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A. Gesellschaftliche Aspekte von HIV und AIDS

A.ER.1
Reency estimations of HIV infections and implications for risk analyses: Results from a pilot study in Berlin 2005 - 2007

Bätzing-Feigenbaum J.1, Kücherer C.2, Loschen S.2, Gohlke-Micknis S.2, Poggense G.1, Jansen A.1, Hamouda O.1

1Robert Koch Institute, Department of Infectious Disease Epidemiology, Berlin, Germany, 2Robert Koch Institute, HIV Variability and Molecular Epidemiology, Berlin, Germany

Objective: The number of newly diagnosed HIV infections in Germany re-increased from 1.444 in 2001 to 2.486 in 2005. However, the true incidence of new HIV infections may not be reflected in these numbers, since the time span between infection and diagnosis is highly variable and is influenced by many factors. Incident infections will be discovered only partly by routine clinical care.

Methods: Blood samples were collected from adult patients (≥18 years) with HIV infections newly diagnosed by practitioners and clinics in Berlin between 2005 and early 2007, and tested at RKI using BED-CEIA. This method allows estimating recency of HIV infections. For BED-CEIA negative samples it can be estimated that infections were acquired not longer than 140 days ago. Clinical data were contributed by the physician and data on knowledge, attitudes and behaviour in terms of HIV/AIDS through a patient questionnaire. Date collection was anonymous and unlinked.

Results: By end of January 2007 116 individuals were enrolled. 102 were MSM (88%). The proportion of recent infections in MSM is 47% (CI [95%]: 38; 56) and 14% (CI [95%]: 32; 0) in individuals from other groups at risk. In the MSM group the proportion of recent infections is higher in the younger age group 20 – 29 years than in the 30 – 44 year range (64 versus 48%). 33% of MSM recently infected with HIV stated to live in non-monogamous partnerships in the past 6 months. 79% had unprotected sex, 64% unprotected anal intercourse. 30% of them had not used condoms consistently in the past 6 months because they didn’t feel at risk and/or believed their sexual partner were not infected with HIV.

Conclusions: Estimating recency of HIV infections allows more relevant analysis of behavioural risk factors for acquiring HIV. This is important since attitudes and behaviour towards HIV change over time. Despite a small number of participants in this pilot study, the results suggest delayed diagnosis in women and other population groups compared with MSM. MSM with recent HIV infections report high risk behaviour with regards to condom use. The findings have implications for prevention strategies and underline the potential usefulness of extending second generation HIV surveillance in Germany.

The study is supported by the BMG

A.ER.2
Intensivierte epidemiologische Surveillance von HIV-Erstdiagnosen in der Schweiz

Gebhardt M.1, Daneel S.2, Vernazza P.2, Schüpbach J.3, Werner M.1, Staub R.1, Boubaker K.1

1Bundesamt für Gesundheit, Übertragbare Krankheiten, Bern, Switzerland, 2Kantonsspital St.Gallen, Infektiologie und Spitalhygiene, St. Gallen, Switzerland, 3Nationales Zentrum für Retroviren, Zürich, Switzerland


- ein kurzer zusätzlicher Fragebogen für den Arzt (AFB)
- ein ausführlicher Fragebogen für den Patienten (PFB)
- Durchführung eines Interviews mit dazu einwilligenden Patienten

Ergebnis: Von 735 neuen HIV-Diagnosen wurden 93% durch EM und 74% durch AFB dokumentiert. Hinsichtlich Geschlecht, Alter und Ansteckungsweg unterschieden sich EM und AFB nicht signifikant. Mit AFB erhöhte sich die Zahl der Fälle mit Information über den Infektionszeitpunkt von 245 (von EM) um 158 (wovon 55% durch Hinweise auf eine Primoinfektion, ansonsten über den wahrscheinlichen Expositions-Zeitpunkt). Aufgrund der AFB erhöhte sich die auf Anamnese beruhende Schätzung des Anteils FI auf 40% auf 46%. Auf 36% der AFB wurde angegeben, der Infektionsort sei im Ausland gewesen, bei 48% im Inland (16% ohne Angabe).

Schlussfolgerung: In der Schweiz werden ab Mai 2007 ein Formular die Fragen über den Infektionszeitpunkt präzisiert, Fragen über den Ort und die Bereitschaft für ein Interview neu hinzugefügt. Patientenfragebogen waren nicht repräsentativ. Der InnoLia-Assay wurde zum Standard für die Bestätigung von HIV-Diagnosen eingeführt, zwecks kontinuierlichem Monitoring von FI.
Trends in the syphilitic epidemic in Germany

Marcus U.1, Schmidt A.J.1, Hamouda O.1

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: Since the implementation of the Protection against Infection Act (IfSG) in 2001 the number of reported syphilis infections in Germany has almost doubled from 1697 in 2001 to 3553 in 2004, and has levelled off since 2004. For 2006 a similar number of reports are expected as for 2004 and 2005.

Methods: Reports on newly diagnosed cases of syphilis are analysed as to gender, mode of transmission (heterosexual or men who have sex with men - MSM), regional distribution and trends. Routine surveillance data are interpreted in the light of additional behavioural surveillance data derived from a large study on knowledge, attitudes and behaviour of German MSM as to sexually transmitted infections (KABaSTI-study).

Results: The proportion of male cases has increased from 81% in 2001 to 90% in 2004 and has stabilized at this level. The proportion of reports without information on mode of transmission has declined from 43% in 2001 to 27% in 2006. The proportion of MSM in the reports with information on mode of transmission has increased steadily from 61% in 2001 to 78% in 2006. An increase in incidence from 2005 to 2006 could be observed in central, western and southern parts of Germany (regions around Freiburg, Stuttgart, Trier, Düsseldorf, Cologne, Arnsberg, Detmold) while other regions reported similar numbers or less cases than in 2005. Slight increases in the number of heterosexual cases were registered mainly in metropolitan areas. A sex work related outbreak in the region of Aachen which began in 2004 is still ongoing. In metropolitan areas half of the reported new cases among MSM in 2006 were re-infections. According to KABaSTI results currently up to 50 % of syphilitic cases among MSM are diagnosed in HIV positive MSM. More than half of these HIV positive MSM with syphilis coinfection are not yet treated with antiretroviral therapy.

Conclusions: Syphilis among MSM seems to circulate mainly in a core subgroup of men at increased risk due to high levels of risk behaviour. However, local and regional outbreaks in MSM in less affected areas do still occur. Smaller and larger outbreaks among heterosexual men and women require continuous epidemiological vigilance and intensified and coordinated local/regional control measures.

Sexually transmitted infections in female sex workers in Germany – results of the STI sentinel surveillance

Bremer V.1, Marcus U.1, Hofmann A.1, Hamouda O.1

1Robert Koch-Institut, Abt. für Infektionsepidemiologie, Berlin, Germany

Objectives: Approximately 2-400,000 female sex workers (FSW) work in Germany. We described FSW with STIs (FSWS) as collected by the German sentinel surveillance system and compared FSWS with other female STI patients (OFSP) in order to identify most vulnerable groups among FSW.

Methods: Since 2002, information on STIs is collected through a nation-wide sentinel surveillance system including local health offices, hospital-based STI clinics and private practitioners. For every case of HIV, gonorrhoea, chlamydia, syphilis and trichomonas infection, physicians completed a questionnaire regarding diagnosis, presumed mode of transmission and demographic information. Patients completed an anonymous questionnaire about sexual risk behaviour and the likely route of transmission. FSWS were defined as women diagnosed with a STI, for whom the patient herself or the sentinel physician reported sex work. Data from January 2003 and September 2006 were used to describe FSWS and compare them with OFSP.

Results: Between 1.1.03 and 30.09.06, sentinel sites documented 1,780 FSWS and 1005 OFSP. FSWS had a median age of 27 years and 70.8% were of non-German origin. Of the non-German FSWS, 418 (33.2%), 333 (26.4%) and 257 (20.4%) were of Eastern or Central European or Latin American origin, respectively. 386 (21.7%) FSWS and 158 (15.7%) OFSP reportedly had an STI in the past (Chi-square test; p<0.001). The most frequently diagnosed STI in FSWS were chlamydia (n=697), followed by gonorrhoea (n=341). In OFSP, chlamydia (n=363) were followed by HIV (n=135), 519/803 women who completed the patient questionnaire were FSWS. FSWS were more likely to have a lower school degree than OFSP. 53.7% of FSWS and 9.0% of OFSP reported consistent condom use with other than their permanent partners. FSWS who reportedly never used condoms with other than their permanent partner were more likely to have had no school degree than other FSWS (47.2% vs. 15.4%; p<0.0001).

Conclusion: Though the results from the German sentinel system are not representative, they suggest that FSWS with a migration background or a low education level are a highly vulnerable population for STIs. Targeted prevention efforts including free STI counselling, screening and treatment are needed to reach these women.

Manifestation und Therapie des Zervixkarzinoms

Funke A.-M.1

1Praxis und Tagesklinik, Gynäkologie und Geburtshilfe, Bremen, Germany

Investment Health: HIV/AIDS coaching and training against fears and discrimination at workplaces

Pietschmann H.1

1AIDS Hilfe Wien, Präventionsabteilung, Wien, Austria

Objectives: People living with HIV are still able to work, also under an antiretroviral therapy. Investment Health offers standardised coaching and training for people working in the private industry but also for people working in other professions. The aim is a (re)integration of HIV-positive people into the working environment, to lower fears and insecurities about these colleagues, to avoid discrimination and to build up a safe workplace.

Methods: In standardised lectures people are informed and trained about the medical and biological basics of HIV/AIDS. This includes facts about transmission paths, prevention of risks but also facts about HIV testing and therapy. Further topics included in these trainings are epidemiology, psychosocial and legal aspects. The programme aims to reach the whole staff in small businesses. In larger firms company medical officers act as contact persons.

Results: Lectures for people working in health and social professions are held frequently. For all other professions lectures are held sporadically. The Aids Hilfe Wien also offers regular updates and meetings for doctors and occupational physicians. A further result of this project is an ongoing cooperation with the Austrian Federal Economic Chamber.

Conclusion: Investment health mainly reaches small- and medium-sized enterprises. Networks are successfully being created and in some special professions these lectures have become a permanent feature of advanced training and health promotion. In several cases these coachings have made it possible for people living with HIV to stay in their jobs.

A.E.R.8
(UM)-Wege zum Thema Aids – Migranten/innen in der STD-Sprechstunde

Nitschke H.1, Knappik A.1, Leidel J.2

1Gesundheitsamt Köln, Beratungsstelle zu STD/AIDS, Köln, Germany, 2Gesundheitsamt Köln, Köln, Germany

Ziele: Der Zugang zu Information, Beratung und ärztlicher Versorgung bei STD ist für viele Migranten/innen eingeschränkt durch rechtliche, sprachliche und kulturelle Faktoren. Wir zeigen, dass durch ein kostenlos und anonym zugängliches ärztliches Versorgungsangebot auch solche Migranten/innen erreicht werden können, die in extrem schwierigen Situationen leben.


A.E.R.9
Young girls/young women and STDs - female gynecologists as "ambassador of prevention"?

Klapp C.1, ÄGGF e.V.(www.aeggf.de)

1Humboldt Universität, Charité Campus Virchow Klinikum Geburtshilfe, Berlin, Germany

In spite of all sex education in school, access to media and liberal minded parents, adolescents are not completely aware of the consequences that may arise when engaging carelessly in sexual activities. So the number of pregnancies and abortions in young girls in Germany has increased and sexually transmitted diseases tend to be a major threat. We found f.e.tat 5,4 % of adolescent girls in an urban population had a newly acquired chlamydia trachomatis (CT)infection, depending on increasing age, number of partners and low education rising to 20%. Usually the use of condoms is poor because it is fixed to AIDS and they often feel that this is far away from...
their reality. Thus students, teachers and parents find it very helpful to receive support by professionals, especially medical doctors/gynecologists, who are neutral, experienced and may build up a confidential intimate atmosphere which encourages discussion of personal fears and problems as well. As a means of quality assurance we (AGGF e.V. - www.aeggf.de) have evaluated our work regarding potential gain in knowledge and acceptance by students. We could show that after a 90 minutes intervention, the overall increase of knowledge was extremely high with 32% in grade 9/10 and 84% in grade 6.

Education of young people concerning STI - especially Chlamydia trachomatis infection - promotes using condoms because this infection may cause problems in becoming pregnant and it concerns their plans of life in a direct way - much more than HIV. The findings of our study suggest that prevention and health promoting programs by doctors in a gender specific confidential atmosphere complemented to school programs are very well accepted - in school or in doctor’s office. Prevention and health promoting programs should start at an early age, preferably in elementary schools and continued in accordance with developmental stage over several years. We could show that students accept this way of information very well, find it useful and comprehensive, are able to retain and reproduce these information and feel ensured for caring better for themselves – and this is basic for any change in behaviour. Last year we could increase "female doctor’s lessons" to about 5.600 with more then 100.000 students participating.

**A.E.R.10**

**HIV-Prävention mit männlichen, jugendlichen Flüchtlingen**

Pfefferkorn E.1

1AIDSHILFE OBERÖSTERREICH, Linz, Austria

**Fragestellung:** Gerade in den letzten fünf Jahren ist in den Kernbereichen der oberösterreichischen Aidshilfe-Arbeit (Prävention, Beratung, Betreuung) ein massiver Zuwachs an Kontakten mit MigrantInnen zu verzeichnen. Dieser Zuwachs lässt sich auch durch entsprechende KlientInnendaten der Aidsstation des lokalen Krankenhauses in Linz untermauern. Vor diesem Hintergrund wurde ein präventives Konzept entwickelt, welches sich direkt und indirekt an MigrantInnen richtet.

**Methodik:** Um einen Zugang zu MigrantInnen zu gewinnen, wurden als erster Schritt Weiterbildungen für MitarbeiterInnen von mit MigrantInnen geschäfteten Einrichtungen angeboten und durchgeführt. Bereits im Rahmen dieser Weiterbildungen wurde neben der Vermittlung von Basisinformationen zu HIV/Aids auch auf das Angebot hingewiesen, kostenlose Workshops zu HIV/Aids für KlientInnen der jeweiligen Einrichtungen zu buchen. Die Workshops mit den Klienten selbst wurden im Rahmen dreier Module abgehalten. (Beziehung/ Sexualität, Basisinfos HIV/Aids, Angebote der AIDSHILFE OBERÖSTERREICH). Die Workshops fanden in Kleingruppen mit jeweils 5-10 Personen statt und dauerten je Modul ca. 2 Stunden. Sprachliche Barrieren (v.a. bei Personen aus dem asiatischen Raum) wurden unter Zuhilfenahme eines Dolmetschers überbrückt. Theoretisch orientierten sich die Workshops an den drei Variablen der personzentrierten Gesprächstherapie nach Rogers (Wertschätzung, Empathie, Konkruenz).

**Ergebnisse:** Im Jahr 2005: Weiterbildung für 40 MitarbeiterInnen der Caritas Flüchtlingsbetreuung Oberösterreich, 7 Workshops mit 70 Teilnehmern; im Jahr 2006: 7 Workshops mit 80 Teilnehmern. Die Teilnehmer waren im Alter von 15 bis 19 Jahren und kamen größtenteils aus Asien (Mongolei, Irak, Tschetschenien, Russland) sowie Afrika (Nigeria). Durch obige Angebote wurde eine Öffnung der AIDSHILFE OBERÖSTERREICH und deren Angebote für alle Beteiligten erreicht, was sich in der gestiegenen Anzahl der Nachfragen an HIV-Antikörpertests, Workshops sowie Kondomen niederschlägt.

**Schlussfolgerungen:** Die Annahme gerade bei Flüchtlingen eine besonders behutsame Herangehensweise an das Thema Sexualität/Aids zu wählen, konnte nicht bestätigt werden. Ein Grossteil der Teilnehmer hatte das Bedürfnis ohne große Um- schleife über obige Themen zu reden.

**A.E.R.11**

**Nationwide online counselling as a tool of quality assurance in HIV-prevention**

Lemmen K.1

1Deutsche AIDS-Hilfe e.V., Psychosoziales und Qualitätsentwicklung, Berlin, Germany

**Objective:** To show how a nationwide system of online counselling supports the efforts of quality assurance in the prevention work of the AIDS service organizations (ASO) in Germany.

**Methods:** There are about 120 ASO under the roof of the Deutsche AIDS-Hilfe e.V. (DAH), When implementing HIV prevention in the internet one has to bear in mind that the net “does not know” national borders or distances. The only border which exists there is that of language. This means in the case of German that one ASO which offers counselling in this language is sufficient. In 2005, the DAH therefore built up a national cooperation of 20 ASO in 19 cities from the Danish Border to Lake Constance. Mean-while, 30 counsellors form a nationwide “virtual team” which is organized in 5 day teams (Monday thru Friday). To share the time and money between the participating ASOs each counsellor takes responsibility for only one day of the week. Before starting work all counsellors signed a form which specifies the common standards of quality in online counselling, and attended a special training.

**Lessons learnt:** Within the first 15 months more than 4.000 questions had been sent to www.aidshilfe-beratung.de which the counsellors answered within one or two days. Not only the clients are highly satisfied with this new way of HIV counselling. Evaluation shows that the counsellors appreciate being a member of the virtual team and having the opportunity to discuss questions and problems in HIV counselling with their colleagues which enhances the quality of the prevention work in the regional ASO.

**A.E.R.12**

**Langzeitadhärenz: Safer Sex – eine realistische Forderung?**

Sander D.1

1Deutsche Aids-Hilfe e.V., Abt. 1 MSM Prävention, Berlin, Germany

Im Vortrag wird aus Sicht der Deutschen Aids-Hilfe e.V. der Frage nachgegangen, welche Umstände safer-Sex-Verhalten begünstigen und welche Barrieren es geben kann, sich im Zeitverlauf stabil selbst- und fremdschützend zu verhalten.

Es wird versucht, sich auf mehreren Ebenen dem Thema zu nähern, und die Frage nach den Chancen und Grenzen der HIV-
Prävention unter den Bedingungen des „Neuen AIDS“ aufgegriffen. Muss heute auch die Primärprävention „anders denken“, um die alten Erfolge auch in Zukunft fortschreiben zu können?

A.ER.13
Syphilis und HIV in Südafrika: ein Übertragungsweg, zwei Epidemiologien

Preiser W.1, Allen R.2, van Zyl G.U.1
1Faculty of Health Sciences, Stellenbosch University, Division of Medical Virology, Tygerberg, South Africa, 2University of Stellenbosch, Department of Philosophy, Tygerberg, South Africa


Alljährlich durchgeführte repräsentative Stichproben zur HIV- und Syphilis-Seroprävalenz bei schwangeren Frauen zeigen für HIV einen Anstieg von 17,0% 1997 auf 30,2% 2005; hingegen sank der Wert für Syphilis (Rapid Plasma Reagin-Test) im gleichen Zeitraum von 11,2% auf 2,7%. Der verzeichnete Rückgang der Syphilis-Zahlen wird u.a. der verbesserten syndromischen STI-Behandlung zugeschrieben; ein Erfolg der HIV-Präventionskampagnen allerdings läßt sich durch die Daten kaum belegen.


Nichtsdestotrotz bleiben zahlreiche von Kark’s Beobachtungen und Analysen zur Syphilis weiterhin gültig und nehmen in vieler Hinsicht die Ausbreitung von HIV 40 Jahre später vorweg: "old crisis, new agent".

A.ER.14
Kondom und Sex – gehört das zusammen?

Nagel S.1
1freie Arztpraxis, Düsseldorf, Germany


A.ER.15
HIV und Hepatitis in deutschen Haftanstalten: Verpasste Präventionschancen und mangelndes Äquivalenzprinzip

Weilandt C.1, Stöver H.2
1WIAD Wissenschaftliches Institut der Ärzte Deutschlands, Bonn, Germany, 2Universität Bremen, Bremer Institut für Drogenforschung, Bremen, Germany

“All prisoners are among the most unhealthy places in our societies.” (WHO 2001) In Deutschland sind an einem gegebenen Tag knapp 80.000 Menschen inhaftiert, jährlich durchlaufen ca. 250.000 Menschen die Justizvollzugsanstalten. In den Gefängnissen findet sich eine überproportional starke Verbreitung von gesundheitlichen Belastungen und Erkrankungen wie Drogen- und Alkoholabhängigkeit, Infektionskrankheiten (HIV/Hepatitis), psychischen Störungen, Hygieneproblemen, Überbelegungen, Bewegungseinschränkungen und alle Formen von Gewalt. Gleichzeitig sind die Möglichkeiten zur Bewältigung dieser gesundheitlichen Belastungen stark eingeschränkt (personelle Ressourcen, eingeschränkte Handlungsmöglichkeiten, inadäquate Problembewältigungsmechanismen). Prävention und Intervention im Vollzug sind erschwert aufgrund überwiegender Beliehung mit Menschen aus unteren sozialen Schichten mit geringem Bildungs- und Ausbildungsniveau, und einem hohen Anteil ethnischer Minoritäten.

und Unklarheit über gesundheitliche Versorgungspotentiale, -qualität und -notwendigkeiten. Gefängnisse sind nicht nur Orte mit besonderen gesundheitlichen Belastungen sondern bieten auch Präventionspotentiale, für eine sonst schwer erreichbare Zielgruppe, die bisher jedoch nicht hinreichend genutzt werden.

Die aktuelle Situation bezgl. Prävalenz, Monitoring, Prävention und Versorgung hinsichtlich Erkrankungen wie HIV, Hepatitis in Deutschland und Europa wird dargestellt und im europäischen Kontext diskutiert.

A.ER.16
Risk behaviour and knowledge about blood-borne infections among prisoners in Germany and their seroprevalence regarding Hepatitis B, Hepatitis C, and HIV - preliminary results of a cross-sectional Study

Radun D.1, Weilandt C.2, Eckert J.2, Schüttler C.G.3, Weid F.J.3, Kücherer C.4, Hamouda O.1

1Robert Koch-Institut, Abt. für Infektionsepidemiologie, Berlin, Germany, 2Wissenschaftliches Institut der Ärzte Deutschlands, Bonn, Germany, 3Justus-Liebig-Universität Giessen, Institut für Medizinische Virologie/Konsiliarlabor für Hepatitis B und D, Giessen, Germany, 4Robert Koch-Institut, Projektgruppe Neuartige Erreger/P 11 HIV-Varialibilität und molekulare Epidemiologie, Berlin, Germany

Background: Blood-borne diseases are common among prisoners. This is largely due to a high proportion of injecting drug users among detainees who became infected by sharing needles or paraphernalia. Tattooing, unprotected sexual intercourse and crowded living conditions increase risks for infection.

Objectives: To determine the prevalence of hepatitis B, hepatitis C, and HIV among prisoners in Germany, to identify gaps in knowledge on blood-borne infections among prisoners and staff, to identify risk factors for blood-borne diseases as well as subgroups at particular risk.

Methods: From November 2006 to January 2007, we conducted a cross-sectional study on knowledge, attitudes and risk behaviour among adult detainees in six German prisons. We chose a sample which largely represents the entire adult population of detainees in Germany’s closed institutions. To achieve sufficient statistical power and to reduce random error, we oversampled female detainees and inmates of juvenile prisons. We administered a standardised, pseudonymised questionnaire to all available inmates, and one on knowledge/attitudes regarding blood-borne infections to prison staff. We asked participating inmates to provide a blood drop in order to test filter-dried blood spots for markers for hepatitis B, hepatitis C, and HIV by unlinked anonymous testing (HIV-screening with two ELISAs (Murex® Abbott, Genscreen® Pasteur), confirmation by HIV-1/-2 Western Blot (Bio-Rad)); anti-HBc, HBsAg and anti-HCV testing by AxSYM® Abbott). To identify risk factors, questionnaires’ code numbers and serologic results are related.

Results: We contacted 1,680 prisoners, 1,582 (94%) returned their questionnaires and 1,519 (96%) agreed in blood testing. 233 staff members returned their questionnaires. As of 19 April 2007, 13/1518 (0.9%) prisoners tested positive for anti-HIV (7 tests were indeterminate). 107/1521 (7.0%) prisoners tested positive for anti-HBc (additional 3.1% grey area reactivity), 21/1521 (1.4%) for HBsAg and 247/1521 (16.2%) for antiHCV (additional 2.3% grey area reactivity).

Conclusions: Although serologic analysis is ongoing, results indicate an elevated prevalence of blood-borne diseases, particularly hepatitis C, among prisoners in Germany, compared to the general population.

A.ER.17
Workshops gemeinsam gestalten: Methoden der Partizipativen Qualitätsentwicklung vor Ort. Ein Beispiel aus der Praxis

Block M.1, Thürrer P.2, von Unger H.1, Wright M.T.1

1Wissenschaftszentrum Berlin für Sozialforschung, Forschungsgruppe Public Health, Berlin, Germany, 2AIDS-Hilfe Leipzig, Leipzig, Germany


A.ER.18
Der Umgang mit HIV-Übertragungsrisiken bei NutzerInnen von Kontaktseiten im Internet

Bochow M.1, Grote S.1

1Wissenschaftszentrum Berlin f. Sozialforschung, Forschungsgruppe Public Health, Berlin, Germany


Methodik: Im Frühjahr 2006 wurde ein Online-Fragebogen geschaltet, auf den auf 8 ausgewählten Kontaktseiten mit einem Banner hingewiesen wurde. Der Fragebogen konzentri-

**Ergebnisse:** Das Internet dient vielen Kontaktseitenutzern zur Information über HIV/AIDS. 55% aller Befragten informieren sich gezielt über das Internet. MSM (60%) holen sich zu einem höheren Anteil gezielt Informationen zu HIV/AIDS aus dem Netz als andere Personengruppen (heterosexuelle Männer: 32%; Frauen: 33%). Ein theoretisches HIV-Expositionsrisiko (internetangebante sexuelle Kontakte HIV-negativer Männer und Frauen zu Personen mit unbekanntem oder diskordantem Serostatus ohne durchgängigen Kondomgebrauch – unabhängig von der Anzahl solcher Kontakte) ist bei MSM und heterosexuellen Männern annähernd gleich (25% vs. 26%). Bei anders angebauten Sexualkontakten liegt der Anteil bei MSM unwesentlich höher (26%), bei heterosexuellen Männern dagegen etwas niedriger (22%). Aufgrund kleiner Fallzahlen lassen sich für Frauen keine sinnvolle %-Werte berechnen, die Größenordnung ist jedoch ähnlich. Das HIV-Transmissionsrisiko (internetangebante sexuelle Kontakte HIV-positiver Männer und Frauen zu Personen mit unbekanntem oder diskordantem Serostatus ohne durchgängigen Kondomgebrauch) liegt bei MSM hingegen deutlich höher als bei heterosexuellen Männern (6% vs. 1% Internet, bzw. 9% vs. 0% andere).

**Diskussion:** Unsere Daten liefern Hinweise, die die Rolle des Internets als wichtiges Medium der Prävention bestätigen. HIV-Transmissionsrisiken finden sich aufgrund der dort höheren Prävalenz hauptsächlich bei MSM. Präventives Verhalten von Männern ist bei Kontakten über das Internet nicht seltener als bei anders angebauten Kontakten.

**A.E.R.19**

**Superinfektion: Virologische Grundlagen**

_Gröne M. 1, Korn K. 1_

1Universitätsklinikum Erlangen, Virologisches Institut, Erlangen, Germany


**A.E.R.20**

**Evaluation von Aufklärungsmaßnahmen der BZgA - am Beispiel des Pretests der „Gemüsekampagne“**

_von Rüden U. 1, Töppich J. 1_

1Bundeszentrale für gesundheitliche Aufklärung, Forschung und Qualitätssicherung, Köln, Germany

Die mach’s mit-Kampagne ist heute das sichtbarste und bekannteste Element der 1987 gestarteten Kampagne „Gib Aids keine Chance“ der Bundeszentrale für gesundheitliche Aufklärung (BZgA). Sie hat wesentlich mit dazu beigetragen, Kondome in der öffentlichen Wahrnehmung zum alltäglichen Gegenstand zu machen. Um umfangreichen Dauerkampagne für die Umsetzung des Präventionsansatzes „HIV-Maßnahmen“ zu unterstützen, hat die Bundeszentrale für gesundheitliche Aufklärung (BZgA) die „Gemüsekampagne“ am Beispiel des Pretests der „ „Gemüsekampagne““

**A.E.R.21**

**Wie wird die HIV-Prävention 2015 sein (müssen)?**

_Staub R. 1, Guggenbühl L. 1, Kopp C. 1, Werner M. 1_

1Bundesamt für Gesundheit, Übertragbare Krankheiten, Sektion Aids, Bern, Switzerland

vor HIV und anderen sexuell übertragbaren Infektionen. Die evidenzbasierte Sexualerziehung an den Schulen orientiert sich am Recht auf sexuelle Gesundheit, nachdem Evaluatio-
nen zeigten, dass abstinentorientierte Sexualerziehung wirkungslos ist.

Um die Ausbreitung von HIV in Gruppen mit hoher Prä-
valenz effizienter zu bremsen orientiert man sich an den Län-
dern mit generalisierter Epidemie, welche die Prävention methodisch schon 2010 bedeutend weiter entwickelt hatten. In jedem Land definieren Staat und NGOs aufgrund fundierter und vergleichbarer epidemiologischer Daten des ECDC die Zielgruppen. NGOs haben in einigen Ländern Prozesse gewonnen, welche die Staaten zu evidenz-basierten Program-
men für gefährdete Gruppen verpflichtet. Insbesondere Spritzentausch- und Substitutionsprogramme sind nun eu-
ropaweiter Standard.

Am schwierigsten war es, die behandelnden ÄrztInnen von HIV-PatientInnen in die Prävention einzubeziehen. Dies be-
zezügliche Ziel war zwar unbestritten: «In festen, diskordan-
ten Partnerschaften gibt es keine HIV-Übertragungen». Aber erst allmählich konnte als Konsens etabliert werden, dass mit der Diagnose einer HIV-Infektion auch die Prävention unter Einbezug der festen PartnerInnen von HIV-diagnostizierten PatientInnen zur ärztlichen Daueraufgabe und Verantwortung gehört. Verhältnispräventive Massnahmen ermöglichten, kostenintensive Kampagnen zur direkten Verhaltenseinflus-
zung zurückzunehmen. In der EU gilt z.B. seit 2010 die Vorschrift, dass an Orten, wo Sex ermöglicht wird, gratis Präservative, Gleitmittel und Informationen angeboten wer-
den müssen (Bordelle, Swingerclubs, Saunen, Gaststätten mit Dunkelraum etc.)

Die internationale Zusammenarbeit ist zur Selbstver-
ständlichkeit geworden. Unter anderem haben UNAIDS/ WHO Europa ein vernetztes 3rd Generation Surveillance Sys-
tem eingeführt, das neben Epidemiologie und Verhaltensmoni-
toring auch Interventions-Surveillance beinhaltet.

A.E.R.22

Das deutsche Projekt Lifeboat - ein audiovisueller Wegweiser für positive Mutterschaft

1Projekt Lifeboat, Köln, Germany, 2Paper House Films, Amsterdam, Netherlands

Ziele: Frauen mit HIV und ihr Umfeld wissen oft zu wenig über ihre Möglichkeiten, schwanger zu werden und gesunde Kinder zu bekommen. Auch in der Öffentlichkeit und bei vie-
len Fachleuten sind nicht alle nötigen Informationen vorhan-
den, um betroffenen Frauen die erforderlichen Hinweise und Unter-
sützung anbieten zu können. Das deutsche Projekt Lifeboat will diese Wissenslücken mit einem audiovisuellen Wegweiser auf DVD schließen. Außerdem will das Projekt Lifeboat Frauen und Mütter mit HIV stärken, damit sie die Übertragungsraten für ihre Kinder minimieren können.

Methodik: Das deutsche Lifeboat ist ein Zweig des interna-
tionalen Projekts Lifeboat. Alle Lifeboat-Projekte vermitteln ihre Botschaften und Informationen mit Kurzfilmen. In Deutschland werden bis zu zehn solcher Kurzfilme für eine DVD produziert. Die Inhalte und die Gestaltung dieser Kurz-
filme werden im Rahmen von peer involvement von Frauen mit HIV, auch von Frauen mit Migrationshintergrund, selbst bestimmt; ExpertInnen begleiten das Projekt beratend und zur Qualitätssicherung. Neben den Kurzfilmen enthalten die DVD weiterführende Informationen zum Thema Schwangerschaft und HIV. Alle diese Informationen sind durch aktive Links unmittelbar als Wegweiser zu einschlägigen Seiten im Internet zu nutzen.

Ergebnis: Die DVD eignet sich für vielfältige Ein-
satzmöglichkeiten. Sie kann in der Arbeit von Beratungs-
stellen genutzt werden, um Frauen mit HIV, MultiplikatorIn-
nen und breite Öffentlichkeit über die Themen HIV und Schwangerschaft aufzuklären. Die Kurzfilme sind auch als Spots für Wartezimmer in Medizinbetrieb oder für Spenden-

Schlussfolgerung: DVD sind ein niedrigschwelliges und vielfältig einsetzbares Medium für die audiovisuelle Vermitt-
lung von Inhalten. Die Beteiligung der Zielgruppe an der Entwicklung von Medien für ihre Peers ist essentiell für die passgenaue Formulierung und Präsentation der gewünschten Botschaften und Informationen. Authentische Beiträge wer-
den von Fachleuten in der Beratung, der medizinischen Be-
handlung und in der Öffentlichkeitsarbeit mit größerem Erf-
folg eingesetzt.

A.E.R.23

Neurologische Erkrankungen bei Frauen mit HIV/AIDS

1Universitätsklinikum Düsseldorf, Neurologie, Düsseldorf, Germany

Einleitung: Bei HIV-1-positiven Patienten wird sehr viel über einen geschlechts-spezifischen Krankheitsverlauf speku-
liert. Erwiesen ist, dass Frauen bei einer niedrigeren Pola-
risation und bei der Manifestation neurologischer Sympto-
men niedriger sind als Männer. Ob neurologische Krankheitsmanifestationen ebenfalls geschlechts-spezifische Besonderheiten aufweisen, ist unklar.

Methodik: In der Düsseldorfer Neuro-AIDS-Kohorte wurde die Krankheitsverlauf von 1693 Männern und 253 Frauen hin-
sichtlich Alter bei Diagnosestellung, Mortalität, Krankheits-
dauer, Krankheitsprogression und neurologischer Systemmanifestationen verglichen.

Ergebnisse: Es zeigte sich, dass Frauen bei Diagnosestellung signifikant jünger sind als Männer. Hinsichtlich Krankheits-
dauer, Krankheitsprogression und Mortalität bestanden keine geschlechts-spezifischen Unterschiede. Nach Adjustierung der Daten hinsichtlich Alter, Ausbildung, Hauptbetroffenengruppen, CD4-Zellzahl und HI-Viruslast im Plasma zeigte sich, dass Frauen nach einer sechsjährigen Infektionsdauer signifi-
kant häufiger an einer Demenz erkranken als Männer. Auch cerebrale opportunistische Infektionen sind häufiger. Diese Unterschiede sind sowohl vor als auch nach Einführung der hochaktiven antiretroviralen Therapie (HAART) zu beobachten. Peripher-nervöse Erkrankungen treten bei Män-
nern und Frauen in gleicher Häufigkeit auf.

Diskussion: Bei der Analyse geschlechts-spezifischer Unter-
schiede in einer großen Kohorte HIV-positiver Männer und Frauen zeigten sich Unterschiede insbesondere im Alter bei Diagnosestellung und bei der Manifestation neurologischer Komplikationen nach mehrjährigem Krankheitsverlauf. Da diese Unterschiede unabhängig vom Zeitpunkt des Thera-
piebeginns und der Wahl der applizierten antiretroviralen Medikamente waren, müssen andere Faktoren eine Rolle spie-
Barriers and motivators to participation of women living with HIV in clinical trials and research studies

Kremer H.1, Steffen E.2, for the German Competence Network HIV/AIDS

Background: The worldwide HIV epidemic disproportionately affects ethnic minority women of lower socio-economic status that are underrepresented in HIV research. The review of the literature identified a worrying paucity in studies focusing on why women fail to enroll in these studies. In the German Cohort of people living with HIV, women comprised only 15% of the participants, although women represent 21% of the HIV+ German population. The percentage of women in clinical trials is even smaller, neglecting that the Guidelines of the European Medicines Agency require sufficient participation of women. Gender is also needs persistent consideration in social science studies concerning psychosocial impacts of HIV/AIDS and of cause concerning primary and secondary prevention.

Method: At the German Austrian AIDS Conference 2007, the AAWS workshop will gather representatives from all stakeholders in HIV including patient advocacy, health care providers, medical and psychosocial science, pharmaceutical industry, media, health politics, and others. The meeting will be the second one in this line discussing the topic in two directions. The first direction is to further identify barriers and motivators of women to participation in HIV studies. Second, we will propose minimal gender standards for study designs.

Results: Prior, in the frame of an interdisciplinary meeting during “HIV in Dialogue,” the involvement of community, transparency of studies, practical support, and monetary incentives were named as motivators to participation in research studies. Some perceived barriers were concerns with confidentiality and not receiving direct benefits despite putting in large efforts and taking risks.

Conclusion: The underrepresentation of women in HIV studies is a call for further studies to listen to the voices of women with HIV, not only to enroll them as study participants but also to design studies that meet their specific needs and promise direct benefit to them. Inclusion of women within clinical trials and research design is a step to ensure that patient oriented sex and gender research becomes and integral part, not an after thought of HIV research, which includes patient advocacy, health care providers, media, health politics, and others. The meeting will be the second one in this line discussing the topic in two directions. The first direction is to further identify barriers and motivators of women to participation in HIV studies. Second, we will propose minimal gender standards for study designs.

A.E.R.26

HIV-Test in der Schwangerschaft - ein Trauerspiel? - In Kenntnis der Diagnose kann die HIV-Mutter-Kind-Übertragung vermieden werden

Beichert M.1, Buchholz B.2, Sütterlin M.1

1Universitätsfrauenklinik Mannheim, Mannheim, Germany, 2Universitätskinderklinik, Mannheim, Germany

Nach den Angaben der UNAIDS stirbt weltweit jede Minute ein Kind unter 15 Jahren an AIDS und ein weiteres infiziert sich mit dem HI-Virus. In 9 befragten HIV-Ambulanzen in

In Deutschland kann im Jahr 2007 in Kenntnis der Diagnose eine HIV-Mutter-Kind-Übertragung verhindert werden.

A.E.R.27
HIV und Schwangerschaft - Betroffenenperspektive

Mayer N.1

1Privat, Düsseldorf, Germany


A.E.R.28
HIV und Hämophilie - Konsequenzen des Blut-AIDS-Skandals

Braun U.1

1Deutsche Hämostiliegesellschaft, Hamburg, Germany

In den 80er Jahren wurden in der Bundesrepublik etwa 1400 Hämophile durch verseuchte Bluttransfusionen und Hunderte von Personen, die nach Unfällen oder anlässlich von Operationen Blutprodukte erhalten hatten, mit HIV infiziert.

Wie stellt sich nun heute die Situation für die Betroffenen dar, und welche Konsequenzen wurden aus dem sog. Blut-AIDS-Skandal gezogen?


Mit Hilfe des 2002 in Kraft getretenen Schadensrechtsänderungsgesetzes können die durch Arzneimittel geschädigten Patienten künftig mit größerer Aussicht auf Erfolg gegen die Verursacher eventueller Schäden klagen, als dies für die HIV- und HCV-infizierten Hämophilen möglich war.

A.E.R.29
Direct costs for highly active antiretroviral treatment (HAART) regimens in the German ClinSurv multicenter cohort 1996 – 2006

Stoll M.1, Kollan C.2, Oette M.3, Horst H.-A.4, Schewe K.5, Kuehne A.2, Hamouda O.2, ClinSurv study group

1Medizinische Hochschule Hannover, Zentrum Innere Medizin, Abt. Klinische Immunologie, Hannover, Germany, 2Robert Koch Institut, Abt. Infektionsepidemiologie, Berlin, Germany, 3Universitätsklinikum, Gastroenterologie, Hepatologie und Infektiologie, Düsseldorf, Germany, 4Universitätsklinikum, Medizinische Klinik II, Kieler, Germany, 5Infektsmedizinisches Zentrum St. Georg, Hamburg, Germany

Background: Apart from resource consumption for hospitalisation, HAART has a major impact on direct costs in HIV-in-
fection. Therefore increasing efforts are necessary for a rational allocation of resources in this field.

**Objective:** To evaluate direct costs of HAART in patients treated at specialised institutions by a follow-up until 2006.

**Methods:** Analysis of the complete HAART documentation from 22 centers of the German ClinSurv cohort. HAART-regimens were calculated on a daily base using documented start and stop dates for each ARV. Direct costs of HAART were taken as office based sales prices (including taxes).

**Results:** From 1996 to 2006 overall 3755 individuals have been evaluated quarterly exclusively for those quarters they are on HAART or STI. Thus in an average of 94% of the observed days patients have been treated with HAART. Mean observed duration under HAART was 1309 days. 4,617,366 treatment days generated actual costs of € 178,504,116.€/

Average costs of an entire regimen were € 38,85 per day. Costs increased by +162% from 1996 to 2006, which would be fourfold more as expected in the case that office based prices have been discounted with 4% annually. NNRTI-based HAART (48%) was used in similar frequency as PI based (46%) and most regimens (97%) contain n-RTIs. Calculating a cost-index for each single drug class within a HAART regimen this is highest for fusion inhibitors (FI) with 141 and lowest for n-RTIs with 28. Like n-RTIs also NNRTIs had a relatively constant index (36) over time, whereas the more expensive group of PI s had a higher index of 60, which was highest in the era before boosting came up (1996: 91), dropped to 48 in 2000, and since then increased to 73.

**Conclusions:** Direct costs for HAART regimens increased inflation-adjusted from 1996 to 2006. This could be explained by (a) use of intensified regimens, (b) a slight decrease in use of NNRTIs, (c) licensing of more expensive new ARVs, and (d) increasing prices of licensed ARVs.

**A.E.R.30**

**Poverty: The other sight of HIV/AIDS**

Kuderna C.1, Amort F.M.1

1Aids Hilfe Wien, Wien, Austria

**Objective:** An HIV-diagnosis is no longer a death sentence. Optimistic representations and positive images dominate the general view of ones life with HIV. However it is also a fact that for many HIV-positive persons these images are not congruent with the every day life experiences. AIDS service organisations are getting more and more involved into the fight against poverty. To succeed with this effort one has to analyse the reality of the actual life circumstances of those in need. Aids Hilfe Wien therefor conducts regular a survey of the accurate life circumstances - personal as well as concerning the social surrounding - and the social situation of our HIV-positive clients. The latest edition was performed in January 2007.

**Method:**

a. Evaluation of app. 500 anonymized client files
b. descriptive statistic of a data base
c. correlation and correlative deduction

**Results:** This newest survey shows that the financial situation remains the main problem. The picture of poverty that was framed in the first edition of this survey (eg. .. of our clients are indebted) is even more enhanced. Furthermore the increase of the aged population in the sample shows even more challenges of multi-problematic circumstances, psychological or psychiatrical and alcohol abuse.

**Conclusion:** The latest survey of the circumstances of our clients in social work draws once again a picture of HIV/AIDS that is dominated by poverty. Within a needed lobbying for reintegration of HIV-infected persons into the labour market we have to accept also that for many people this will not be a realistic perspective and poverty is the dominating reality of their lifes.

**A.E.R.31**

**Controlling and AIDS NPOs: Implementation of a standardized controlling system for all AIDS-Hilfen in Austria**

Dax S.1

1Aids Hilfe Wien, Kaufmännische Abteilung, Wien, Austria

**Background:** At present current statistics reporting aggregate numbers of specific contacts etc. on the one hand, accounting on the other hand, are separate fields of documentation in NPOs. Cost accounting is widely seen as a treasury business with no link to the real product sphere. On the whole, Controlling is a rather young tool in AIDS sector. Nevertheless, the relevant environment of an NPO is more and more interested in NPO Controlling.

**Objectives:** The aim of controlling processes is to link cost data and statistic figures by means of ratios and indices. The quality level of production needs to be compiled into the model on all levels of aggregation. Later, these ratios should become the basis of management instruments.

**Results/problems arising:** In the process one has to face problems of
a) the classic stochastics
b) direct costing and dealing with overheads
c) the algorithm of the relation of a) to b) or vice versa considering quality factors.

**Conclusion:** Beside an intelligent design of the controlling model, one has to plan, test, execute, and control cost-effective and time-thrifty strategies of realization. In this part, practical experience in Aids Hilfe Wien will be delivered. Dealing with the fit or lack of fit into general trends of NPO Controlling regarding this specific project is meant to give a further outlook as a resume.
A.ER.32
AIDS-Phobie und –Hypochondrie in der HIV-Testberatung
Stummer K.,\textsuperscript{1}
\textsuperscript{1}Aidshilfe Oberösterreich, Linz, Austria

Fragenstellung: AIDS eignet sich, wie kaum eine andere schwere chronische Erkrankung, als besondere Projekitions-
fläche diffuser, und (un)bewusster Ängste und Befürchtun-
gen. Würde zu Beginn der Epidemie zu diesem Thema inten-
siv geforscht, finden sich in aktuellen Publikationen, wenn
überhaupt, nur marginale Beiträge. In der Beratungspraxis
zeigt sich nach wie vor und in unverminderter Stärke das
Phänomen der AIDS-Phobie und –Hypochondrie, welches
durch Wissensvermittlung und wiederholten HIV-Testungen
allein, nicht nachhaltig zu beeinflussen ist.

Methoden: Durch Studium der einschlägigen Fachliteratur und
ausgewählten Einzelfallanalysen aus der alltäglichen Testbe-
ratungspraxis wurden in einer Arbeitsgruppe der AIDSHILFE
OBERÖSTERRICH Ansätze zu einem besseren Verständnis
der Phänomenologie, der Nosologie, der Psychodynamik, des
Verlaufs und möglicher Interventionsformen erarbeitet und
kritisch reflektiert.

Ergebnisse: Die AIDS-Phobie und –Hypochondrie stellt ein
komplexes Phänomen dar, das sich in seinen individuellen
Ausprägung sehr divergent manifestieren kann. Es lassen sich
leichte von schwereren Formen differenzieren. Eine psy-
chotherapeutische Behandlung schwererer Beeinträchtigun-
gen erfordert viel Geduld und einen langen Atem seitens des
Behandlers, da den Betroffenen anfänglich die psychische Di-
nension des Geschehnens nicht zugänglich ist bzw. dieselbe
nimmer wieder zur Disposition gestellt wird und es vorerst
nicht selten zu einer narrativen Fixierung „ad nauseam“ auf
die vermeintliche Infektionssituation, als Ausdruck einer
Ichdystonie real oder phantasiierten Erlebens, kommt.

Schlussfolgerungen: Die AIDS-Phobie- und -Hypochondrie
muss als schwerwiegende Beeinträchtigung der psychosozialen
Befindlichkeit der Betroffenen und als krankheits-
wertig wahrgenommen und respektiert werden. In der Test-
beratung Tätigkeiten sollten deshalb über eine hohe psycho-patho-
logische Qualifikation verfügen. Die oft bizarr erscheinenden
„Infektionsdramen – und – dramatisierungen“ können in ihrer
Symbolisierung sowohl auf der Subjekt- wie auf der Objekt-
stufe gesehen, sollten aber nie vorschnell als solche kommu-
niziert werden. Eine psychotherapeutische Behandlung lege
artis sollte den Betroffenen eröffnet und ermöglicht werden.

A.ER.33
Maßnahmen und Strategien zur Erhöhung der Teilhabe von Menschen mit HIV und Aids am Erwerbsleben: Erfahrungen aus der Projektarbeit der EQUAL-Entwicklungspartnerschaft LINK-UP
Krone M.,\textsuperscript{1}
\textsuperscript{1}Deutsche AIDS-Hilfe e.V., EP LINK-UP, Berlin, Germany

Fragenstellung: Menschen mit HIV und Aids treten, ähnlich
wie auch Betroffene anderer chronischer Erkrankungen, bei
den medizinische Entwicklungen zu einer besseren Behan-
delbarkeit führen, in der Welt der Arbeit in Erscheinung: als
Arbeitssuchende und dadurch als arbeitsmarktpolitisch rele-
vante Gruppe, aber auch als im Erwerbsleben stehende, die
ihre Erwerbsfähigkeit so lange wie möglich zu erhalten

Patient safety in clinical studies – concern for erosion of trust?
Salzberger B.\textsuperscript{1}, Rockstroh J.\textsuperscript{2}, Jäger H.\textsuperscript{3}
\textsuperscript{1}Universitätsklinikum Regensburg, Klinik I für Innere
Medizin, Regensburg, Germany, \textsuperscript{2}Universitätsklinikum Bonn,
Klinik und Poliklinik für Innere Medizin, Bonn, Germany,
\textsuperscript{3}Praxisgemeinschaft Karlsplatz, München, Germany

Serious adverse events (SAE) to drugs can emerge in clinical
practice as well as in clinical studies. Damages to patients due
to SAEs in clinical studies are treated differently in regard to
refunding: damages to patients in clinical studies have to be
covered by an insurance policy and refunds can be claimed. A
HIV-infected patient was hospitalized due to a SAE in a clinical
trial for several weeks with a complicated clinical course
and long period of recovery. After recovering, he claimed a
refund for his income losses during hospitalization and reha-
bilitation. This claim was not accepted by the insurance compa-
y as several non-expert medical witnesses could not iden-
tify a causal relationship between the SAE and hospital ad-
mission.

As expert witnesses in this claim, we came rapidly and in
unison to the conclusion, that a causal relationship did exist.
In examining the history of the claim we found several inher-
ent pitfalls in the process of refunding patients for SAEs in
clinical trials. These pitfalls might erode patients’ trust for
Results:

weeks of age and 4-6 months of age. Babies was reported back to our program by HIV PCR at 2-4

Cesarean because of HIV status, and Cesarean for obstetric reasons.

Objectives: To evaluate rates of HIV transmission associated with three modes of delivery in HIV-positive women: vaginal, Cesarean because of HIV status, and Cesarean for obstetric reasons.

Methods: Retrospective chart review was done to analyze the outcomes of five years of births to HIV-positive women in a prenatal care program in Houston, Texas. The HIV status of babies was reported back to our program by HIV PCR at 2-4 weeks of age and 4-6 months of age.

Results: Between June of 2001 and December 2006 the Harris County Hospital District Women’s Program supervised the deliveries of 131 pregnant women. Standard treatment in our program is administration of highly active antiretroviral therapy (HAART) during pregnancy, IV zidovudine in labor, and six week oral prophylaxis with zidovudine for the baby. Following the ACOG guidelines, 76 (58%) of the women delivered vaginally and 55 (42%) delivered by Cesarean section. Among those who underwent Cesarean, 13 (10% of all pregnant women and 24% of all Cesareans) had a Cesarean for HIV-related reasons, i.e. viral load greater than 1000. The remaining 42 Cesareans (32% of all pregnant women and 76% of all Cesareans) were done for obstetric reasons.

There was a single case (0.7%) of mother to child transmission in a woman in the Cesarean group. She had arrived from another country at 36 weeks gestation with a viral load of 640,000. Because of bureaucratic obstacles she was unable to obtain oral therapy before 38 weeks. She underwent elective Cesarean at 38 weeks after administration of 3 hours of IV zidovudine and her baby was HIV-positive at birth.

Conclusions: Perinatal transmission of HIV is negligible in HIV-positive women treated with HAART during pregnancy who have viral loads less than 1000 and who undergo vaginal delivery.

B. Klink der HIV-Infektion

B.ER.1

Perinatal transmission of HIV and vaginal delivery: the Houston experience

Levison J.1, Beasley A.2, Giordano T.3

1Baylor College of Medicine, Department of Obstetrics and Gynecology/ Department of Family and Community Medicine, Houston, TX, United States of America, 2Baylor College of Medicine, Department of Obstetrics and Gynecology, Houston, TX, United States of America, 3Baylor College of Medicine, Department of Internal Medicine/Infectious Disease, Houston, TX, United States of America

Objectives: To evaluate rates of HIV transmission associated with three modes of delivery in HIV-positive women: vaginal, Cesarean because of HIV status, and Cesarean for obstetric reasons.

Methods: Retrospective chart review was done to analyze the outcomes of five years of births to HIV-positive women in a prenatal care program in Houston, Texas. The HIV status of babies was reported back to our program by HIV PCR at 2-4 weeks of age and 4-6 months of age.

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Conclusions: Perinatal transmission of HIV is negligible in HIV-positive women treated with HAART during pregnancy who have viral loads less than 1000 and who undergo vaginal delivery.

B.ER.2

Psychiatrische Aspekte bei HIV und AIDS: Psychotrope Behandlungsstrategien, psychiatrische Nebenwirkungen der antiretroviralen Medikamente und Behandlung von Schlafstörungen

von Einsiedel R.1, Jordan W.1

1Städtisches Klinikum Magdeburg, Klinik für Psychiatrie und Psychotherapie, Magdeburg, Germany


B.ER.3

Lipodystrophiesyndrom und Möglichkeiten der Behandlung aus der Sicht Betroffener

Schwarze S.1

1Projekt Information e.V., München, Germany


B.ER.4

**Verborgene Resistenz: Die Bedeutung minorer Quasispezies für den Erfolg der antiretroviralen Therapie**

Metzner K. J.

1Universität Erlangen-Nürnberg, Institut für Klinische und Molekulare Virologie, Erlangen, Germany


B.ER.5

**Hepatitis B new treatment options and new preventive approaches by vaccination**

Mauss S.

1Center for HIV and Hepatogastroenterology, Düsseldorf, Germany

The treatment of chronic hepatitis B is characterised by a rapid increase in the number of available antiviral drugs be longing to the class of HBV-polymerase inhibitors. Due to the better tolerance and more convenient application compared to interferon alfa HBV-polymerase inhibitors account today for the vast majority of prescribed therapies in chronic hepatitis B in Western countries. However particularly in HBe-antigen negative patients harbouring the precore mutant long-term suppression of HBV is needed. This is due to the high relapse rate after discontinuation of antiviral therapy in the absence of HBs-seroconversion which is a rare event during the first years of treatment. For this the development of resistance and cross-resistance against HBV-polymerase inhibitors is a rele vant issue for long term strategies to treat chronic hepatitis B. Suboptimal antiviral therapy resulting in the development of early resistance will harm future treatment options and lead to progressive liver disease in patients running out of effective treatment options. Sequential monotherapy or primary combin ation therapy with HBV-polymerase inhibitors are the curr ent treatment options having different pros and cons. In HIV coinfected individuals in the absence of antiretroviral therapy the treatment options are limited to adefovir and telbivudine due to interaction with HIV for the other available agents. In antiretrovirally treated patients HBV is usually simultaneously treated by NRTIs used to treat HIV. In these patients lamivudine monotherapy of HBV should be avoided except for patients in whom full viral suppression is reached with this approach. Changes of antiretroviral therapy must take the effect on HBV into account.

Vaccination against HBV is associated with a non-response rate of 10-15% in the general population. In HIV-coinfected patients the degree of immunodeficiency is an important pre dictor of antibody response against the vaccine. However vac cines in development may reach higher response rates in par ticular by using new adjuvant.

B.ER.6

**Pro Mono = pro bono, Risikominimierung durch Monotherapie**

Stoll M.

1Medizinische Hochschule Hannover, Zentrum Innere Medizin, Abt. Klinische Immunologie, Hannover, Germany


Schlussfolgerung: Das Dogma einer "obsoleten Monotherapie" wackelt. Evidenz gegen Monotherapie kommt bisher aus Studien mit nRTI und NNRTI. PI/r haben demgegenüber eine höhere Resistenzbarriere. Für (oder gegen) eine Monotherapie mit neuen, teilweise weit potenteren Substanzen fehlen bisher die Daten. Die Entwicklung zahlreicher neuer Substanzklassen lässt das Risiko zudem vertretbar(er) erscheinen, eine einzelne Substanzklasse in einem Monotherapieansatz (frühzeitiger) zu verlieren. Ein Vorteil der Monotherapie wäre sogar, dass nur die eine verwendete Substanzklasse von Resistenz betroffen wäre. Für HAART gilt, dass Toxizität und Non-Adhärenz die wichtigsten Therapie-limitierenden Faktoren sind. Potentiell...
bedrohliche Langzeittoxizitäten sind somit ebensoliche hypothetischen Risiken wie die Risiken eines (früheren) Therapieversagens. Zu guter Letzt darf der Patientenwille zu einer Monotherapie nicht geringer wiegen als das Dogma einer Leitlinie. Dort wo Evidenz fehlt, gilt für den Arzt das "primum non nocere". Diesem Grundsatz ist die Monotherapie alle Male näher als die Kombination mehrerer Substanzen.

B.E.R.7
Gene therapy for HIV-infection
van Lanzen J.1, Glaunsinger T.1, Hermann F.2, Egerer L.2, Newzela S.2, Kimpel J.2, von Laer D.2
1Universitätskrankenhaus Eppendorf, Infektiologie, Hamburg, Germany, 2Georg-Speyer-Haus, Frankfurt am Main, Germany

Drug toxicity and viral resistance limit long-term efficacy of antiviral drug treatment for HIV infection. Thus, alternative therapies need to be explored. Here, we tested the infusion of T lymphocytes transduced with a retroviral vector (M87o) that expresses an HIV entry inhibitory peptide (mac46). Gene-modified autologous T cells were infused into 10 HIV-infected patients with advanced disease and multidrug resistant virus during antiretroviral combination therapy. T cell infusions were tolerated well with no severe side effects. A significant increase of CD4 counts was observed post infusion. At the end of the one-year follow-up, the CD4 counts of all patients were still around or above baseline. Gene-modified cells could be detected in peripheral blood, lymph nodes and bone marrow throughout the one-year follow-up, whereby marking levels correlated with the cell dose. No significant changes of viral load were observed during the first four months. Four of the seven patients that changed their antiviral drug regimen thereafter responded with a significant decline in plasma viral load. In conclusion, the transfer of gene-modified cells was safe, led to sustained levels of gene marking and may improve immune competence in HIV-infected patients with advanced disease and multidrug resistant virus. However, the low level of gene marking and the lack of a substantial in vivo accumulation of gene-protected cells induced us to return to the bench and further improve our strategy. Different configurations of gammaretroviral SIN vectors were cloned and analyzed for improved long-term expression in vivo in mouse T-cell and stem-cell transplantation models. In addition, several variants of the M870 transgenes were generated that lead to shedding/secretion of the antiviral C peptide and thus protect non-gene-modified cells in the vicinity. Finally, several humanized mouse models were compared for their suitability for preclinical testing of gene therapy regimen for HIV infection.

B.E.R.8
European study about mitochondrial toxicity in HIV-negative children born to HIV-1-infected mothers (MITOC)

Buchholz B.1, Wintergerst U.2, Brockmeyer N.3, Competence Network for HIV/AIDS and MITOC
1Kindermodul, Universitätskinderklinik Mannheim, Mannheim, Germany, 2Kindermodul, Dr. von Haunersches Kinderklinik, München, Germany, 3Dermatologische Klinik der Ruhr Universität, St. Josef Hospital, Bochum, Germany

In Europe the low rate (1-2%) of vertical transmission of HIV in pregnant women has been achieved by the combination of anti-retroviral therapy of these women (including nucleoside reverse transcriptase inhibitors/NRTI), caesarean section, anti-retroviral post exposition prophylaxis (with NRTI) in the newborn and refraining from breast-feeding. Mitochondrial toxicity in children associated with in utero/postnatal exposure to NRTIs (as cause of affinity for mitochondrial g-DNA polymerase inducing mitochondrial depletion/dysfunction) was recovered during a screening in the French Perinatal Cohort in 1999+2003: The estimated incidence of mitochondrial dysfunction up to the age of 18 months was 0.26% (95% confidence interval, 0.10-0.54) among these NRTI-exposed children, of whom 21/2644 had established or possible mitochondrial dysfunction. In April 2001 the Pharmacovigilance Working Party of the European Committee for Medicinal Products for Human Use requested further investigation of mitochondrial toxicity in children associated with in utero/postnatal exposure to NRTIs. Accordingly the Collaborative Committee for Mitochondrial Toxicity in Children (MITOC) with representatives from all companies distributing NRTIs (BMS, Gilead Sciences, GSK) and from European cohorts collecting prospective data on these children (French Perinatal Cohort Study, Spanish Perinatal Cohort Study, Swiss Mother and Children HIV Cohort Study, Italian Registry for HIV Infection in Children, German Competence Network for HIV/AIDS) was established. In the protocol developed by MITOC these children will be examined in a cross-sectional evaluation at a single visit between the ages of 18-24 months
- to determine the prevalence of neurological symptoms of cognitive or motor delay (=cases)
- to categorize these cases into explained and unexplained neurological symptoms
- to estimate the proportion of the unexplained cases whose symptoms are suggestive of mitochondrial disorder
- to assess the association between type, duration of ART exposure in utero and/or postnatally and unexplained mitochondrial disorder-related cognitive/motor delay. Based upon information provided by the cohorts/studies, the study will enroll approximately 2500 to 3000 eligible children over a two-year period.

B.E.R.9
Herausgesetzte periphere Nervenregeneration in HIV-Patienten nach experimenteller Denervierung

Hahn K.1, Brown A.2, Hauer P.2, McArthur J.C.2, Polydefkis M.2
1Charité, Humboldt Universität Berlin, Neurologie, Berlin, Germany, 2Johns Hopkins Universität, Neurologie, Baltimore, United States of America


Methodik: Die chemische Axotomie erfolgte durch topische Capsaicinapplikation am distalen lateralen Oberschenkel in 71 Kontrollen und 22 HIV-positiven Probanden. Über den Zeitraum von 100 Tagen wurde die Nervenfaserrégeneration
in multiplen Hautstanzbiopsien quantifiziert. Zur Erzeugung
einer mechanischen intrakutanen Axotomy erhielten 5 Kon-
trollprobanden und 5 HIV-positive Probanden eine 3 mm
große Hautstanzbiopsie am distalen Oberschenkel. 2 Monate
später erfolgte eine 4 mm große überlappende Biopsie in der
die kollaterale Nervenregeneration quantifiziert wurde.

Ergebnisse: Die Nervenfaserregeneration nach chemischer
Denervierung durch Capsaicin war am höchsten in den gesun-
den Kontrollen (0.17 ± 0.073 Fasern/mm/Tag), gefolgt von
den HIV positiven Probanden ohne Neuropathie (0.13 ± 0.06)
den HIV+ Probanden mit Neuropathie (0.097 ± 0.077)
(ps<0.002). Dabei zeigte sich eine signifikante Korrelation mit
der basalen epidermalen Nervenfaserdichte aber keine Korre-
lation mit der Dauer der HIV-Erkrankung, der HIV Viruslast
oder der CD4 Zellzahl. Darüber hinaus zeigte sich, dass
Probanden mit einer HIV-Erkrankung im Vergleich zu Gesun-
den eine reduzierte Regeneration nach mechanischer De-
nervierung aufweisen (5.31µm ± 0.73 im Vergleich zu 9.78
µm ± 1.5/Tag, p = 0.03).

Zusammenfassung: Patienten mit einer HIV-Erkrankung
weisen Abnormalitäten in der Nervenfaserregeneration auf,
die sich bereits vor dem klinischen Auftreten einer sen-
sorischen Polyneuropathie nachweisen lassen.

B.ER.10
Nierenfunktion bei HIV und Begleiterkrankung
Rieke A.1
1Klinikum Kemperhof, Immunologische Ambulanz, Koblenz,
Germany

Neben der HIVAN als direkt HIV assoziierte Nieren-
erkrankung überwiegend bei Afroamerikanern sind Verän-
derungen der Nierenfunktion bei HIV – Patienten häufig: 30% aller Patienten haben eine Proteineurie, ein Viertel entwickeln eine Einschränkung der GFR. In einer Zusammenstellung der Zulassungsstudien und Analyse der Subgruppen darin ist für die Substanz TDF bei farbigen Patienten keine erhöhte Nephrotoxizität erkennbar. Für eine Toxizität unter TDF scheint das Ausmaß der Vorbehandlung u.a. auch mit Ind., das Lebensalter > 45 Jahren und Diabetes mellitus, nicht je-
doch Art. Hypertonie, Geschlecht, Hepatitis – Coinfektion,
Art der HIV Transmission und Gebrauch von NRTI oder ge-
boosterter PI verantwortlich zu sein, so Kohortenanalysen.
Die aktuellen Studienergebnisse werden zusammengestellt.

C. Koinfektionen /Komorbidität
C.ER.1
HSV-Infektion bei HIV-Trägern
Rabenau H.F.1
1Institut für Medizinische Virologie der Universitätsklinik,
Frankfurt am Main, Germany

Infektionen mit den Herpes simplex Viren (HSV) Typ 1 oder
Typ 2 sind beim Menschen ubiquitär verbreitet. Die Übertra-
gung des HSV-1 erfolgt durch Speichelkontakt mit den Eltern
bereits ab dem frühen Kindesalter. Junge Erwachsene sind in
Deutschland zu ca. 80% HSV-1 Antikörperträger. Das HSV-2
wird in der Regel durch Intimkontakte übertragen. Der Mani-
festationsindex wird bei der Primärinfektion sehr unter-
chiedlich eingeschätzt (10-50%). Der Herpes genitalis wird
überwiegend durch HSV-2, kann jedoch auch Folge einer
HSV-1 Infektion sein, welche einen milderen Verlauf haben
soll. Bei Immunsuppression in Folge einer HIV-Infektion
can der Herpes genitalis massiv und länger persistierend
 ausgeprägt sein, bei AIDS-Patienten auch als Herpes anogeni-
tals. Epidemiologische Untersuchungen zur HSV-2-Seroprä-
valenz zeigen, dass in Industrieländern heute im Mittel etwa
20 %, in einzelnen Risikogruppen bis zu 60 % der Bevölke-
rung postpubertär spezifische Antikörper aufweisen. Bei HIV-
positiven Patienten (n = 369) des Universitätsklinikums
Frankfurt wurde mit einer Prävalenz von 31,6 % ein sig-
nifikanter Wert gegenüber dem „Normalkollektiv“
beobachtet. Personen, die sowohl HIV, als auch HSV-2 in-
fi ziert sind, zeigen häufiger HSV-Rezidine, als solche, die nur
HSV-2 alleine infiziert sind. Gleichzeitig ist die Anzahl der
Rezidine mit der CD4-Zahl und damit mit der Immunsuppres-
sion korreliert. Verschiedene Studien belegen, dass eine HSV-
2-Seropositivität sowohl das Risiko einer HIV- Akquirierung
erhöht, als auch das Risiko HIV zu übertragen. Letzteres
scheint u.a. dadurch bedingt zu sein, dass durch HSV-2-regu-
latorische Proteine die HIV Replikation erhöht werden kann,
was wieder rum zu einer Erhöhung der HI-Virustiter an der
Mukosa führt und zur häufigeren HIV-Ausscheidung. Dies
cann sowohl bei klinisch apparenten als auch inapparenten
HSV-Reaktivierungen auftreten. Versuche mit antiperpetis-
cheren Therapien die HIV-Übertragung zu reduzieren zeigen
viel versprechende Erfolge.

C.ER.2
ART bei HCV- und HBV-Koinfektion
Vogel M.1
1Universitätsklinikum Bonn, Medizinische Klinik und
Poliklinik I, Bonn, Germany

Hepatitis-Koinfektionen stellen für HIV-Patienten ein erhöh-
tes Risiko für Transaminasenerhöhung nach Einleitung einer
hochaktiven antiretroviralen Therapie (HAART) dar. Den-
noch überwiegen die Vorteile einer HAART, so dass bei
bestehender Hepatitis-Koinfektion grundsätzlich keinem Pa-
tienten die Therapie vorenthalten sollte.

Eine Hepatitis-Koinfektion sollte jedoch die Auswahl
der antiretroviralen Medikamente beeinflussen. So ist bei
behandlungsorientierten HBV-Infektion und gleichzeitiger In-
dikation für eine HAART an die Gabe von 3TC oder FTC in
Kombination mit TDF als Bestandteil der HAART zu denken.
Bevor Vorliegen einer HCV-Infektion ist bei geplanter PegIFN /
RBV Kombinationstherapie nach Möglichkeit eine AZT und
d4T-freie HAART zu wählen. AZT erhöht das Risiko für
Leukopenien und Anämien, während d4T das Risiko für mito-
chodriale Toxizität erhöht. Die Gleichzeitige Gabe von ddL
und RBV ist aufgrund des erhöhten Risikos für Pankreatitiden
und Laktatidosen kontraindiziert.

In der Klasse der Proteaseinhibitoren weisen vor allem
RTV in therapeutischer Dosierung und TPV, in der Klasse der
NNRTI vor allem NVP ein erhöhtes Risiko für Transami-
nasenerhöhungen auf, so dass entsprechende Kontrollen der
Leberwerte erfolgen sollten. Patienten mit fortgeschrittener
Leberfibrose / -zirrhose weisen besonders hohe Risiken für
Transaminasenerhöhungen unter HAART auf und sollten eng-
maschig überwacht werden. Spiegelkontrollen vorrangig
hepatisch eliminierten Substanzen können hier im Einzelfall sin-
nvoll sein, um eine individuelle Dosisanpassung zu erreichen
und eine dosisabhängige Lebertoxizität zu minimieren. Auch
sollte bei Patienten mit fortgeschrittener Fibrose / Zirrhose nach Möglichkeit die Gabe von d4T oder ddI aufgrund des erhöhten Risikos einer Laktatazidose vermieden werden.

Nach Beginn einer HAART bei einem Hepatitis-koinfizierten Patienten sollten in den ersten 3 Monaten alle 2 - 4 Wochen Kontrollen der Lebertransaminasen erfolgen, um eine schwere Hepatoxizität nicht zu übersehen. Differentialdiagnostisch sollte insbesondere bei Vorliegen einer chronischen Hepatitis B Koinfektion oder bei höhergradigen Immunodefekten an ein Immunrekonstitutionssyndrom oder schwellende opportunistische Infektionen mit Leberbeteiligung gedacht werden.

C.E.R.3 Therapie der Syphilis bei HIV-Infektion: Konsequenz nach Leitlinien oder doch anders? Schöfer H.1

1Klinikum der J.W. Goethe-Universität Frankfurt/M., Zentrum der Dermatologie und Venerologie (ZDV), Frankfurt/M., Germany

Seit vielen Jahrzehnten gilt Penicillin unangefochten als Therapie der Wahl zur Behandlung der Syphilis. Resistenzentwicklungen wurden nicht beobachtet. Als Voraussetzung für eine erfolgreiche Behandlung gilt ein treponemizider Serumspiegel (>0,03 IE/ml) über mindestens 10-11 Tage. Durch die Einstellung der Produktion von Clemizol- und Procapipenicillin stehen aktuell nur noch kristalloides Penicillin G und Benzathin-Benzylpenicillin (BBP) zur Syphilisbehandlung zur Verfügung. Sie unterscheiden sich in ihrer Anwendung in zwei wesentlichen Punkten:
1. der Applikationsweise und
2. der Erreichung treponemizider Wirkstoffkonzentrationen im Liquorraum.


C.E.R.4 Syphilis und HIV Bickel M.1

1UCLA, Infectious Disease, Los Angeles, United States of America


C.E.R.5 Fallpräsentation zur Interpretation bildgebender Verfahren in der HIV-Behandlung Prosch H.1, Steuer A.2, Schmied B.2, Mostbeck G.1

1Otto Wagner Spital, Röntgen, Wien, Austria, 2Otto Wagner Spital, II. Pneumologische Abteilung, Wien, Austria

Die Einführung der hochaktiven antiretroviralen Therapie (HAART) Mitte der 1990 Jahre führte zu einer signifikanten Abnahme der Mortalität und Morbidität der HIV-Infektion. Bei einer geringen Anzahl der HIV-infizierten Patienten führt das Wiedereinsetzen der Immunabwehr jedoch zu einer gesteigerten inflammatorischen Reaktion, die als Immunrekonstitutionssyndrom (IRIS) bezeichnet wird. Meist präsentiert sich das IRIS als Mycobacterium avium Lymphadenitis, als paradoxe pulmonale oder extrapulmonale Tu-

D.ER.6

The virological feature of human immuno deficiency virus type-1 (HIV-1) pre and post treatment of tuberculosis in coinfected patients

Biru T.1, Petros B.2, Messele T.3, Pollakis G.4, Tilahun T.3, Wolday D.5

1Johann Wolfgang Goethe Universität, HIVCenter, Zentrum für Innere Medizin, Frankfurt, Germany, 2Addis Ababa University, Biomedical Sciences, Addis Ababa, Ethiopia, 3Ethiopian Health and Nutrition Research Institute, Ethiopia, 4Netherlands AIDS Research Project (ENARP), Addis Ababa, Ethiopia, 5University of Amsterdam, Dept. of Human Retrovirology, Academic Medical Center, Amsterdam, Netherlands

The association between HIV and Tuberculosis (TB) is complex and bi-directional. Recent studies demonstrated that TB accelerates the course of AIDS. In the present study we sought for virological and immunological features of HIV in TB co-infected individuals. The study subjects are selected from Ethiopia-Netherlands AIDS research project (ENARP) cohort. 8 HIV/TB co-infected individuals prior to diagnosis of TB, during and after completion of successful TB chemotherapy and 7 CD4 matched HIV-1 only with one year follow-up were involved. As routine laboratory analysis viral load and CD4+ cell count were done at the time of blood sample collection. For this study, RNA was isolated from plasma and the C2V3 region of HIV-1 envelope gene was amplified by nested polymerase chain reaction (PCR). Direct sequencing was performed for all the PCR positive products. The HIV/TB co-infected individuals showed a significantly elevated plasma HIV-1 viral load (P<0.05) during treatment of TB with steeper decline in CD4+ cell counts (P<0.05). However, the ds (synonymous nucleotide substitution) and dns (non-synonymous nucleotide substitution) comparison between the study groups and the controls at intake (before start of treatment) and 12 months later (after completion of TB treatment) didn’t show a significant difference between the two groups. The ratio of ds and dns between the two time points for both groups was approximated to 1, which shows a positive but weak selection of evolution of the virus. We conclude therefore that plasma HIV-1 viral load is elevated during and after treatment of active tuberculosis, but this may not be due to the presence of highly replicative HIV viruses. We recommend future research should focus on isolating the different HIV quasi-species so that one can see if there is a difference in HIV genetic diversity, diversification and diversification rate between the HIV/TB and HIV only study population.

D. Therapie der HIV-Infektion

D.ER.1

Therapiestrategien bei vorbehandelten Patienten

Gute P.1

1Praxis, Frankfurt am Main, Germany


Dies bedeutet dass trotz der Verfügbarkeit der neuen Medikamente diese nicht zwingend immer eingesetzt werden müssen. Insbesondere sollte der Einsatz nicht unkritisch erfolgen da bei diesen Medikamenten noch vieles unbekannt ist (Langzeit-NW?) und diese Substanzen meistens in nicht in Studien erproben Kombinationen eingesetzt werden müssen.

Die Behandlung von vorbehandelten Patienten sollte primär auf Strategischen Gesichtspunkten erfolgen und das Ziel einer Jahrzehnten langen Therapie ermöglichen.


D.ER.2

Patientenkohorte – Klinische Relevanz

Skoretz N.1, Bergmann U.1, Denecke S.1, Michalik C.1, Theisen D.1, Wiegelmann S.1, Paulus U.1, Competence Network for HIV/AIDS

1Universität zu Köln, Köln, Germany

Hintergrund: Das Kompetenznetz HIV/AIDS hat seit Förderbeginn durch das Bundesministerium für Bildung und Forschung (BMBF) ein primäres Anliegen: Eine umfassende, repräsentative Patienten kohorte zu etablieren, von der Forschung, Wissenschaft, die klinische Versorgung und insbesondere die Patienten profitieren.


Der Einfluß einer Hepatitis auf die HIV-Infektion wird in einem weiteren Projekt spezifiziert; bedeutsam, da über 3600 Patienten eine Hepatitis B und über 350 eine Hepatitis C Koinfektion aufweisen. Die Kohorte wird zur Hypothesengenerierung genutzt und zum gezielten Rekrutieren von Patienten für klinische Studien. Testdatensätze für internationale Kooperationen zeigten, dass die Qualität der Daten gut ist und die Datenerfassung internationalen Standards genügt.

**Schlussfolgerungen:** Die Daten werden zur Hypothesengenerierung, für Studien, Publikationen, und zur Information der Öffentlichkeit genutzt. Dies alles dient der Beschreibung der HIV-Versorgungssituation in Deutschland und der Optimierung und Standardisierung der HIV-Therapie. Die Kohorte trägt somit zum vertikalen und horizontalen Wissenstransfer sowohl national, als auch international bei.

**D.E.R.3**

New HCV antiviral therapies

*Zeuzem S*.1

1Klinikum d. J.W. Goethe-Universität, Med. Klinik I, Frankfurt, Germany

In the first decade after isolation and characterization of the hepatitis C virus many compounds were empirically tested in clinical trials for anti-HCV activity. Only interferons alone and in combination with ribavirin showed significant antiviral efficacy. With the current standard of care – pegylated interferon alfa in combination with ribavirin – excellent sustained virologic response rates of 80-90% are achieved in patients chronically infected with hepatitis C virus (HCV) genotype 2 or 3 isolates. However, virologic response rates in patients infected with the most prevalent genotype HCV-1 are only around 50%. Thus, specifically for HCV-1 infected patients improved therapeutic options are needed.

Basic to the development of new specific anti-HCV drugs is the understanding of the viral life cycle, in particular the genomic organization and the polyprotein processing. Major progress in this field was achieved due to the development of sub-genomic and more recently full-genomic replica systems. The HCV genome is a single-stranded RNA molecule that contains a single open reading frame encoding a polyprotein of about 3000 amino acids. The polyprotein is subsequently processed at the level of the endoplasmatic reticulum (ER) by cellular and viral proteases to yield 4 structural and 6 non-structural proteins. The open reading frame is flanked by 5’ and 3’ untranslated regions. Each single HCV structure represents a potential antiviral target. Antisense oligonucleotides, ribozymes, siRNA, and small molecules have been targeted in particular against the 5’-noncoding region with substantial success in vitro but not yet in vivo. Inhibition of nucleocapsid formation to the icosaedral viral coat is an attractive target, however, no specific molecules have yet been developed. Envelope proteins HCV E1 and E2 are the basis for the development of prophylactic and/or therapeutic vaccines.

NS3 and NS4A are cleaved by the catalytic activity of the NS3 protease domain. In addition to the protease domain located in the 189 aminoterminal amino acids, NS3 also possesses a helicase domain located in the 442 carboxyterminal amino acids. The NS3 protease domain is responsible to completely the polyprotein processing down to NS4B, NS5A, and NS5B. Despite the fact that the catalytic site is a shallow and largely hydrophobic groove and therefore very difficult to target several compounds have been successfully designed (BILN 2061, VX-950, SCH503034, etc.). The NS5B RNA-dependent RNA polymerase is the key enzyme for synthesis of a complementary minus-strand RNA using the genome as template, and the subsequent synthesis of genomic plus-strand RNA from this minus-strand RNA template. The active site of the enzyme is a target for nucleoside/nucleotide analogue inhibitors. Nucleoside inhibitors were recently reported to bind at a surface site in the thumb approximately 30 Å from the active site. This site is very close to a allosteric GTP site suggesting that nonnucleoside inhibitors may act by blocking the enzyme in the initiation mode through inhibition of a conformational change needed to proceed with elongation.

**D.E.R.4**

Gentherapie bei Immundefizienzen – Chancen und Risiken

*Baum C*.1

1Medizinische Hochschule Hannover, Hannover, Germany

Discovery and optimization of a natural HIV-1 entry inhibitor targeting the gp41 fusion Peptide


1 University Clinic Ulm, Institute of Virology, Ulm, Germany, 2 Hannover Medical School, Division of Experimental and Clinical Peptide Research, Hannover, Germany, 3 University of Erlangen-Nürnberg, Institute for Clinical and Molecular Virology and Nikolaus-Fiebig-Center, Erlangen, Germany, 4 University of Lübeck, Institute for Chemistry, Lübeck, Germany, 5 University of Hamburg, Organic Chemistry, Hamburg, Germany, 6 Hannover Medical School, Clinical Immunology and Rheumatology, Hannover, Germany, 7 VIRO Pharmaceuticals GmbH & Co. KG, Hannover, Germany

A variety of molecules in human blood have been implicated in the inhibition of HIV-1. However, it remained elusive which circulating natural compounds are most effective in controlling viral replication in vivo. To identify natural HIV-1 inhibitors we screened a peptide library generated from large quantities from patients with chronic renal failure. HF-derived peptide libraries contain essentially all circulating blood peptides smaller than 30 kDa. We identified a natural peptide in HIV-1-infected individuals. This peptide specifically binds to the HIV-1 gp41 fusion peptide, further optimization of VIRIP might lead to the development of another class of antiretroviral drugs. One of its derivatives with enhanced antiviral activity has been characterized in preclinical experiments for its tolerability and safety. Based on the outcome of these studies, a plan for a proof-of-concept clinical phase I/II study is currently being developed to investigate the efficacy of this novel antiviral peptide in HIV-1-infected individuals.

D.E.R.6

Mitochondrial toxicity of antiretroviral therapy

Sternfeld T.1

1 Klinikum rechts der Isar, Technische Universität München, Infektionsambulanz, II. Medizinische Klinik und Poliklinik, München, Germany

Despite the initial positive impact of highly antiretroviral therapy (HAART), serious side effects, like lactic acidosis, hepatic steatosis, myopathy and lipodystrophy, which appear to originate in the mitochondria and lead to dysfunction of the organelle were observed. As the AIDS epidemic continues, and survival is prolonged by treatment with antiretroviral therapy, long-term side effects of HAART may become increasingly common, especially in developing countries where the latest and less toxic generations of antiretroviral drugs are not available. Because of the poor prognosis without therapy, the long-term impact of mitochondrial toxicity it is outweighed by the success of HAART. Pathogenesis of mitochondrial toxicity caused by HAART is complex and despite research efforts not fully understood. Clinical phenotype is heterogeneous due to genetic predisposition to HAART toxicity, direct effects of the HIV virus on mitochondria, oxidative stress, the immune status of the patient and the used drug combinations. Several molecular and cellular techniques are currently available to analyze mitochondria, but extrapolation to clinical practice is complicated.

In order to develop tools for assessing mitochondrial toxicity in the clinical setting, we analyzed the influence of HIV infection on mitochondrial membrane potential (MMP) as a marker of energization state of the mitochondria, and on the rate of apoptosis of peripheral mononuclear cells. Hepatic mitochondrial function was assessed using 13C-methionine breath test in HIV negative healthy subjects, HIV positive, treatment naive, and HIV positive patients on ART as well as hepatitis co-infected patients. Results were correlated with HAART, clinical and immunological parameters and the different forms of lipodystrophy.
D.E.R.7
Zentrale und periphere Neurotoxizität von HAART

Hahn K.1

1Charité, Humboldt Universität, Neurologie, Berlin, Germany


D.E.R.8
Update Lipodystrophie aus ärztlicher Sicht

Bickel M.1

1UCLA, Infectious Disease, Los Angeles, United States of America


D.E.R.9
Trends in the transmission of drug-resistant HIV strains: Increase of NNRTI resistance accompanied by a decrease of NRTI resistance (German HIV-1 seroconverter study)

Kuecherer C.1, Poggensee G.1, Bartmeyer B.1, Somogyi S.1, Fleischhauer C.1, Korn K.2, Dupke S.3, Cordes C.4, Jessen H.3, Klausen G.6, Hamouda O.1, German HIV-1 Seroconverter Study Group

1Robert Koch-Institute, Berlin, Germany, 2Institute of Clinical and Molecular Virology and National Reference Center for Retroviruses, University Erlangen-Nürnberg, Erlangen, Germany, 3Medical Practice Driesener Str., Berlin, Germany, 4Medical Practice Kubenner Str., Berlin, Germany, 5Medical Practice Motzstr., Berlin, Germany, 6Medical Practice Kaiserdamm, Berlin, Germany

Objective: Development of resistance due to insufficient drug levels during antiretroviral treatment of HIV infected patients results in treatment failure and is a major source for transmission of resistant HIV. Trends of transmission of resistant HIV were analysed in drug naive patients with a known date of infection. Methods: Population sequences of the protease and the first 1000 nucleotides of the reverse transcriptase were analysed in 827/885 drug-naive HIV-1 seroconverters infected between 1996 and 2005. Resistance mutations and the expected phenotypic resistance profiles were predicted using the Stanford algorithm (version 4.2.1).

Results: The majority of the study patients were men (94%), of German origin (88%) and infected with subtype B (93%). 86% of the patients were men, who have sex with men. Overall, 14% of the seroconverters were infected with resistant HIV of which the activity of at least one drug was reduced. NRTI-resistant strains were most frequently observed (7.8% NRTI, 2.4 % PI and 2.1% NNRTI). Resistance to more than one drug class was identified in 14 (1.7%) of HIV strains and transmission of drug-resistant strains was only rarely observed (n=3). No increase or decrease in the overall transmission frequency of resistant HIV was observed during time (p=0.09). However, HIV-strains showing only resistance to NRTI seemed to decrease since 2001 (p=0.03), whereas resistance to NNRTI occurring alone or combination with other classes of resistance seemed to increase during time (p=0.04). The decline of NRTI resistant HIV was mainly due to a decrease in the frequency of thymidine-analogue resistance mutations (8.4% in 1996-2000 to 4.8% (2001-2005). Nevertheless, NRTI resistance was predominant from 1996 to 2005.

Conclusion: The decrease in NRTI resistance and increase in NNRTI resistance might be explained by the changing patterns of drug use. Since 1996 PI and NNRTI were part of HAART concepts, whereas “triple nuke” regimens were not recommended anymore. The lower genetic barrier to develop NNRTI resistance as compared to PI resistance could contribute to the rise of transmitted NNRTI resistance. These trends need to be confirmed by further investigations.

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Primary drug resistance has been demonstrated in acutely infected patients, e.g. in the German Seroconverter study, that found a prevalence of about 14%. For the clinician, the more common situation is deciding about first-line HAART in chronically infected patients with immune deficiency. The German prospective study RESINA showed a prevalence of about 10% in these cases. Further investigations demonstrated an even higher prevalence using ultra-sensitive testing. Because of these facts, revised FDA-guidelines for trials on antiretroviral therapy in treatment-naive patients require separate analyses of the treated population according to the presence of baseline genotypic resistance.

Several studies showed reduced virological efficacy of HAART in patients with primary resistance, compared to patients infected with wild type HIV. In these investigations, the decision for a certain combination therapy was not based on genotyping. As a consequence, first-line antiretroviral therapy should not be administered without prior resistance testing. To date, only two prospective studies evaluated the use of genotyping for choosing a first-line regimen. One of these was undertaken in seroconverters (Shet A, JAIDS 2006), the other in chronically infected patients (Oette M, JAIDS 2006). Both compared efficacy of HAART guided by genotypic resistance testing between patient groups harboring mutant virus and wild type virus. In both studies, treatment was equally potent in the two patient groups.

In summary, the prevalence of primary HIV drug resistance is 10-14% in Germany. Success of first-line HAART is suboptimal in patients carrying mutated virus. In contrast, application of resistance testing may lead to equal efficacy in groups with and without primary drug resistance. Thus, routine genotyping in untreated HIV-positive patients should be performed before administration of first-line HAART.

**E. Virologie**

**E.E.R.1**

Einfluss von CTL Escape Mutationen auf die virale Fitness von HIV

Schneidewind A.1, Brockman M.A.1, Allen T.M.1

1Harvard Medical School, Massachusetts General Hospital, Partners AIDS Research Center, Boston, United States of America


Diese Daten verdeutlichen, dass wichtige Wechselwirkungen zwischen Capsid und Proteinen der Zielzelle durch CTL Escape verändert werden. Strukturelle und funktionelle Einschränkungen bei der Selektion für Escape Mutationen verkleinern die virale Variationsbreite und führen gleichzeitig zu Mutanten mit eingeschränkter Fitness. Die Identifizierung weiterer Escape Mutationen in Gag, die mit einer Fitnessreduktion einhergehen oder die die Interaktion zwischen Capsid und zellulären Proteinen verändern, kann dazu beitragen, Zielstrukturen für effektive Impfstoffe zu charakterisieren.

**F. Immunologie**

**F.ER.2 Immune weapons in HIV-induced neuropathogenesis**

*Speth C.*, *Hagleitner M.1, Wehinger A.1, Mohsenipour I.2, Arendt G.3, Dierich M.P.1, Maier H.4*

1Medizinische Universität Innsbruck, Department für Hygiene, Mikrobiologie und Sozialmedizin, Innsbruck, Austria; 2Medizinische Universität Innsbruck, Department für Neurochirurgie, Innsbruck, Austria; 3Heinrich-Heine-Universität, Düsseldorf, Germany; 4Medizinische Universität Innsbruck, Institut für Pathologie, Innsbruck, Austria

**Objectives**: Complement synthesis and astrocytic phagocytosis are the most important local immune weapons in CNS and form an interactive network. This mutual immune network can limit viral spreading and virus-induced neural damage. Since the spontaneous complement production in the brain is low the expression level of complement in the virus-infected brain is an important parameter to evaluate the effectiveness of innate immune response. Therefore we quantified cerebral complement concentrations in HIV-infected patients and investigated the effect of complement on astrocytic phagocytosis.

**Methods**: The expression of complement was analysed immunohistochemically in post-mortem brain tissue derived from HIV-infected patients and compared to control tissue from uninfected individuals. Phagocytosis by astrocytes was quantified using fluorescent opsonized beads.

**Results**: The immunohistochemical analysis showed a strong upregulation of complement factors in the brain parenchyma of HIV-infected patients. Whereas only weak spontaneous complement expression was detected in uninfected control brains, a strong signal was obtained in the tissue of HIV-infected patients. All resident cell types (astrocytes, microglia, oligodendrocytes and neurons) contributed to the local complement synthesis with differences between the various complement factors. The increase of complement production seems to be an early event in HIV-induced neuropathogene-

**Conclusion**: Our data suggest that HIV infection of the brain induces local synthesis of complement factors. Thus, complement can play an important role as antiviral weapon. However it also inhibits local phagocytosis and thus support viral spreading and neurodegeneration.
Increased IFN-alpha expression in circulating plasmacytoid dendritic cells of HIV-1 infected patients despite selective loss

Lehmann C.1, Taubert D.2, Hartmann P.1, Fäktenheuer G.1, van Lunzen J.3, Stellbrink H.-J.1,5, Gallo R.C.4, Romero F.4

1Klinikum der Universität zu Köln, Klinische Infektiologie, Köln, Germany, 2Klinikum der Universität zu Köln, Institut für Pharmakologie, Köln, Germany, 3Medical Center Hamburg-Eppendorf and Heinrich-Pette-Institute for Experimental Virology and Immunology, Hamburg, Germany, 4University of Maryland, Institute of Human Virology, Baltimore, United States of America

Objective: Plasmacytoid dendritic cells (PDC) induce innate and adaptive immune responses through production of interferon alpha (IFNa). To date, the role of PDC and IFNa in human immunodeficiency virus 1 (HIV-1) infection remains unclear and even paradoxical. Indeed, HIV-1 disease progression is associated with a decline of PDC, which display reduced ability to produce IFNa when challenged with reference viruses. However, high levels of IFNa in sera of HIV-1 infected individuals are associated with disease progression.

Methods: We sought to determine whether disappearance of PDC in HIV-1 disease is due to homing in lymphoid tissues. We also studied steady-state IFNa and myxovirus resistance protein A (MxA) expression, and correlated the results with selected clinical and laboratory parameters.

Results: We found a marked decrease of PDC in peripheral blood of HIV-1 infected individuals progressing to disease, but steady PDC counts in lymphoid tissues. Loss of circulating PDC correlated strongly with CD4+ T cell counts. However, PDC from HIV-1 infected individuals progressing to disease expressed IFNa and MxA levels markedly higher than control individuals, although this did not correlate with viremia.

Conclusions: Despite selective loss of peripheral PDC during progression to HIV-1 disease, the residual cells express high levels of IFNa, which may contribute to immune suppression.

Natural killer cells and natural killer cell receptors in HIV-1 infection

Nattermann J.1, Spengler U.1, Rockstroh J.K.1

1Universitätsklinikum Bonn, Medizinische Klinik und Poliklinik I, Bonn, Germany

Natural killer (NK) cells represent a first line of defense against viruses and regulate adaptive immune responses. Recent epidemiologic data indicate that NK cells may have the potential to influence the natural course of HIV-1 infection. NK cell function is regulated by the balance between inhibitory and stimulatory receptors triggered on their cell surface. Inhibitory NK cell receptors (NKR) are specific for MHC class I molecules and comprise two families: the killer-cell immunoglobulin-like receptor (KIR) family and the C-type-lectin family of receptors. Activating receptors such as NK2D and the recently discovered natural cytotoxicity receptors (NCRs) NKp30, NKp44 and NKp46 provide the “on signal” for NK cell stimulation during interaction with their target cells. Of note, NK cell receptors are heterogeneously expressed on individual NK cells enabling further phenotypic distinction of NK cell subsets based on the constitutive or inducible expression of the various NK cell receptors. In addition, accessory NK cell receptors (e.g. NKp-80, CD161, CD96 and CD244) can enhance NK cell activation induced by the other receptors.

HIV-1 infection is associated with substantial changes in expression of NKR and NKR ligands. Reduced expression of NKp30 and NKp46 in progressive HIV-1 infection has been shown to impair lytic activity of NK cells. However, HIV-1 infection is also associated with an up-regulation of KIR which has been suggested to rendering NK cells more sensitive to virally infected target cells. Expression of the NKR ligands HLA-A and -B is down-regulated in HIV-1 infection. In contrast, expression of the non-classical HLA-E molecule is increased on HIV-1 infected CD4+ lymphocytes. This might be of special relevance as increased HLA-E expression has been shown to impair antibody dependent cytotoxic activity of NK cells, reduce direct lysis of infected CD4+ lymphocytes by NK cells, and affect cytokine secretion of NK cells, which in turn affects NK cell cross-talk with CD8+ T lymphocytes and dendritic cells.

Overall, HIV-1 infection is associated with perturbations in the expression of NKR, leading to functional abnormalities of NK cells, which possibly contribute to the impairment of innate host defenses in HIV-infected individuals.

The role of dendritic cells in the blood

Schmidt B.1

1Virological Institute, Clinical and Molecular Virology, National Reference Centre for Retroviruses, Erlangen, Germany

Stem cells differentiate into a common myeloid (CMP) and a common lymphoid precursor (CLP). The CMP develops into the tissue-associated institial dendritic cells (DC), the skin-related Langerhans cells, and the pre-DC1 or myeloid dendritic cells (MDC). The latter are mainly localized in the peripheral blood until they migrate to secondary lymphatic tissue and mature into myeloid DC1 after encounter of their specific antigen. The CLP develops into the pre-DC2 or plasmacytoid dendritic cells (PDC), which are depleted from the peripheral blood to the lymph nodes after stimulation and maturation into lymphoid DC2.

Upon stimulation, both DC populations in the blood upregulate the chemokine receptor 7 (CCR7), which binds to the ligands CCL19 and CCL21 expressed on high endothelial venules of lymphatic tissue. The myeloid DC are mainly involved in adaptive immune responses by antigen endocytosis, processing and presentation to naïve T lymphocytes, whereas the lymphoid DC are crucial for innate immune responses. Innate immunity is an evolutionary conserved system which generates a rapid response after recognition of certain molecular patterns, e.g. CpG motifs. In contrast, adaptive immunity is only present in vertebrates and responds to specific epitopes presented in the MHC context. Memory and booster responses are well-known for adaptive, but not innate immunity.

In HIV infection, both numbers and function of PDC as well as MDC are reduced. Recent data indicate that both PDC and MDC can be infected by CXCR4-tropic and in particular CCR5-tropic viruses. Thus, they represent a major HIV-1 reservoir and their migration to lymphatic tissue contributes to HIV dissemination. PDC are the main type 1 interferon (IFN) producing cells in the blood, which upon viral stimulation elicit a Th1-based immune stimulation. IFNs exhibit a strong antiviral capacity in vitro, however the dominant effect in vivo is antiproliferative which prevents a CD4+ cell increase. In addition, IFNs induce an upregulation of CD253 (TRAIL), which enhances the apoptosis of CD4+ cells.
In conclusion, the alteration of innate and adaptive immune responses which result in reduced antigen presentation as well as unspecific immune stimulation appear to be a major factor in HIV-1 pathogenesis.

**F.E.R.7**

Veränderung immunologischer Parameter von akuter zur chronischer HIV-1 Infektion

Streeck H.¹, Altfeld M.¹

¹Partners AIDS Research Center, Massachusetts General Hospital/HMS, Boston, United States of America


**F.E.R.8**

Immunodominance in Primary HIV-1 Infection

Streeck H.¹, Altfeld M.¹

¹Partners AIDS Research Center, Massachusetts General Hospital/HMS, Boston, United States of America

Unter Immunodomination versteht man die Fähigkeit einzelner HLA-abhängiger Immunantworten anderer HLA-abhängiger Immunantworten in ihren Anwesenheit zu unterdrücken. Aktuell ist wenig über den Mechanismus der Immunodominanz bekannt. Ein eingehenderes Verständnis dieses Phänomens ist jedoch in Fragen effektiver Impfstoffentwicklung überaus relevant, da potentiell neben immunologisch irrelevant auch relevante Anteile aktiv supprimiert werden können. Hierbei spielt vor allem die Phase der akuten HIV-1 Infektion eine wichtige Rolle, da hier nicht nur die ersten HIV-spezifischen CD8⁺ T Zellantworten gegen das Virus aufkommen, sondern diese ersten Immunantworten in der Kontrolle der viralen Infektion auch weitaus effektiver zu sein scheinen als neu entstandene Immunantworten zu einem späteren Zeitpunkt im Krankheitsverlauf. In der hier präsentierten Studie wurden über 300 Patienten während der ersten Phase der HIV-1 Infektion auf ihre HLA-abhängigen CD8⁺ T Zellantworten mittels IFN-γ ELispot untersucht. Hierbei konnten klare Immunodominanzmuster einiger HLA Allele über andere HLA Allele nachgewiesen werden. Interessanterweise zeigten besonders die HLA-Typen, die mit einer langsamere Krankheitsprogression assoziiert sind, wie zum Beispiel HLA-B27 und HLA-B57, diesen Effekt. Im Falle von HLA-B27 und –B57 kann die Dominanz dieser HLA Allele auf die Rolle einiger weniger Epitope zurückgeführt werden, die in einer hochkonservierten Region von p24/Gag zu finden sind. Auch wenn andere HLA Allele Epitope in p24 präsentieren und CD8⁺ T Zellantworten gegen diese Region gebildet werden können, entstehen diese meist jedoch nicht während der akuten HIV-1 Infektion.

**F.E.R.9**

Probleme und Lösungswege bei der Erzeugung von breit neutralisierenden Antikörpern gegen HIV

Denner J.¹

¹Robert Koch-Institut, Berlin, Germany

**Fragstellung:** In Anbetracht der hohen Zahl der HIV-Infizierten weltweit und der entsprechenden humanitären und ökonomischen Folgen sowie wissend, dass die gegenwärtigen Kombinationstherapien keine Heilung bieten und mit vielen Nebenwirkungen verbunden sind, ist eine Prävention durch einen Impfstoff dringend erforderlich. Obwohl noch unklar ist, ob eine humorale oder zelluläre Immunantwort zum Schutz vor HIV führen, hat die humorale Immunantwort auf der Basis neutralisierender Antikörper den Vorteil, dass die Infektion von Zellen, in die HIV als DNA-Kopie integriert und lange Zeit persistieren kann, von vornherein verhindert wird. Da das Oberflächenhülprotein gp120 äußerst variabel ist, stellt das konservierte transmembrane Hüllprotein gp41 ein besseres Zielmolekül für die Gewinnung neutralisierender Antikörper dar. Vor mehr als 10 Jahren wurden bei HIV-infizierten zwei Antikörper identifiziert, 2F5 und 4E10, die an hochkonservierte Epitope in der Membran-proximalen externen Region (MPER) von gp41 binden und bis zu 95% aller HIV-Stämme neutralisieren. Als monoklonale Antikörper wurden beide erfolgreich bei passiven Immunisierungen und klinischen Immuntherapien eingesetzt, allerdings, gelang es bisher nicht, derartige Antikörper zu induzieren.


**Schlussfolgerungen:** Diese Daten eröffnen neue Möglichkeiten für die Gewinnung breit neutralisierender Antikörper gegen HIV.
A. Gesellschaftliche Aspekte von HIV und AIDS

A.1 (Vortrag)

High extent of clustering of patients with HIV seroconversion in Hamburg in 2005 and 2006

Noah C.1, Korn K.2, Meyer T.1, Scheewe C.3, Fenske S.3, Plettenberg A.4, Hoffmann C.5, Stellbrink H.-J.6

1IPM (Institute for Immunology, Clinical Pathology, Molecular Medicine), Hamburg, Germany, 2Nationales Referenzzentrum für Retroviren, Erlangen, Germany, 3ICH (Infektionsmedizinisches Centrum Hamburg), Hamburg, Germany, 4IF (Institut für Interdisziplinäre Medizin), Hamburg, Germany

Objective: To assess the relative contribution of clusters of patients with HIV seroconversion regionally in Hamburg in the years 2005 and 2006 and to assess the local prevalence of transmitted resistance as well as of non-B HIV strains.

Methods: Phylogenetic analysis of reverse transcriptase (RT) and protease sequences of subjects with HIV seroconversion diagnosed in a diagnostic laboratory in Hamburg in 2005 and 2006. Seroconversion was defined as a first positive HIV-1 serology with an evolving western blot pattern or a positive HIV-1 PCR in the absence of HIV antibodies or a first positive HIV-1 serology in conjunction with clinical signs and symptoms compatible with acute HIV infection. Subjects were included if a genotypic resistance analysis result was available or if a stored serum or plasma sample was available for genotypic analysis. 39 subjects originating from 16 different physicians fulfilled the inclusion criteria (38 male, 1 female). RT and protease sequences were analysed using BCM Search Launcher and Phylop.

Results: Three definitive clusters were identified, comprising 5, 3, and 2 subjects, respectively. Three additional subjects probably also belonged to a cluster (divergence <1% in RT and 1.1-1.8% in protease). Two subtype C infections had identical protease sequences but 3.3% divergence in RT. NNRTI resistance was detected in 2 subjects, corresponding to a rate of 5.1%. Neither of the resistant strains belonged to a cluster. 4 of the 39 (10.3%) were non-B strains.

Conclusions: In this non-selected group of seroconverting subjects, 10-13 of 39 seroconversions (26-33%) belonged to clusters. This highlights the relatively high contribution of a limited number of virus strains to local virus spread. If resistant strains were involved in these events, they could rapidly gain high prevalence rates.

A.2 (Poster)

Clinical surveillance of HIV (ClinSurv HIV)

Kühne A.1, Kollan C.1, Bärzing-Feigenbaum J.1, Hamouda O.1

1Robert Koch Institut, Infektionsepidemiologie, Berlin, Germany

Background: In 1999 the ClinSurv HIV multicenter cohort was established to collect information on HIV-infected persons treated in major German HIV centres.

Objectives: To assess the number of HIV-patients in clinical care and to monitor demographic characteristics, clinical outcome, antiretroviral regimens and potential risk factors for HIV progression and death over time.

Methods: Currently 17 treatment centres biannually provide anonymous standardised data of patients who attended a treatment centre since January 1st 1999. Data include information on demographics, routes of infection, laboratory parameters (CD4- and CD8-cell counts, viral load), HIV- and AIDS related diagnoses and treatment as well as death cases. All compiled data have been systematically examined for plausibility and completeness by means of a computerised algorithm. Results (Data as of Dec 31st 2005): In total 17,063 patients have been included in the analysis. Among these 10,614 attended a treatment centre the first time after January 1st 1999 (incident patients). Of these 80% were men. When attending a centre for the first time 24% had already suffered from an AIDS defining disease. After the first attendance AIDS defining diseases have been diagnosed the first time in 14.7% of the incident patients. Of 997 patients reported to have died, 29.5% had no documented AIDS-defining disease. 75.2% of all patients received HAART, 82.2% of those on HAART started 1999 or after. At the time of the first documented HAART date the median CD4-cell count was 250 cells/μl, the median viral load 53,000 copies/ml.

Conclusions: The ClinSurv database constitutes an epidemiological basis for long term analysis of HIV patients who are in medical care in Germany providing valuable information about clinical practise outside randomised clinical trials. To improve the research on national HIV epidemiology the database is available for the participating treatment centres. The development and maintenance of this network is able to contribute data for multidisciplinary and multicenter projects.

A.3 (Poster)

Primary resistance and HIV-1 subtypes in Germany (2005-2006)

Knechten H.1, Ranneberg B.2, Ehret R.1, van Lunzen J.3, Fätkenheuer G.4, Klaucke S.5, Mauss S.6, Kirsch M.7, Braun P.1

1FZB Aachen, Aachen, Germany, 2Gilead Sciences, München, Germany, 3UKE, Hamburg, Germany, 4University of Cologne, Köln, Germany, 5Infektiologicum Frankfurt, Frankfurt, Germany, 6Praxisgemeinschaft Düsseldorf, Düsseldorf, Germany

Background: Genotyping in therapy-naive HIV-1 infected patients is strongly recommended by different treatment guidelines, due to prevalence of primary resistance. Purpose of this analysis was to evaluate the prevalence of different subtypes and primary resistance in Germany between 2005 and 2006.

Methods: Genotypes of 265 therapy-naive HIV-1 infected patients were analysed. From May 2005 to August 2006 samples from 37 medical centres from all over Germany were genotyped either with TruGene (Bayer) or ViroSeq (Abbott). Resistance was interpreted via Stanford database, Version 4.2.5 (low level resistant was classified as resistant), and by
following a list of resistance associated mutations proposed by Bennet et al. (13th CROI; 2006). This algorithm classifies mutations as resistance relevant, which meet the following criteria: Mutations should be associated with HIV drug resistance and selected by ART, non-polymorph and applicable to all subtypes. Results of both methods were compared. Non-B subtypes were additionally analysed with NCBI subtype tool.

**Results:** The following subtypes were determined: B (212; 80%), A (6; 2.3%), D (12; 4.5%), C (4; 1.5%), G (2; 0.8%), K (1; 0.4%), CRF02_AG (10; 3.8%), CRF01_AE (10; 3.8%), CRF05_DF (2; 0.8%), CRF06_CPX (2; 0.8%), CRF08 (1; 0.4%), PR:F/RT:B (2; 0.8%) and 14BG (1; 0.4%)(Table 1).

**Conclusion:** In this study the prevalence of primary resistance in Germany is 10.2% (Stanford) or 8.7% (Bennett). The results of the two different algorithms differ slightly, due to the fact that Stanford db regards other additional secondary mutations and thus found more isolates with PI mutations than Bennett. Most resistance mutations were found against NRTIs and least against PIs. 2% of all patients have resistance mutations against more than one drug-class. The analysis of HIV-Subtype becomes more important in Germany, since every fifth patient is infected with HIV non-B subtype.

**A.4 (Poster)**

**Establishing large-scale cohorts in Africa to prepare for HIV vaccine efficacy trials**


**Objectives:** To develop cohorts and collect data on HIV-related risk behaviors, HIV incidence, cohort recruitment and retention for future HIV vaccine efficacy trials.

**Methods:** Since 2004, eight sites in east and southern Africa have developed clinical, laboratory, and counseling capacity to prepare for large-scale HIV vaccine trials in collaboration with IAVI. After providing informed consent, adult, HIV-negative potential trial volunteers are recruited, receive HIV voluntary counseling and testing, and are followed quarterly. Demographic and risk behavior data are collected through structured questionnaires; specimens are collected for HIV-testing. Volunteers who become HIV-infected are followed to collect viral and immunopathogenesis information on early HIV infection. All sites operate according to good clinical and laboratory practices.

**Results:** As of January 2007, 5,615 at-risk volunteers are enrolled: 2,783 (50%) HIV-discordant couples, 1184 (21%) rural residents in high HIV-prevalence area, 178 (3%) men who have sex with men (MSM), and 1,196 (21%) other at-risk participants. With over 8,500 person-years of observation (PY), HIV incidence in sites with more than 100 PY ranged from 1.0 to 11.3 cases/100 PY. Despite shorter duration of follow-up, MSM have the highest incidence, 8.2 cases/100PY. Over 160 volunteers with a documented duration of HIV-infection of less than 385 days are being followed.

**Conclusions:** Eight sites in sub-Saharan Africa have successfully engendered research facilities capable of recruiting thousands of potential volunteers for vaccine clinical trials. The lessons learned from this work will guide the development of upcoming efficacy trials.

**A.5 (Vortrag)**

**Entwicklung von Morbidität und Mortalität in der Frankfurter Kohorte**

*Stephan C.1, Khaykin P.1, Staszew ski S.1, Klauke S.2, Gute P.3, Helm E.B.3*

1HIVCENTER, Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt, Germany, 2IFS Praxis Stresemannallee, Frankfurt, Germany, 3HIV Schwerpunkt-Praxis Friedensstrasse, Frankfurt, Germany

**Ziel:** Identifikation von Trends in der HIV-Epidemiologie anhand einer Kohorte.

**Methodik:** Analyse von Morbiditätsfaktoren und Mortalität bei 9000 HIV-infizierten Patienten der Frankfurter Kohorte ab 1982.


A.6 (Vortrag)
Transmission of drug resistant HIV in Austria

Sarcletti M.1, Sturm G.2, Geit M.3, Rieger A.4, Schmied B.5, Puchhammer-Stöckl E.4, Zangerle R.1

1Medizinische Universität Innsbruck, Innsbruck, Austria, 2Österr. HIV-Kohortenstudie, Innsbruck, Austria, 3AKH Linz, Linz, Austria, 4Medizinische Universität Wien, Wien, Austria, 5OWS Wien, Wien, Austria

Aim of the study: To evaluate the frequency of transmitted drug resistant HIV in patients in Austria.
Method: We analyzed all resistance tests performed until January 1st 2007 in 5 HIV treatment centres in treatment naïve patients. The rate of resistance was calculated by number of patients with resistance mutations divided by the number of patients with a resistance test (genotypic resistance). Mutations were judged as resistant according to Shafer R et al (AIDS 2007, 11:215-23). We divided the patients in two groups: patients with ‘recent infection’ (primary HIV infection or a last negative test within 3 years before the first positive test) and patients with infection of unknown date. For the patients with recent infection the year of infection was obtained by the date of acute HIV infection or the median point in time between negative and positive HIV test. For the patients with infection of unknown date the rate of resistance was plotted against the year of the HIV test.

Results: Of the 4336 HIV infected persons with unknown date of infection 818 had an amplifiable resistance test before antiretroviral therapy; in 102 patients (12,5%) at least one resistance mutation against NRTI or NNRTI or PI could be detected, with the highest rate (17,1%) among those who had their HIV-test in 2002. In the 682 patients with ‘recent infection’ 331 resistance tests were amplifiable and 33 patients (10,0%) had at least one resistance mutation against one drug class. 5,4% of the patients had at least one resistance mutation against NRTIs, 2,4% against NNRTIs and 2,4% against PIs. In 1 patient (0,3%) a virus with resistance mutations against NRTI and PI was transmitted. No transmission of resistance against 3 drug classes was found. Among patients with ‘recent infection’ transmission of resistant HIV occurred in 11,1% of patients in 2001 and since then in about 5% every year.

Conclusions: Transmission of resistant HIV was found more frequently in patients with unknown date of infection compared to patients with ‘recent infection’. Overall, transmission of antiretroviral resistance appears to be stable, if not declining. No three-class transmitted resistance and no difficult to treat cases of transmitted resistance has been observed.

A.7 (Vortrag)
HIV progression and mortality in a community-based cohort in Lusaka, Zambia: gender specific differences

Kitchen M.1, Mwinga A.2, Quigley M.3

1Universitätsklinik Innsbruck, Dermatologie, Innsbruck, Austria, 2UTH, Lusaka, Zambia, 3LSHTM, London, United Kingdom

Background: The growing feminization of AIDS is most apparent in Africa, where UNAIDS estimates that 57% of all individuals living with HIV/AIDS are female. In Africans aged 15-24, women account for 76% of all infections. In this paper we compare HIV progression and mortality in women and men in Zambia.

Methods: 974 HIV-1 seropositive individuals were reviewed every 3 months at the University Teaching Hospital, Lusaka. A social history was taken at recruitment, progression markers (CD4 count, hemoglobin, neopterin) were measured every 6 months. The endpoint of the study was death.

Results: 43% of patients were female. Women tended to be younger than men (mean age 28 vs. 32 years, p<0.001) and were more likely to be widowed, divorced, or separated than men (25% vs. 8%, p<0.001). They were more likely to have no education at all (8% vs. 1%) and less likely to have reached grade 8 (42% vs.66%). At baseline, females had lower hemoglobin levels than men (113g/L vs. 134g/L, p<0.001), there was no difference between the sexes in the other laboratory parameters. During 3138 person-years of follow-up 281 deaths occurred. The crude death rate was slightly higher in women than in men (9.9 vs. 8.4 per 100 person-years), and after adjusting for age this difference was significant (RR 1.29, p<0.05). When stratified by CD4 count, the death rate in patients with CD4 count ≥ 200/μL was significantly higher in women than in men (3.7 vs. 1.2; adjusted risk ratio RR = 4.23, 95% CI 1.38-12.97)), but in patients with CD4 < 200/μL the death rates did not differ significantly. The annual loss of CD4 cells was faster in
women (-36.0/μL vs. -27.1/μL in males, p<0.05). This difference was marked in patients with baseline CD4 counts ≥ 200/μL (-46.4/μL in females and 32.9/μL in males, p<0.05) but was not significant in patients with CD4 counts < 200/μL.

Conclusions: This poorer overall prognosis in women appears to be due to socio-economic factors. Many deaths in women might be unrelated to the HIV infection. Better access to medical facilities and basic drugs could improve survival until antiretroviral treatment will be available for a greater number of HIV-infected Africans.

A.8 (Poster)
The Berlin-Donetsk (Ukraine) co-operation project

Arasteh K.1, Graziadano N.2, Kuzenova O.2, Solodenko K.2, Träder C.1, Banczyk I.1, Weber C.1, Stocker H.1, Müller M.1, Kowol S.1

1Vivantes Auguste-Viktoria-Klinikum, Berlin, Germany,
2Donetsk Regional Aids Center, Donetsk, Ukraine

The Ukraine reports the highest number of annual AIDS deaths in the European Region. The most affected regions in the Ukraine are Dnipropetrovsk, Donetsk, Odessa, Mikolaev and Crimea. Injecting drug use remains the most common mode of HIV-transmission. In the administrative district of Donetsk approx. 250,000 people are infected with HIV (estimated by the Donetsk Regional AIDS-Center). The district has a population of 4.8 Million people.

The Donetsk Regional AIDS-Centre is not capable of providing inpatient care at present. Therefore, the AIDS-Centre cooperates with 20 departments in the field of internal medicine in the district of Donetsk since 1990 in which AIDS-patients can be hospitalized. This cooperation offered many participating physicians the opportunity to gain experience within the treatment of HIV/AIDS.

Since 2002 the Department of Gastroenterology and Infectious Diseases of the Vivantes Auguste Viktoria Hospital in Berlin cooperates with hospitals in Kiew and Odessa in the context of medical exchange programmes. 2003 our department was involved in the elaboration of the WHO guidelines for implementation of HIV/AIDS treatment in the Ukraine. Since the beginning of the cooperation our physicians and nurses have been providing training and education in the field of HIV/AIDS in all regions of Eastern Europe within the framework of the WHO Knowledge Hub.

The initiation of the project took place at the Donetsk AIDS Center in January 2006 during a visit of our delegation. We plan to invite physicians and nurses of the Donetsk Regional AIDS Centre to Berlin for training programmes of 5- or 10-week duration each. The education contents are clinical diagnostic of opportunistic infections, treatment of HIV/AIDS and related diseases as well as HIV health care based on the local resources available in Donetsk.

The centre-periphery structure of the AIDS health care in the district of Donetsk allows for an effective spreading of the acquired know-how and the specialists trained in Berlin are suitable to act as education multipliers in this region.

The project evaluation will be accomplished by a physician and a public health care specialist. The project will be monitored and evaluated by the Public Health Institute Berlin.

A.9 (Poster)
Erhebung und Auswertung von Routinedaten zur Qualitätssicherung der Behandlung HIV-infizierter Patienten

Währmann A.1, Schneisser N.1, Rohlfing F.1

1Medeora GmbH, Köln, Germany

Ziele: Die Diskussion um die Sicherung der Qualität medizinischer Behandlungen nimmt durch die rapide Kostensteigerung im Gesundheitswesen im Allgemeinen, aber auch wegen der hochpreisigen Behandlung HIV-infizierter Patienten im Speziellen stetig zu. Eine unverzichtbare Informationssquelle auf dem Weg zu gesicherter Qualität ist dabei die Auswertung von Daten aus der Behandlungsroutine. Die Nutzung dieser Daten wird dabei durch verschiedene Faktoren wie mangelnde Dokumentation während der Behandlung, schlecht definierte Schnittstellen und inhomogene medizinische Kataloge erschwert.


Ergebnisse/Schlussfolgerung: Die vorgestellte Lösung ermöglicht auf komfortable Weise die Übernahme und Harmonisierung von Daten HIV-infizierter Patienten aus heterogenen Quellsystemen. Eine ausreichende Datenqualität kann durch verschiedene Validierungsfunktionen sichergestellt werden und gestattet so die fundierte Bewertung klinischer Informationen im Rahmen der Qualitätssicherung.

A.10 (Poster)
Dramatic development of the HIV epidemic in Ukraine: Relation of explosive increase and socioeconomic factors in Ukrainian medical society

Tsoukas B.1, Kricheldorff I.1

1Private Universität Witten/Herdecke, Fakultät für Medizin, Witten, Germany

Primary research goal of our survey will be the identification of indicators and trends among medical doctors why the HIV epidemic in Ukraine could reach such dramatic figures.

In 2006 almost 1.4 % of the Ukrainian people where infect- ed with HIV/suffering from AIDS. This number will increase further. Our preliminary work is the establishment of the initiative Students Health Dialogue that we founded in 2004. We established a sufficient peer education program network throughout urban Ukraine. In this process the issue whether the vast spread of HIV in Ukraine was a lack of governmental action or of civil engagement came up. Believing that medical staff plays a key role in public coping with diseases, our interest will aim at physicians.
Method of data collection will be a questionnaire filled out by doctors in Ukraine and Germany. A number of n = 100 in each country is seen to be powerful enough for significance of conclusions. Questions will be e.g. First reported case of HIV in individual commemoration.


Our expectation is the identification of reasons - besides the general problem of a weak health care system and political insecurity - why the HIV epidemic existing in Ukraine has such a severe course.

A.11 (Poster)
HIV und AIDS in der Ukraine - neure Entwicklungen
Alberth F.1
1Connect plus e.V., Augsburg, Germany

Ziele: Informationen über die epidemiologische Entwicklung in der Ukraine

Methodik: Präsentation

Ergebnis: In der Ukraine und in der Russischen Föderation steigen die Neunfektionshäufigkeit o or die Menschen mit HIV und AIDS erfasst, die sich beim Gesundheitsystem registrieren lassen und Kontakt zu den Kliniken oder Ärzten haben. Die antiretroviralen Medikamente sind vorhanden, erreichen jedoch nicht in ausreichendem Maße die Patienten, die dringend eine Therapie brauchen. Die Entwicklung in einem Hochprävalenzgebiet der Ukraine (Odessa) und in einem Niedrigprävalenzgebiet (Lemberg) werden dargestellt und die Reaktion des Staates und der NGO-Landschaft auf diese Herausforderung aufgezeigt.

Verschiedene in- und ausländische Akteure entwickeln auf nationaler und lokaler Ebene Programme. Eine kurze Übersicht zeigt den momentanen Stand dar.

Schlussfolgerung: Connect plus arbeitet seit 6 Jahren in der Qualifizierung von medizinischem und sozial-psychologischen Fachkräften. Projekte, die auch modellhaft übertragen werden können werden vorgestellt.

A.12 (Vortrag)
KABASti-study results: Self reported incidence of bacterial sexually transmitted infections (STIs) in German men who have sex with men (MSM) - influence of HIV serostatus and sexual risk taking
Marcus U., Schmidt A.J., Hamouda O.

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: An increase of STIs in MSM has been reported from many Western industrialised countries in recent years. Repeated behaviour surveys in MSM have demonstrated increasing numbers of sexual partners and declining use of condoms for anal intercourse. To better understand the reasons for increasing rates of STIs in MSM and to identify potential new approaches to STI prevention, a survey on knowledge, attitudes and behaviour as to STIs (KABASti-study) in MSM was conducted in 2006.

Methods: Participants were recruited on German internet MSM contact sites (n=5,928) and country-wide through private medical practices (n=723) with a high proportion of MSM clients. 6,833 completed questionnaires were analysed. Sexually transmitted infections diagnosed in the previous 12 months were assessed.

Results: From all responding participants (n=4,648), 5% each reported a diagnosis of syphilis or urethral gonorrhoea, and 5% a diagnosis of Chlamydia infection. Incidence of these bacterial STIs (bSTI) was significantly higher in HIV positive (HIV+) compared to HIV negative (HIV-) or untested men, as well as in men who reported more than 10 compared to 10 or less partners (OR=4.9; 95%CI:4.0-5.9), and in men who reported 5 or more episodes of unprotected anal intercourse (UAI) compared to less than 5 during the last 12 months (OR=7.3; 95%CI:5.9-9.1). HIV+ men without antiretroviral treatment (ART) reported higher incidences than HIV+ men receiving ART (OR=2.0; 95%CI:1.5-2.7). The highest incidences of bSTIs among HIV+ and HIV- men were reported by participants recruited through a bareback website. After controlling for number of partners and frequency of UAI, HIV+ (OR=2.1; 95%CI:1.3-3.3) and HIV- (OR=2.4; 95%CI:1.5-3.9) men from bareback sites had higher risks of having been diagnosed with bSTI than men recruited from other sites.

Conclusions: Incidence of bSTI is higher in HIV+ than in HIV- MSM. This can be explained by higher number of partners, more unprotected intercourse, less intention to use condoms for prevention of STIs, and formation of high risk sexual networks in which unprotected sex is common. Receiving ART may not only reduce the risk of further HIV transmission, but also the risk for acquisition of STIs by unknown mechanisms.

Study supported by BMG

A.13 (Poster)
Highly variable use of diagnostic methods for sexually transmitted infections – results of a nationwide survey, Germany 2006
Gilsdorf A., Hamouda O., Bremer V.

1Robert Koch-Institut, Abt. für Infektionsepidemiologie, Berlin, Germany

Objective: Syphilis and HIV are the only notifiable sexually transmitted infections (STI) in Germany. Further data for STI are collected through a sentinel surveillance system. The use of diagnostic methods with high sensitivity and specificity are needed for high data quality and early detection. We asked sentinel and other physicians about the current use of diagnostic methods for STIs in order to recognise potential problems and provide recommendations.

Methods: We performed a nationwide cross-sectional survey among randomly chosen physicians with a specialisation in gynaecology, urology and dermato-venerology (DV) as well as sentinel physicians. We asked physicians about the methods and the type of samples used to diagnose HIV, chlamydia (CT), gonorrhoea (GO) and syphilis (SY) and whether they would perform STI testing in asymptomatic patients. The results were stratified by medical speciality.

Results: A total of 691/2228 (31.0%) physicians participated. 80.1% participants offered tests for HIV, 84.0% for CT,
83.1% for GO and 83.5% for syphilis. Of all participants who performed HIV testing, 89.5% ordered an antibody test, 3.2% a rapid test and 1.2% a nucleic acid amplification tests (NAAT). For CT testing, NAAT were used in 33% and rapid tests in 34.0%. Gynaecologists used more often rapid CT tests (48.1% vs. 17.3%; p<0.02) and less often NAAT than other physicians (29.4 vs. 38.0%; p<0.0001). Overall, 33.2% of the participants reported performing GO resistance testing. 98.1% of participants offer SY serology. DV reported more often to do dark-field microscopy than other physicians (42.1% vs. 7.1%; p<0.00001), 65.4%, 33.4% and 65.2% of physicians tested asymptomatic patients for CT, GO and SY. In 53.0%, the reason for testing was antenatal care. There was no difference between sentinel and other physicians.

**Conclusion:** Used diagnostic methods for STI are highly variable among medical specialties. NAAT for CT, GO resistance testing or screening of high-risk patients were rarely part of the daily routine. Physicians should be further trained in STI diagnostics. Diagnostic guidelines of different clinical bodies should be reviewed and harmonised, if needed, to ensure the evidence-based use of the optimal STI diagnostic methods.

**A.14 (Vortrag)**

Sexually transmitted infections (STIs) in west-eastern EU border regions: results of the bordernet sentinel-surveillance

**Jansen K. 1, Gilsdorf A. 1, Steffan E. 2, Hamouda O. 1, Bremer V. 1**

1Robert Koch-Institute, Department for Infectious Disease Epidemiology, Berlin, Germany, 2SPI Research gGmbH, Berlin, Germany

**Objective:** With the EU enlargement new challenges in dealing with STIs have arisen. The border regions between new and old EU-members are characterised by cultural, economic and political differences, also in respect of spreading STIs. Bordernet, an EU-funded project, aims at standardising and improving counselling, diagnosis and therapy of HIV and STIs in 6 involved EU member states. A sentinel surveillance system for HIV and other STIs was set up to monitor trends and the effect of interventions.

**Methods:** A sentinel surveillance system was established in 2005 in four model regions between Germany-Poland (n=2), Austria-Slovak Republic and Italy-Slovenia. Via several questionnaires clinical data regarding Chlamydia (CT), Gonorrhoea (GO), HIV and Syphilis (SY) are gathered from physicians; information on risk of infection, risk behaviour and social background from patients. Monthly number of patients, sex distribution, numbers of examinations and positive tests are reported also.

**Results:** In 2006, 47,350 examinations in 27,782 patients were reported by 60 sentinel sites. Most frequent infection was CT (680 pos. tests), followed by SY (293), GO (243) and HIV (157). HIV (77.8%) and SY (75.7%) were mainly diagnosed in men, CT in women (60.6%). A previous STI was reported for 32.0% of men and 24.7% of women (p<0.01). Proportion of men was 56.5%, mean age 32.2 years. Proportion of migrants was 20.5% in men and 49.5% in women (p<0.01). 66.4% of migrants originated from Central Europe. Most important risks of infection in men were sex with men (37.8%) and heterosexual contacts (32.7%), in women commercial sex work (41.6%) and heterosexual contacts (37.7%). 78.8% of commercial sex workers were migrants. A non regular condom use with casual sex partners was stated by 39.9% of men and 29.8% of women.

**Discussion:** Already in its first year, important epidemiological data were gained which are not represented by the national reporting systems. Migration and prostitution turned out as highly relevant influencing factors for epidemiological events within the specific border regions, especially in women. Some of the results were already implemented within the scope of the overall project Bordernet as a basis for planning in prevention and for improvement of diagnostics of STIs.

**A.15 (Vortrag)**

KABaSTI-study results: Regional differences in sexual risk behaviour, incidence of sexually transmitted infections (STIs) and HIV prevalence in an internet-recruited sample of German men who have sex with men (MSM)

**Schmidt A.J. 1, Marcus U. 1, Voss L. 1, Hamouda O. 1**

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

**Objectives:** Incidence and prevalence of diagnosed HIV infections and other STIs in MSM are usually related to total population or specified age groups. However, MSM are not equally distributed in the population, but are concentrated in larger cities. Since MSM population distribution is usually unknown, it is difficult to define the relative incidence and prevalence of STI and HIV in this population.

**Methods:** An internet survey on knowledge, attitudes and behaviour of German MSM as to sexually transmitted infections (KABaSTI-study; n=5,928) collected data on residence (first two digits of the postal code), HIV serostatus, STI history, and sexual risk taking. In a first step, the particular geographical distributions of survey participants and the general adult population (20-50 years old) were compared to find out where MSM concentrate. Then, the respective geographical distribution of men positive for HIV or with a history of syphilis in the previous 12 months (both from survey and routine surveillance data) was related to the regional distribution of MSM.

**Results:** The highest concentrations of MSM (factor 2 to 7 times higher than expected if assumed that MSM represent a constant proportion of the general population) are found in the centres of Germany’s 5 largest cities (Berlin, Hamburg, Munich, Cologne, Frankfurt). Geographical distribution of HIV prevalence as determined by either survey or routine (2nd and 1st generation) surveillance data are very similar. Syphilis incidence distribution shows larger variation, probably due to a relatively small number of reported infections in the internet survey. HIV prevalence and syphilis incidence in cities with the highest concentration of MSM again are about 2-fold higher than to be expected from MSM distribution as calculated above. Also, the proportion of men reporting frequent (>4) episodes of unprotected anal intercourse with a partner of unknown HIV status in the previous year is significantly higher in larger cities (>500,000 inhabitants; OR=1.7;95%CI: 1.4-2.2).

**Conclusions:** Taking into account the distorted MSM population, “risk maps” for MSM can be constructed on the basis of internet surveillance data. These “maps” may help to target and prioritize prevention activities.

KABaSTI-study was supported by BMG
**A.16 (Poster)**

The bordernet sentinel-surveillance: Experiences in building up an international reporting system for sexually transmitted infections (STIs)

*Jansen K.1, Gildorf A.1, Steffen E.2, Hamouda O.1, Bremer V.1*

1Robert Koch-Institute, Department for Infectious Disease Epidemiology, Berlin, Germany, 2SPI Research gGmbH, Berlin, Germany

**Objective:** Bordernet, an EU-funded project, aims at standardising and improving counselling, diagnosis and therapy of HIV/AIDS and STIs in 6 involved EU member states. A sentinel-surveillance system for STIs has been established to provide a solid data basis for developing new approaches in these fields as well as for monitoring their success.

**Methods:** In four model regions between Germany (G) - Poland (Poster) (n=2), Austria (A) -Slovak Republic (SK) and Italy (I) –Slovenia (SI), an international sentinel surveillance system was established in 2005. Data are gathered via monthly, diagnosis and (voluntary) patient questionnaires.

**Results:** By now, the surveillance-system consists of 60 sentinel sites which reported 47,350 examinations in 27,782 patients in 2006. There are 15 resp. 11 sites in the 2 regions in G, 2 in each region in P, 10 in A, 12 in SK, 6 in I and 2 in SI. In G and A, private practitioners and public health care institutions are represented equally, in all other regions sites are public. 20 sites only test for HIV, 13 only for other STIs.

Response rates of patients qu. were very high in I (92.3%), P (96.0%), SK (98.5%) and SI (100%), much lower in G (24.7%) and A (17.6%) (p<0.01). Obligatory case definitions for Chlamydia based on amplification methods were applied at 11/11 sentinel sites testing for Chlamydia in A, 5/21 in G, 1/4 in I, 0/1 in P, 3/7 in SK and 0/0 in SI.

**Discussion:** Building up a cross-border sentinel surveillance is challenging. Population density, national health systems, number of potential and recruited sentinel sites and repeating completeness vary greatly. Frequent separation of diagnostics and treatment of HIV and other STIs cause underdiagnosing and underreporting. Different resources in diagnostics and treatment hampered the use of standardised case definitions. The high response rates of patient qu. of countries with solely public health care institutions as sentinel sites and other countries must be questioned.

Comparison of epidemiological data between different countries is laborious. However, this study provides much more information than national reporting systems, espec. regarding border specific phenomena like prostitution and migration. It is a big step for developing health care efforts in the participating regions.

**A.17 (Poster)**

High seroprevalence of Herpes simplex virus typ 2 in HIV-1 infected men

*Müller M.1, Enders M.2, Ulmer A.1*

1Praxis Ulmer, Frietsch, Müller, Stuttgart, Germany, 2Labor Prof. Enders und Partner, Stuttgart, Germany

**Background:** Genital Herpes simplex Virus Typ 2 (HSV-2) infection increases the risk of HIV-1 transmission.

**Methods:** HSV type-specific IgG antibodies were determined in a cohort of HIV-1 infected male outpatients by a commercial immunoblot assay. Information on general demographic factors, sexual behavior, intravenous drug use (IVDU), previous clinical episodes of herpes simplex, and the knowledge about genital herpes as a potential risk factor for HIV infection was obtained by interview.

**Results:** In total 215 patients agreed to be investigated. The HSV-2 seroprevalence of the cohort in total was 47.7%, 52.1% (62/119) in men who have sex with men (MSM), 51.1% (24/47) in heterosexual men, 10.7% (3/28) in patients, who were infected by intravenous drug use and 61.9% (13/21) in another heterogeneous subgroup including 11 patients of African origin. The HSV-2 seropositivity was lower in the IVDU subgroup (p=0.0001, Likelihood-Ratio-Test), and increased significantly with age in all subgroups. In total, 113 patients reported at least one clinical episode of Herpes - infection. The manifestation site was in 2.7 % of the patients perianal (3/3 patients HSV-2 antibody positive), in 19.5 % genital (21/22 patients HSV-2 antibody positive) and in 81.4 % perioral (42/52 patients HSV-2 antibody positive). Only 3 of 215 patients were aware, that genital herpes is associated with a higher risk for HIV transmission.

**Conclusions:** The HSV-2 seroprevalence is considerably higher in HIV-infected men compared to the general population in Germany. HSV-2 seropositivity differs not between MSM and heterosexual men. Most HIV-1 positive men with HSV-2 infection do not remember a clinical episode of genital herpes. The synergistic effect of genital herpes on HIV transmission is largely unknown. Patients from risk groups should be offered additional HSV type-specific testing and counselling on possible prevention and treatment options.

**A.18 (Poster)**

Turkish migrant women in Vienna and HIV prevention

*Kilaf E.1*

1Stadt Wien, Integrations- und Diversitätsangelegenheiten, Wien, Austria

**Background:** The objective of the study was to observe the knowledge about sexually transmitted diseases from the perspective of socio-economic and integration in relation to ethnic Turkish women living in Vienna, Austria.

**Method:** Data was collected by using an open and closed questionnaire, as a part of the Turkish Migration to Austria and Women’s Health Study 2003. The interview partners (n=145 between 15 and 56 years of age, with a mean age of 31) of this study were met at two different types of organizations as well as house visits. These two types of organizations were namely religious and governmental facilities. The interviews were made during the day, so full time workers could not be included in the survey.

**Results:** The ethnic Turkish women reported a poor knowledge about the sexually transmitted diseases (45.8% Hepatitis and 42.4% HIV/AIDS). Interestingly, the older the women are the more they knew about the HIV (35.9% to 51.7%) whereas the knowledge about Hepatitis does not show any pattern in any age relation. The spent years in Vienna shows the more the women have been living in Vienna the more they knew about HIV if the educational level is ignored. Higher the educational level is the more women reported knowledge about sexually transmitted diseases. This is also true for German knowledge and annual check-up, where the socio-economic conditions were inversely related to self-rated health.
Conclusion: Socio-economic status have an impact on knowledge about health and as expected integrated (well German speaking) women are observed to be also integrated into the health system; they knew more about the illnesses. The most important challenge for AIDS prevention is to spread intensively the knowledge about AIDS and for better results in the mother language of migrants.

A.19 (Poster)

Prevalence of Neurosyphilis (NSI) diagnosed by Cerebrospinal Fluid (CSF) and clinical neurological examinations in HIV-positive patients with primary or secondary infectious Syphilis (SI) and CSF-repuncture for therapy control after treatment

Esser S.1, Jablonka R.1, Körber A.1, Ross B.1, Obermann M.2, Hagedorn H.J.3, Grabbe S.1

1Universitätsklinikum Essen, Dermatologie und Venerologie, Essen, Germany, 2Universitätsklinikum Essen, Neurologie, Essen, Germany, 3Medizin-Untersuchungsstelle im Regierungsbezirk Detmold, Konsiliarlabor Dr. Krone & Partner, Herford, Germany

Objectives: Since 2000 prevalence of SI increased in Germany. SI cases showed rapid progression of SI to NSI and therapy failure in HIV-infected patients. The aim of the study is to evaluate signs for NSI in CSF in patients with co-infection of SI and HIV from January 2000 till February 2006.

Methods: This prospective ongoing study included HIV-positive Patients with serological (TPHA, VDRL, IgM Western Blot) and clinical diagnosed primary or secondary SI. Neurological examinations and CSF puncture were performed and repuncture 12 months after treatment (TPHA, TPHA ratio, FTA-ABS-19s-IgM, blood-CSF-barrier).

Results: 94% of the 47 male patients (CDC WHO stage A 17%, B 68%, C 15%; mean age 37 yrs) were described as men who have sex with men, three were heterosexual. Mean CD4-cell count was 469/μl (range 81-1164) and mean HIV-RNA 48497 copies/ml (range 50-500000). 31 (66%) patients were treated with antiretroviral therapy. Nine patients (19%) showed infectious seropositive SI without dermatological symptoms and 35 (74%) showed makulo-papular exanthema. All IgM-Western Blots were positive. Mean TPHA was 1:1299885 (range 1:1280-1:41943040), mean VDRL 1:634 (1:1-1:8192), Mean CSF-TPHA was 1:387 (range 1:2-1:8192), in repuncture of actual 13 patients 1:32 (range 0-1:128). Nine (19%) patients had a positive FTA-ABS-19s-IgM in CSF. Neurological symptoms were verified by a neurologist in three patients. At least a neurological attendance of SI was diagnosed in seven cases (15%) followed by intravenous Penicillin G therapy for 21 days. The others got intramuscularly treatment with Benzathinpenicillin for 14 days. In repuncture one year after treatment neither treatment failure nor positive CSF-FTA-ABS-19s-IgM titer was observed after therapy.

Conclusions: 15 % of the HIV-positive patients with infectious SI had signs of early NSI. No treatment failure was observed in repuncture. This survey shows increased risk of NSI in HIV-Infected patients but obviously no treatment failure after sufficient therapy.

A.20 (Poster)

Impact of GB virus-C co-infection and quality of life in a cohort of HIV infected patients in a private clinic in Germany
Kaiser T.1, Kahmann B.2, Holm S.2, Weimann M.2, Stoll M.3, Tillmann H.L.1

1Universitätsklinikum Leipzig, Medizinische Klinik & Poliklinik II, Leipzig, Germany, 2Internistische Gemeinschaftspraxis Georgstraße, Hannover, Germany, 3Medizinische Hochschule Hannover, Klinische Immunologie, Hannover, Germany

Objective: GB Virus C is a non-pathogenic Flavivirus genetically closely related to the Hepatitis C Virus, which was found in relation to a better clinical course of infected HIV-patients in the pre-HAART era. Aim of this study was to investigate the effect on the HIV viral load, CD4 and CD8 cells and also the quality of life in a cross sectional patient cohort from a private clinic in Germany in HAART era.

Methods: 248 patients were analysed for HIV and GBV-C viral load, CD4 and CD8 cells. In addition, quality of life has been evaluated in 115 cases by using the SEL questionnaire and analysed in relation to GBV-C status.

Results: There was a trend though not significant towards better results for HIV-viral load, CD4 and CD8 cells in the GBV-C positive patients. Although not reaching the level of significance in this study, the positive trend was the same in whatever sub analysis performed.

Likewise, the quality of life was better, though not significantly, for GBV-C co-infected patients. Limiting the analysis to patients not yet receiving HAART showed even significant better QoL for GBV-C viraemic patients (p=0.039).

Discussion: The availability of HAART seems to diminish but not eliminate GBV-C’s role in slower disease progression and better quality of life in HIV infected patients.

Key words: GBV-C, HGV, HIV, co-infection, QoL, quality of life.

A.21 (Vortrag)

KABaSTI-study results: Barebacking among German men who have sex with men (MSM) - risk reduction intentions and practice
Marcus U.1, Schmidt A.J.1, Hamouda O.1

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: During the last decade “barebacking” (intentional non-use of condoms for anal intercourse with casual partners in MSM) has become increasingly popular. There has been no study on sexual risk behaviour and risk management strategies in MSM with bareback identities in Germany so far.

Methods: Within a larger internet survey on knowledge, attitudes, and behaviour of German MSM as to sexually transmitted infections, we analysed reported sexual risk behaviour and risk management intentions of survey participants recruited on bareback websites (BBW) compared to participants recruited on other websites (OW).

Results: BBW (n=564) were significantly older (77% vs. 59% older than 30 years), had been tested for HIV more frequently (91% vs. 67%), a much higher proportion was HIV positive (59% vs. 10%), and were living more often in metropolitan areas (37% vs. 24%) than OW (n=5364). BBW report-
ed more sex partners in the previous 12 months (61% vs. 25% with >10 partners), and a higher proportion of unprotected anal intercourse with anonymous partners than OW (71% vs. 30%). BBW met a larger proportion of partners via offline-cruising than OW (56% vs. 47%). Asked, under which conditions they would skip condom use for anal intercourse, the predominant reason given by HIV positive as well as HIV negative BBW was HIV seroconversion, followed by strategic positioning, and the decision of the partner not to insist on condom use. Asked for the reason for non-use of a condom during the last episode of UAI with a casual partner, the most frequent reasons were erection problems (31%), feeling that condom use would have been disruptive (30%), partner decision (27%), knowledge/assumption that during this specific episode UAI would not involve HIV transmission risk (26%), and unavailability of a condom (12%).

Conclusions: On the intentional level, “barebacking” seems to be predominantly serosorting. However, it remains unclear, how effective and how reliable HIV serostatus disclosure takes place. Situational factors not directly related to disclosure of HIV serostatus are frequently reported as reasons for non-use of condoms. Particularly questionable is the efficiency of serosorting with anonymous casual partners.

Study was supported by BGH

A.22 (Poster)

HIV-Postexpositionsprophylaxe (PEP) nach sexueller Exposition: Information und Beratung zu jeder Tages- und Nachtzeit

Lemmen K.1, Gekeler C.1

1Deutsche AIDS-Hilfe e.V., Psychosoziales und Qualitätsentwicklung, Berlin, Germany


A.23 (Vortrag)

Combating Syphilis in Vienna with information and promoting testing

Zagler C.1, Amort F.M.2

1SMZ Otto-Wagner-Spital, Wien, Austria, 2Aids Hilfe Wien, Prävention, Wien, Austria

Objective: Europe has seen an increase of new HIV-infections and the return of Syphilis infections especially within the gay communities in different European capital cities over the last years. Vienna has seen a Syphilis outbreak in 2002, however no specific data for MSM are available. Nevertheless experts agreed that specific information should be spread and that free and anonymous Syphilis testing should be offered to the gay community.

Method: The organisation Homed developed an information campaign using the iconography of the TV series “Sex and the city”. The motives were available as posters, postcards and on the internet site www.syphilis.at. The homepage offers a FAQ-section and e-mail counselling regarding Syphilis is offered. Aids Hilfe Wien as logistic partner of this project distributed 500 cruising packs with free condoms and lubricant and the informative postcard from July 2006 till October 2006 per week, reaching in total 10.000 face-to face contacts. In October the free and anonymous testing offer was established on 3 days per week for 12 hours per week. All of this activities were accompanied by comprehensive information activities using existing resources (e.g. online prevention, internet, ...)

Results: Through the comprehensive activities the access to the information related to Syphilis, 2000 persons visited the homepage www.syphilis.at, weekly e-mails with questions regarding Syphilis were answered. With outreach activities 10.000 face to face contacts were attained and since October 2006 monthly 40-50 MSM showed up for free and anonymous testing. A review of the first 150 men using this service showed that 5,36% of all tests were reactive towards Syphilis and that 7,38% of the sample were diagnosed as HIV-positiv.

Conclusion: It was observed that MSM are very thankful for information regarding Syphilis. The campaign could easily be transferred to other cities as its iconography is known all over Europe. Furthermore it was shown that the need of regular testing has to be promoted more offensively and should be included in the promotion of HIV-testing as it seems yet to be standardised handling in the health promotion of MSM. Beside the achieved successes, further activities are needed.

A.24 (Poster)

2 years of students health dialogue - first results of a German-Ukrainian prevention campaign by medical students

Doll H.1, Dahmen J.1

1Universität Witten/Herdecke, Students Health Dialogue, Witten, Germany

Objective: The rate of HIV/AIDS infections in Ukraine is one of the highest in Europe with almost 1,4% of the adult
population, aged 15-49 years, representing a number of 410,000 HIV-carriers (Estimate, UNAIDS/WHO 2006). The epidemic has evolved from a specialized problem of vulnerable groups (IDUs, men having sex with men, sex workers) to a generalised epidemic affecting all social ranks and ages. HIV/AIDS prevention campaigns in the Ukraine are insufficient. Social ignorance and stigma are detectable towards people living with HIV/AIDS (PLWAH).

Methods: The first fact-finding tour took place in 2004. Contacts with Ukrainian students were established. In 2005 the Students Health Dialogue (SHD) signed a contract with the IFMSA Ukraine (International Federation of Medical Students Association) to build up and adopt HIV/AIDS prevention in the Ukraine. German and Ukrainian students developed the concept at the first German-Ukrainian peer-education conference at the University Witten/Herdecke including a first 3-phase model and a peer-to-peer education program.

Results: In a first step Ukrainian students who visited the conference trained 45 trainers from 5 different faculties in Kiev. The second phase included peer education training in schools and universities. Over 800 pupils and students could be educated in HIV/AIDS prevention until the end of December 2006. In a third phase a group of 6 SHD-activists visited the local projects, took part in prevention courses and gathered facts about the prevention campaigning. Evaluation protocols of the former phases with the development and adoption facts about the prevention campaigning. Evaluation protocols of the former phases with the development and adoption of the HIV/AIDS prevention campaign in the Ukraine are in progress. A train-the-trainers workshop is planned in Charkiv in April 2007.

Conclusions: Further faculties are invited to participate and more trainers are to be educated to generalise HIV/AIDS prevention campaigning by international student coalitions. Peer-organised prevention campaigns are a very important part of sexual health education and availability should be widened. Further research on outcome, evaluation and cultural adoption should be done.

A.25 (Poster)
Empowerment in der HIV/STD Prävention durch Peer Education und Labeling am Beispiel von DARKANGEL im realen und virtuellen Raum
de Witt R.

Allgemein wird eine Tendenz zu mehr unsafem Sex bei Männern, die Sex mit Männern haben (MSM) festgestellt (so genannte „Kondommäßigkeit“). Erfolgreiche Primärprävention muss einen positiven Gegentrend setzen.

Fragstellung: Führt die Einführung eines „Labels“ und eines Markennamen für „Safer Sex“ zu Empowerment bei der Zielgruppe?

Methode: Projekt DARKANGEL

Ziel: MSM, die Safer Sex praktizieren unterstützen und stärken. Sichtbar machen von Safer Sex praktizierender (Statement). Gegengewicht zum proklamierten Trend „unsafem Sex“.

5 Phasen:
1. Postkarten, T-Shirts, Leuchtsticker „Safe Tonight“, eigene „Cruising-Packs“ (Gleitgel und Kondom) werden produziert. Sowie ein „Vertrag“, den der zukünftige DARKANGEL ausfüllt. Inhalt: Ja, ich will DARKANGEL sein
2. Ich werde andere akzeptieren
3. auch wenn sie anderer Meinung sind
4. meine Überzeugungen nicht teilen
5. keine Gespräche wollen

Nach Unterzeichnung erhält man „Cruising Packs“ und Sticker „Safe Tonight“. Die Leuchtsticker können beim „Cruisen“ (suche von sexuellen Kontakten), getragen werden. Aussage: „Mit mir nur Safer Sex.“

2. gayromeo, ein Chatportal, wird für eine Zusammenarbeit gewonnen. Userprofile, einer Art Visitenkarte, können mit einem DARKANGEL Button versehen werden. Aussage: „Mit mir nur Safer Sex.“

3. Internetseite www.DARKANGEL.eu
   - Möglichkeit der Online-Registrierung
   - Vertrag direkt abrufbar
   - wird online ausgefüllt und versandt
   - nach Reaktion auf eine Bestätigungsmail ist man DARKANGEL und bekommt sein „Starter Pack“(s.o.).

4. DARKANGEL-Club bei gayromeo
   - Club News
   - Forum: Diskussionsmöglichkeit zu Safer Sex (peer-to-peer).

5. Newsletter

Ergebnis: Online-Label bei „gayromeo:
   - innerhalb eines Jahres über 85.000 Nutzer
   - Möglichkeit der Online-Label bei „gayromeo: erreich so Empowerment für die 70% der MSM, die nach wie vor grundsätzlich Safer Sex wollen.

A.26 (Poster)
Lust or trust? Adolescents’ sexual risk behaviour – a project overview

Brunner E.1, Brunner C.1, Kada O.1, Jenull-Schiefer B.1

1Alpen-Adria-Universität Klagenfurt, Institut für Psychologie, Abteilung für Angewandte Psychologie und Methodenforschung, Klagenfurt, Austria

Objective: Health psychology uses social cognitive models (Schwarzer, 2004) to explain risky behaviours such as defaulted condom use. These models emphasise the role of rationality in the decision for or against a condom. Emotional and interactive components are neglected. Sexuality is characterised by complex emotional events, usually experienced in a dyadic setting (Pant, 2005). Therefore the project “Lust or trust?” highlights emotions and interactive aspects like communication besides rational components.

Methods: The project consists of six studies: Experts (n = 7) were interviewed regarding the preventive landscape and youth sex education in Austria. Using questionnaires adolescents were asked for their motives for and against condom use (N = 175) and for their emotional experiences regarding their first and last sexual intercourse (N = 144). Two interview studies were conducted – one, investigating girls’ emotional experiences before, during and after the first sexual intercourse (n = 32), and another exploring interactive components in casual sex encounters (n = 30). At last 1089 Carinthian adolescents were surveyed considering variables such as con-
Jährlicher Vor-Ort-Überblick

Inhalt des SE-Standards: Kondome, Gleitmittel und ggfls. Methoden:

- Durch das kostenlose und am Ort des sexuellen Geschehens in allen schwulen Betrieben, die ihren Gästen die Zugängliche Präventionsmaterial (Kondome, Latexhandschuhe) soll der Einzelne in seinem Schutzverhalten verbessern und unterstützen. Fortschreibung der Verantwortungsbewusstsein der Betreiber unterstützt werden und sich auch in persönlich schwierigen Situationen, leichter für den Schutz entscheiden können.

Schlussfolgerung: Die Erfahrung zeigt, dass die Betreiber im Rahmen einer public-private Partnership zur Etablierung des SE-Standards motiviert werden können, es aber auch der Kontrolle bedarf, damit die dargestellten Verpflichtungen eingehalten werden. Fortentwicklung von SE zu einem allgemeinen Präventionsstandard in Deutschland und Europa.

A.27 (Poster)

"Safe Environment" (SE) - Eine ständige Erinnerung in schwulen Unternehmen Safer Sex zu praktizieren

Ehrlé F.-J.¹, Engel H.¹

¹AK AIDS Köln e.V., Köln, Germany

SE wurde initiiert durch die AIDS-Koordination des Gesundheitsamtes in Zusammenarbeit mit dem AK AIDS Köln e.V.

Ziele:

- der seit 2001 steigenden HIV-Infektionsrate bei MSM gegensteuern
- In allen schwulen Betrieben, die ihren Gästen die Möglichkeit zum Sex-Vor-Ort bieten (Bars mit Darkrooms, Saunen etc) durch Verbesserung/Standardisierung der AIDS- und STD-Prävention in diesen Betrieben ein SE zu schaffen
- Bedingt durch HAART hat AIDS seinen Schrecken vielerorts verloren und zu einem Nachlassen der Prävention geführt, während die Möglichkeiten zur sexuellen Begegnung in kommerziellen Rahmen sich beständig erweitern. SE setzt einen ständigen unbewusst wirkenden Erinnerungsimpuls an das Vorhandensein von AIDS und die Notwendigkeit von Safer Sex
- Durch das kostenlose und am Ort des sexuellen Geschehens zugängliche Präventionsmaterial (Kondome, Gleitgel, Latexhandschuhe) soll der Einzelne in seinem Schutzverhalten unterstützt werden und sich auch in persönlich schwierigen Situationen, leichter für den Schutz entscheiden können.

Methoden:

- Implementierung des SE-Standards in den oben genannten schwulen Betrieben durch Gespräche mit den Betreibern
- Inhalt des SE-Standards: Kondome, Gleitmittel und ggfls. Latexhandschuhe werden kostenlos via Spender unmittelbar am Ort des sexuellen Geschehens zur Verfügung gestellt. Aushang/Auslage von Präventionsplakaten/-broschüren zu HIV und STDs jährliche Fortbildung des Personals zum Themenkreis HIV/STDs
- Jährlicher Vor-Ort-Überblick

- Betriebe, die die SE-Standards erfüllen, erhalten vom Gesundheitsamt ein Gütesiegel

Ergebnis: Die Umsetzung von SE in der schwulen Szene ist möglich und wird von Gästen gut angenommen.

Practise of HIV post-exposure-prophylaxis in a HIV-specialized clinic in Berlin

Rittweger M.¹, Masuhr A.¹, Schulbin H.¹, Arastéh K.¹

¹Vivantes Auguste-Viktoria-Klinikum, Klinik für Innere Medizin - Infektiologie, Berlin, Germany

Objective: Guidelines help in the assessment of the indication for PEP, even though the application is often limited due to the unique setting of cases and frequently missing or incomplete information about the index-person (IP).

Methods: Presented is a retrospective analysis of consultations after potential exposure to HIV in occupational and non-occupational settings to assess the application of the guidelines for PEP, the availability of information on the IP and their influence in the PEP-recommendation.

Results: From 08/2005 to 12/2006 145 consultations for PEP were documented: 64 cases of occupational exposure (oPEP) and 81 cases of non-occupational exposure (nPEP). Indication for PEP was assessed according to the german-austrian guidelines for PEP. Information about the IP for oPEP was available in 53 cases. Indication for PEP was given in 38 cases, in 2 cases PEP was started without indication according to the guidelines. No information about the IP was available in 11 cases, for which in 4 cases potential of HIV exposure was given. 3 of these exposed persons decided against PEP. In the 41 cases of oPEP 27 patients received standard PEP and 14 patients received PEP divergent to the ART of the IP. Prior HIV-Genotypes where available only in 11/64 cases and led only in 4 cases to an adjusted PEP. In 3 cases additional Enfuvirtide for 5 days was applied in a setting of high risk and IPs with multiple resistant HIV. Information about the IP was available in 43 cases of 81 consultations for nPEP. An indication for PEP was assessed in 50 cases, 2 patients did not to start PEP, 1 patient started PEP without clear indication. Of 49 patients starting PEP 39 received standard PEP due to incomplete or missing information about the IP. In 10 cases a divergent PEP was recommended where information about the ART of the IP was available.

Conclusions: The guidelines for PEP were frequently applied in the recommendation and application of PEP. When PEP was indicated, almost all patients started PEP. In most cases standard PEP was applied due to missing or incomplete information about the IP. When information on current ART and prior resistance was available mostly a divergent PEP regimen was chosen.
A.29 (Poster)

BORDERNET- cross border cooperation in HIV/AIDS and STI prevention, diagnostic and therapy

Steffan E.1, Arsova-Netzelmann T.1
1SPI Forschung gGmbH, Berlin, Germany

Objectives: BORDERNET aims to enhance HIV/AIDS and STI-Prevention, diagnostic and therapy in regions across the old and the current EC-outer borders, funded by the EU, MOH Germany etc. BORDERNET takes into consideration the specific differences in cultural, legal and social aspects and the regional distinctions of border regions. The project operates in four cross-border model regions, connecting Germany and Poland, Austria and the Slovak Republic, Italy and Slovenia.

Methods: The project addresses relevant agents in the field of HIV and STI prevention, diagnostic and therapy. The cooperation is based on regional interdisciplinary networks to strengthen capacity building, prevention measures, collection of epidemiological data, improvement of STI diagnostic and counselling offers and carry out of KAB surveys outlining sexual risk indicators and prevention potentials among special target groups.

Results: Cross-border networks create synergy effects beyond the concerned regions. In the KAB-Surveys around 1700 persons from 6 countries were questioned. The results delivered insights into the specific risk related contexts regarding mobility, sexual risk behavior, access and utilisation of HIV/STI services. The Sentinel Surveillance on STI provides important knowledge about the state of diagnostic offers and the epidemiological development in the model regions. In order to improve services’ accessibility and quality, additional pilot diagnostic offers especially for hard to reach groups and uninsured persons were established.

Discussion: In all the model regions a necessary integration or at least a harmonisation of the existing HIV/AIDS prevention and diagnostic offers on the one side and the STI offers on the other should be attempted out of efficiency reasons. The integration of STI into a holistic concept of “Sexual Health” is of particular importance in the whole of Europe, especially for (young) women. The considerable deficiencies in STI diagnostic in all the participating model regions lead to an under-registration of STI. The assessed approaches in HIV Voluntary Counselling and Testing (VCT) highlighted some quality discrepancies and should be improved through the introduction of uniform VCT quality standards.

A.30 (Poster)

"Love knows no boundaries": a project by migrants for migrants in the prevention of sexually transmitted diseases (STD)

Traub U.1, Körber J.2, Schmolz G.3
1County Health Department, Ludwigsburg, Germany, 2State Health Department, Stuttgart, Germany, 3currently State Health Department, Stuttgart, Germany

The incidence of STD is increasing amongst young migrants. Informative media in their own language that appeal to migrants is scarce in Germany.

Objective: To increase awareness about STD in school children and young adults from Turkey and Russia.

Methods: A physician from the Health Department trained pupils from two schools using several self-developed, interactive games. Turkish and Russian pupils developed media for use in migrant populations.

Results: Six posters and flyers dealing with different STDs were designed and printed in Russian. Language and pictures were selected by pupils for their own age group. A Turkish DVD featuring pupils and a representative from the Turkish consulate was produced. There are short sequences on Chlamydia, Herpes, Hepatitis etc based on day-to-day situations at school. The media were distributed to over 100 schools and youth centres all over Germany. The participating pupils and initial schools were questioned on the impact of the project.

Conclusions: Media developed by pupils from migrant families for other migrants are very effective in improving knowledge about STD. The actively involved pupils gained tremendous self confidence. There is further demand for similar sources of information in other languages.

A.31 (Poster)

Condom use self-efficacy: Global or specific measuring?

Brunner E.1, Jenull-Schiefer B.1
1Alpen-Adria-Universität Klagenfurt, Institut für Psychologie, Abteilung für Angewandte Psychologie und Methodenforschung, Klagenfurt, Austria

Objective: Self-efficacy means subjective perception of one’s competence to show certain behaviour (Bandura, 1977, 1990) and is a core determinant of health behaviour. Research has shown that the use of health-specific self-efficacy scales leads to a better prediction of health behaviour than the use of scales which measure only global self-efficacy (Brunner, 2006; Schwarzer, 2004). Therefore, it is essential to develop specific measuring methods subject to the investigated health behaviour (Farmer & Meston, 2006).

Methods: One of the studies of the project "Lust or trust? Adolescent sexual risk taking" investigates condom use self-efficacy as a determinant of sexual risk behaviour. 1089 pupils and students of Carinthia, Austria were surveyed using a questionnaire about; condom use, intention to use a condom, emotional experiences regarding intercourse, self-efficacy etc. On the one hand, the questionnaire asked about the global condom use self-efficacy (one item asking for the ability to use a condom in general). On the other hand, it asked about the ability to use a condom in different specific situations (specific condom use self-efficacy; seven items; e.g. the ability to use a condom if the person is intoxicated, sexually aroused, or in love).

Results: A factor analysis was conducted to identify the structure of the seven items, asking for specific condom use self-efficacy. One factor forms the basis of the seven items; with a Cronbach’s Alpha of $\alpha = .78$ the scale shows a satisfying reliability. As expected, the correlation between the specific condom use self-efficacy and the global condom use self-efficacy is positive ($r = .57$, $p = .000$). Regression analysis pointed out that the specific condom use self-efficacy is a better predictor of condom use than the global condom use self-efficacy.

Conclusions: The investigation of health behaviour requires specific self-efficacy scales. Asking about subjective perception of one’s competence, in using a condom in different situ-
search about HIV-protection behaviour of male sex workers

Objective: In Austria the latest study investigating sexuality in a broad way was conducted in the late 90ies (Ludwig Boltzmann-Institut für Frauenforschung, 1997). Due to the increasing number of STDs in young people (UNAIDS, 2006) and a lack of recent data new studies are urgently required. Therefore the project “Lust or trust? Adolescents‘ sexual risk taking in Carinthia” provides actual data.

Methods: The study explores sexual behaviour in adolescents. 1089 Carinthian pupils and students (age: M = 18.73, SD = 2.85; 67 % female) were surveyed. The sample consists of respondents from all regions of Carinthia to assure the generalisation of the results.

Results: 80 % of the participants are sexually experienced. They are significantly older than the inexperienced group (t (709.89) = 14.85, p < .01). The mean age at the first sexual intercourse was 15.75 (SD = 1.42). On average the sexually experienced respondents had 4.55 sexual partners (SD = 6.62). 79 % used a condom at the first intercourse, whereas only 47 % used a condom at the last intercourse. In general 25 % used condoms always, however 39 % seldom or never. 22 % of the respondents drank alcohol always or often before having intercourse, while 78 % reported rare or no presexual alcohol consumption. Analysing gender differences we found that men are more likely to drink before having sex (z = -3.33, p < .01). Furthermore men use condoms more often in general (z = -3.75, p < .01), regarding the first sexual intercourse no gender differences exist (p = .95). Women are more likely to have a steady relationship (Chi2 (1, 852) = 38.39, p < .01).

Conclusions: The framing of a sexual encounter by MSW has an impact on their HIV-protection behaviour. Prevention messages or social counselling for MSW should not only address them as men who sell sex to other men but also as persons who have to select among competing frames of sexual scripts, HIV-protection strategies and HIV-protection behaviour. While certain transactional frames have a positive impact on HIV-protection behaviour (sex work as profitable opportunity to earn money & sex work as a delivery of a qualified service) others (sex work as opportunity to earn money & sex work as enjoyable opportunity to earn money) give way to unsafe sex.

A.34 (Poster) Is knowledge about HIV/AIDS and willingness to protect by using condoms in young German people decreasing?

von Rüden U.1, Töppich J.1

1Bundeszentrale für gesundheitliche Aufklärung, Köln, Germany

To examine whether the public awareness of AIDS (especially in young people), the level of knowledge about HIV infections and protection, as well as the intention to use condoms has changed since the early 1990’s.

Knowledge, attitudes towards HIV and AIDS, and protective behaviour has been studied by the Federal Centre for Health Education (BZgA) since 1987 by means of the study “Public Awareness of AIDS”, an annual, nationwide survey conducted among the general population over the age of 16 in Germany. The multi-stage random sample (based on the ADM telephone sample system, random selection of persons in the household) is disproportionately stratified as regards age (16 to 44 year-olds: 2,276 cases of 3,600 in total). Data from 1991 until 2006 show:

In the early 1990s two-thirds of the general population over the age of 16 and about 80% of the young people (16 to 20
A substantial increase in condom possession can be determined. In 1991, 32% of the general and 37% of the young population said they had condoms at home or with them. In 2006 46% of the general population and 68% of the younger people had condoms available.

AIDS is considered to be far less of a threat than in the past decade. Nevertheless, the majority of the German population still views HIV/AIDS as a fatal disease. Preventive health care aims at achieving and maintaining a high level of public knowledge about HIV/AIDS. Promoting safer sex constantly has lead to increased experience with and availability of condoms especially in young people.

A.35 (Poster)
Knowledge, attitudes and behaviour with regards to HIV and STIs among young adults in Germany, Poland Austria, Slovak Republic, Italy and Slovenia – a BORDERNET cross border survey

Sokolowski S
Steffan E.
Arsova Netzelmann T.

SPI Forschung gGmbH, Berlin, Germany

Objectives: Young people’s risk exposure to HIV/AIDS and STI is confirmed not only by recent data on new HIV infections, but also by a variety of socio-demographic, cultural and psychosocial factors related to the age of experimentation and unsettled search of (sexual) identity. Carried out in the frame of the EC-funded Project BORDERNET, the survey aims to identify sexual risk indicators related to knowledge, attitudes, sexual practices and cross-border mobility of European young adults from 6 EU member states.

Methods: A KAB survey comprising additional items on cross border mobility conducted through a self-administration questionnaire. Based on preliminary defined selection criteria of risky youth venues, 1085 young adults aged 18 to 25 years were recruited in border regions of Austria, Germany, Italy, Poland, Slovakia and Slovenia.

Results: Young adults exhibit in general high basic knowledge of HIV/STIs. At the same time various uncertainties exist related to widespread myths of infection and protection, which influence respondents from the new EU member states stronger. About a quarter (26%) of the young adults (with a considerable share of Germans among them) does not have information about the availability of anonymous and free-of-charge HIV counselling and testing offers. This may impact negatively their help-seeking behaviour. Gender and cross-country comparisons show that the young women and the respondents from old EU member states (especially the Austrians and the Germans) tend more to single-partner relationships as a risk management strategy and state to choose more often the “no condom, no sex” self-protective behaviour. Young men, as well as respondents from Mediterranean countries (Italy, Slovenia) predominate among those with multiple sexual partners, and partly with condom-unfriendly attitudes. Nevertheless, men in general report more often condom use than women and rely more on their assertiveness skills at the condom negotiation.

Conclusions: The identified narrow link between condom use and prevention of unwanted pregnancy confirms unambiguously the importance of integrative prevention approaches, which embed the HIV/AIDS and STIs education into the wider frame of the sexual and reproductive health of young adults.

A.36 (Poster)
HIV prevention among MSM in the Ukraine

Traute A.

An Ukrainian-German working group conducted a study among HIV-positive and HIV-negative MSM (men who have sex with men) per in-depth interviews and questionnaires between August and November 2006. The aim was to obtain information about prevention deficits and ways to HIV prevention among MSM in the Ukraine - a work that has long been neglected and only recently is conducted with the aid of international donors. 16 in-depth interviews about all aspects of sexual experience and sexual behaviour, safer sex and the perceived attitude of Ukrainian society and MSM communities were conducted. Parallel, 200 MSM were interviewed per paper and pencil questionnaire about the same aspects. During the recruiting phase, stress was laid on the goal to recruit MSM from various social sub-groups (MSM identified as gay, bisexual, hidden, with incarceration experience, sex workers). The in-depth interviews were performed by trained peers of the respective sub-group in order to allow access to that scene. The project also served as capacity building measure for the Ukrainian project partners.

One of the main results was that risky sexual behaviour takes place, when sex partners feel being or are discriminated by the society because of to their sexual preferences, or by the MSM community due to their HIV-Status. In these cases, for example no communication about safer sex and protection steps takes place in sexual situations. Psychological factors of risky behaviour are perceived chronic stress (tension), perceived discrepancies between own knowledge, own beliefs and principles and performed behaviour. The group of not-tested MSM can be silhouetted against tested MSM with regard to anonymity of sexual contacts and lacking protective behaviour. Knowledge deficits seem to play no role in risky behaviour. In general, initiation of sex contacts via internet has become widespread. Prevention measures should first of all be implemented on accordant websites.

The study was supported by UNAIDS (No. IR.UKR.USC.226.UA.04.G (999.51)) by funds from the German Federal Ministry of Health, and was scientifically supervised by a member of Public Health Group at Centre for Social Studies (Wissenschaftszentrum) Berlin.
A.37 (Poster)

Modellprojekt: Deutschsprachige Prävention im Internet

Sindelar C.¹

1Deutsche AIDS-Hilfe, Zielgruppenspezifische Prävention, Berlin, Germany

Fragestellung: Darstellung des Modellprojektes Internetprävention für Schwule, Bisexuelle und MSM in Kooperation mit dem größten Internetkontaktportal für Schwule im deutschsprachigen Raum www.gayromeo.com, durch der User und der Internetanbieter transparent erfahrbar, wer mit welcher Eignung die Beratung anbietet und seine Abgrenzung zur Beratung


A.38 (Poster)

Follow-up of stab victims injured by a knife contaminated with HIV-infected blood at the opening of Berlin central railway station does not reveal transmission of bloodborne viruses

Jorgensen P.¹, Schürmann D.², Hoffmeister B.², Hamouda O.¹, Suckau M.³, Marcus U.¹

¹Robert Koch-Institut, Berlin, Germany, ²Charité - Universitätsmedizin, Berlin, Germany, ³Infektionsschutz Senatsverwaltung für Gesundheit, Soziales und Verbraucherschutz, Berlin, Germany

Background: At the opening of Berlin’s new railway station in May 2006, a 16-year old man randomly stabbed 33 persons with a knife. On the following day one of the victims revealed that he was HIV-infected. HIV post exposure prophylaxis (PEP) with Kaletra®+Combivir®, and active/passive Hep. B vaccination, if necessary, was offered to all injured victims except the one already HIV-positive, and on request to persons with cutaneous contact to blood of victims. RKI and Charité initiated an investigation to evaluate the possibility of blood-borne virus transmission during the incident. HIV-PEP compliance and tolerability were also analysed.

Methods: All PEP recipients were followed up. Data evaluated included the severity of injury, location at the time of assault, PEP compliance, side effects, and serological test results (HIV, HBV, HCV) up to 6 months following exposure. Location of victims at the time of attack along with the presumed route of the perpetrator was used to establish the sequence of stabbings.

Results: Thirty-two stab victims and 8 persons with bloodskin contact received HIV-PEP. All cases initially tested negative for HIV, HBV, and HCV. Six-month follow-up was completed in 32 of 40 cases (80%) by the end of January 2007. Compliance with PEP among stab victims was 93% compared to 75% among persons with blood-skin contact. Five cases stopped PEP prematurely, 3 of these had blood-skin contact only. Side effects associated with PEP were reported by 97%. None of the 26 of 32 stab victims who had their follow-up completed showed serological evidence of infection with HIV, HBV, or HCV.

Conclusions: In the reported incident the risk of acquiring HIV after being exposed to an HIV-contaminated knife may have been lower than the risk estimated for percutaneous needle-stick injuries in health care settings (0.3%). Clothing may have acted as a barrier reducing the quantity of inoculated blood. Further, the HIV-infected victim had a low viral load (174 copies/ml) due to ART. While none of the injured received PEP within the optimal time frame, all received the first dose within 48 hours. PEP compliance was high, even though side effects were frequent. Public health issues, management of the incident, and economic issues will be discussed.

A.39 (Poster)

The balance of errors. Combining psychological methods and health economics to evaluate interventions in HIV prevention

Scambor C.¹

¹Steirische AIDS-Hilfe, Graz, Austria

Objective: Evaluation studies using quantitative methods normally report the results referring to standard levels of significance (e.g. “significant on 5 % level”). However, if these values are chosen in an arbitrary way, the whole study design may turn out as inappropriate for the evaluation of HIV-preventive interventions. A new strategy was developed to base evaluation studies on health-economic comparisons: The costs of preventive interventions and the economic benefit of prevented HIV-infections were combined to find appropriate study designs.

Methods: Within a series of studies (1998-2006), a simple HIV preventive intervention for men who have sex with men was evaluated. Condoms and lubricant were displayed for free in a darkroom. The condoms that were used and thrown on the floor by MSM each night were counted in the next morning. As a result, a series of “used condoms” to compare
pre- and post-intervention phases was obtained. Economic estimates were used to design the studies: The (moderate) costs of applying effectless interventions (type-I-error rate) and the (very high) theoretical costs of new HIV-infections without the intervention (type-II-error rate) were “translated” into designs with increased levels of significance (up to 30 %), which is unusual in conventional experimentation.

**Results:** An effect of the intervention could be detected. Model estimations showed that between 2 and 8 HIV-infections were prevented by the intervention in the period from 1998 to 2005, and thus had saved costs up to 5.9 million Euros, with project costs of 30.000,--.

**Conclusions:** The current practice of an arbitrary specification of error rates may result in wrong decisions with the detrimental consequence of stopping effective interventions.

Thus, an interdisciplinary strategy for specifying an appropriate level of significance was developed, by combining psychological methodology and health economics. The risk of “reporting effects that don’t exist” and the risk of “failing to see existing effects” are balanced by using the monetary values of each error’s respective consequences. In general, even very small effects “pay for the investment” in HIV prevention, but such effects often can not be detected when conventional levels of significance are used.

### A.41 (Poster)

**Seroprevalence of HIV infection among patients attending the pre-pregnancy class at prenatal diagnosis and therapy centre, college of medicine, University of Lagos. A nine years review**

Ajayi G.1, Omilabu S.1, Alamu D.1, Balogun Y.1, Badaru S.1

1Prenatal Diagnosis and Therapy Center, Tertiary Hospital, Lagos, Nigeria

**Objective:** To study the sero prevalence of HIV infection in the pre-pregnancy period in a tertiary care centre in Lagos.

**Setting:** Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos.

**Design:** A cross sectional study.

**Materials and methods:** Blood samples of males and females referred to pre-pregnancy class with written consent were collected and tested for HIV antibodies between 1997 and 2005. Only those who are HIV sero positive were included in this study. Partners of sero positive were also counseled and tested. Statistical analysis was done using Chi-square test.

Result: Out of a total of n=1868 screened, n=73 (3.87%) were found to be sero reactive or sero positive. The highest sero prevalence of HIV was in the year 2004 with (n=17) 9.39%. The majority of sero active n=39 were in the age group 26-35 years. The total male: female ratio was 1:2.7(20:53).

**Conclusion:** In the present study, sero prevalence of HIV infections was found to be high (3.87%) among pre-pregnancy class in Lagos. There is need to reduce this high prevalence by targeting an intervention program towards high risk and vulnerable groups in the society. Apart from these patients attending such pre-pregnancy class, patients should consider this and be screened before and after any procedure.

### A.42 (Poster)

**Effect of Zinc therapy in HIV positive pregnancies**

Ajayi G.1, Omilabu S.1, Alamu D.1, Balogun Y.1, Badaru S.1

1Prenatal Diagnosis and Therapy Center, Tertiary Hospital, Lagos, Nigeria

**Objective:** To measure the concentration of Zinc in HIV positive pregnant women and the effect of Zinc replacement therapy.

**Design:** Longitudinal Study

**Setting:** Prenatal Diagnosis and Therapy Centre in Tertiary Hospital in Lagos.

**Materials and methods:** In HIV positive patients, Zinc concentrations were determined by Atomic Absorption Spectrophotometry (AAS) and patients were treated with 20-30mgZn/day orally for an average of 10 weeks apart from the Antiretroviral drug they were on.

**Result:** Zinc concentration improved and was accompanied by a statistically significant increase from 0.846 to 1.031mg/ml or 84.6 to 1031mg/l (9ppm)

**Conclusion:** Our result shows that trace element deficiency of Zinc is present in HIV positive patients and correlates with the CD4 count. The effect of adjuvant Zinc replacement therapy should be recommended.
**A.43 (Vortrag)**

**Ante- und peripartale Komplikationen bei HIV-positiven Schwangeren in der Schweiz**

Aebi K.1, Lapaire O.1, Höslti I.1, and MoCHIV (Mother and Child HIV Cohort Study)

1Women`s Hospital, University Hospital, Basel, Switzerland

**Einführung:** In der Ära der hochwirksamen antiretroviralen Therapie (HAART) ist das Transmissionsrisiko von HIV von Mutter zu Kind unter optimalen Bedingungen unter 2%. Unklar bleibt, wie häufig schwangerschaftsspezifische Probleme wie z.B. Frühgeburt und Präeklampsie bei HIV-Positivität auftreten und wie gut diese in den letzten Jahren im Rahmen der pränatalen Vorsorge in unserem Kollektiv erkannt und behandelt wurden.

**Material und Methoden:** Seit 2003 wurden mittels Fragebögen der Mutter-Kind-HIV-Kohortenstudie, welche in die Schweizerische HIV-Kohortenstudie integriert ist, Daten zu Schwangerschaft und Geburt erfasst. Eingeschlossen wurden HIV-positive Schwangere mit vitaler Schwangerschaft > 24 SSW nach erfolgtem „written informed consent“.

**Ergebnisse:** Von 133 eingeschlossenen HIV-positiven Frauen hatten 83,4% eine Spontankonzeption, 17,3% IVF/ICSI und 7,4% eine intrauterine Insemination. Die erste Schwangerschaftskontrolle erfolgte durchschnittlich in der 11. SSW (5 bis 19 SSW). 42 Frauen (31,6%) hatten nach der 24. SSW schwangerschaftsspezifische Probleme. Analog einem Normalkollektiv konnten 1 Patientin mit HELLP Syndrom, 3 Schwangerschaften mit schwangerschaftsinduzierter Hyper tonie (2,3%) und 4 Schwangerschaften mit Gestationsdiabetes (1,8%) beobachtet werden. Eine vaginale Bakteriologie peripartal ergab bei 12 (8%) Frauen einen positiven GBS-Nachweis und in 8 (6,0 %) Fällen eine bakterielle Vaginose.

Auffällig häufig wurde bei 24 HIV-positiven Schwangeren (16,5%) vorzeitige Kontraktionen, bei 15 (11,3%) eine Verkürzung der Zervix (<25 mm), bei 10 (7,5%) ein vorzeitiger Blasensprung und bei 4 (3 %) eine vaginale Blutung verifiziert. Eine antibiotische Therapie im 3. Trimenon erhielten 30 (22,6%) der Frauen, eine Lungenreifungsinduktion 18 (13,5%) und eine Tokolyse 20 (15,0 %). Eine Cerclage wurde in 3 Fällen gelegt. Insgesamt hatten 31 (23,3%) Patientinnen Frühgeburten vor der vollendeten 37. SSW.

**Schlussfolgerung:** Trotz optimaler Therapie sind Schwangerschaftskomplikationen bei HIV-positiven Schwangeren mit 31% häufig. Das Frühgeburtsrisiko ist mit 23% ca. 3-fach höher als in einem nicht infizierten Kollektiv. Besonders im Hinblick auf die Frühgeburtlichkeit sind in Zukunft weitere Analysen der Risikofaktoren geplant.

**A.44 (Vortrag)**

**HIV infections in newborns and children born in Germany from 2004-2006 – missed opportunities**

Marcus U.1, Voss L.1, Hamouda O.1

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

**Objectives:** It has been well known for more than 10 years, that HIV transmission from mother to child is largely preventable by combined interventions such as antiretroviral treatment/prophylaxis during pregnancy and delivery, planned caesarean section, formula feeding of the neonate and postnatal antiretroviral prophylaxis. Many cases of HIV transmission to the neonate in developed countries are therefore due to failure to diagnose HIV infection during pregnancy or to implement prophylactic measures.

**Methods:** For all HIV infections in neonates and children born in Germany and diagnosed from 2004 through 2006 which have been reported to the Robert Koch-Institut (n=41) we tried to obtain additional information on possible reasons for failed transmission prophylaxis by contacting paediatricians or gynaecologists involved in care for mother or child.

**Results:** The number of newly diagnosed infections in neonates or children born in Germany ranged from 11 in 2004 to 17 in 2005 and 13 in 2006. In 20 cases an HIV test was probably not offered to the mother during pregnancy. In 8 cases prophylactic measures were implemented too late or incomplete due to various reasons. In 4 cases HIV testing or medical interventions were declined by the pregnant woman or her partner. In 4 cases prophylactic measures were unsuccessful for undetermined reasons. 3 women seem to have acquired HIV infection after a negative screening test in early pregnancy. In 2 cases HIV infection had been diagnosed during pregnancy, but for unknown reasons no adequate care was provided. As to the risk factors for the mothers, 22 women originated from high prevalence regions, 8 from other foreign countries, 4 German women had a partner from a high prevalence region, and 2 women were intravenous drug users.

**Conclusions:** Failure to offer HIV testing during pregnancy and inadequate implementation of prenatal care for infected women were the main reasons for mother-to-child transmissions of HIV in Germany. The prenatal care guidelines in Germany need to be updated urgently in order to adequately address the problems and improve the management of HIV-infected pregnant women.

**A.45 (Vortrag)**

**Berufstätigkeit und Bildungsniveau bei HIV-infizierten Frauen und Männern in Deutschland**

Mueck B1, Balogh A.-M.1, Wolf E.1, Koegl C.1, Jaeger H.1

1MUC Research, Muenchen, Germany, 2Gemeinschaftspraxis Dr. Jaeger-Guedes - Dr. Jaeger, Muenchen, Germany

**Fragstellung:** Zeigen sich in einer Kohorte von 1056 HIV-Patienten soziodemografische Unterschiede zwischen Frauen und Männern?

**Methode:** Prospektive, monozentrische Beobachtungsstudie von HIV-positiven Frauen und Männern, die seit Oktober 2004 innerhalb der deutschlandweiten Patientenkohorte des Kompetenznetzes HIV/AIDS in unserer Praxis erfasst werden (HIV-Kohorte muench01).

**Ergebnisse:** 20% der Patienten (N=209) sind Frauen, 80% Männer (N=847). Das Durchschnittsalter der Frauen beträgt 42, das der Männer 46 Jahre. Die mittlere Infektionsdauer liegt in beiden Gruppen bei 10 Jahren. Die Arbeitslosenquote der erfassten Frauen beträgt 18%, die der erfassten Männer 9%, und ist jeweils höher als die gesamtdeutsche Arbeitslosenquote (Frauen 10%, Männer 12%, Stat. Bundesamt 2004). Der Anteil ohne Schulabschluss liegt bei den Frauen mit 12% deutlich höher als bei den Männern mit 2%, ebenso ist der Prozentsatz ohne Berufsabschluss mit 29% signifikant höher als bei den Männern mit nur 7%. Das niedrigere Bildungs- und Ausbildungsniveau der erfassten HIV-positiven Frauen liegt in der ethnischen Zusammensetzung begründet:

**MUC Research, Muenchen, Germany, 2Gemeinschaftspraxis Dr. Jaeger-Guedes - Dr. Jaeger, Muenchen, Germany**
Trotz schlechteren Bildungsniveaus der schwarzen und asiatischen Frauen sind diese mit 54% in gleichem Maße berufstätig wie die kaukasischen Frauen mit 56% (Tabelle 1).

**Schlussfolgerungen:** Die Arbeitslosenquote in unserer HIV-Kohorte entspricht in etwa der gesamtdeutschen Arbeitslosenquote. Die berufstätigen HIV-Patienten arbeiten häufiger Teilzeit im Vergleich zur deutschen Gesamtbevölkerung. Das Bildungsniveau der in der Kohorte erfassten schwarzen und asiatischen Frauen ist wesentlich niedriger als das der Kaukasierinnen; der Anteil der berufstätigen Frauen unter- schied sich jedoch nicht nach Ethnizität.

### A.46 (Poster)

**Migration and prostitution – not a topic in the HIV/AIDS discourse?**

*Stefan E., Sokolowski S.*

1SPI Forschung gGmbH, Berlin, Germany

**Background:** The share of migrants among the sex workers in Germany has increased from 30% in the 90ies up to 70-80% to date. The legal framework regarding this particular group has also become a subject of change meanwhile. The law for protection of infectious diseases, the prostitution law and not least the EU Eastern-Enlargement have a massive impact on the living conditions of the sex workers with migration background as well as on their accessibility for prevention and health care offers. Both laws are currently in process of amendment, which encourages a stronger focus on the HIV and STI prevention aspects for this particular group to be additionally undertaken.

**Method:** Our thesis is based on the achievements and outcomes of several of our own studies. A total number of 157 sex workers (including 28 males) with migration background were interviewed in the frame of the projects “Migration and HIV” (2004) and “BORDERNET” (2006). We tackled the issue of the change in the AIDS and STI counselling centres in the study “Health care services in transition” (2003) and the reorganisation of the AIDS/STD counselling centres in North-Rhein–Westphalia (2006)

**Results:** According to our data the migrant sex workers are relatively often affected by STIs, whereas Gonorrhoea and Chlamydia trachomatis represent the most often diagnosed STIs in the group. Around 65% of the respondents have a good basic knowledge of HIV/AIDS and STIs infection and prevention but myths and fears are widely spread among the group. More than 75% of the interviewees reported that every 5th to every 2nd client offers to pay more for unsafe sex or refuses condom use. The lacking or insufficient adjustment of the public health care offers to the new legal and political framework deteriorates the access to the STI counselling services by the migrant sex workers.

**Discussion:** Sex workers with migrant background should rely on voluntary and anonymous health care services. The latter can achieve only a certain coverage given that the services have to adapt to the new legislative conditions in the prostitution milieu. Besides the establishment of outreach services, further offers have to be developed, which assure accessible thresholds to the available health services for the sex workers.

### A.47 (Vortrag)

**Transcultural intermediary training HIV/AIDS: A key-model for intercultural education**

*Kimil A., Wienold M., Salman R.*

1Ethno-Medizinisches Zentrum, Migrant-AIDS-Project in Hannover to bridge the knowledge gap between the native German and the immigrant population. The training also aims to stimulate solidarity in response to a perceived lack of support of migrants with HIV/AIDS in their own communities. Has this approach been successful?  

**Methods:** Qualitative and quantitative data from five training courses (each 50 hrs, 2002-2006) and from the intermediaries’ campaigns (2006) were systematically evaluated. Feedback was also sought from public and private funders.

**Results:** Over 100 intermediaries have participated in the project since 2002 in Hannover and Hamburg. The trainings have been highly appreciated by participants. Intermediaries have become involved in (self-) evaluation and in continued education (voluntarily). More than 200 group sessions were conducted in community settings. Data confirm earlier findings of deficits in specific sub-populations and groups. They also point to a high potential for discrimination and confirm a great distance to people with HIV. The increasing depth of evaluation now brings forward detailed information on knowledge, behaviours and attitudes. Data from Hamburg
(2006, N=200) confirm (1) the need for further education in HIV/AIDS issues in ten language groups, and (2) the high success rate of community group sessions prepared and conducted by intermediaries. The formalized feedback of intermediaries to the local co-ordinator of project activities allows for insights into migrants’ AIDS-issues on a real-time basis. Transferring the idea to Hamburg was identified as a “Best Case” for integration by the German government. (Potential) Funders were interested in expanded services (e.g. geographically) and in developing longer term support for the model.

**Conclusion:** Intermediary training is able to successfully establish targeted campaigns in diverse populations traditionally hard to reach for HIV/AIDS-prevention. Relevant outcome data can be collected effectively. Further efforts are needed to follow the impact of training on the professional careers of highly skilled intermediaries and to develop train-the-trainers concepts.

**A.48 (Vortrag)**

**Vorstellung eines neuveröffentlichten Mediums der BZgA für Multiplikatoren und Multiplikatorenbildung: Präventionsmappe Sexuell übertragbare Krankheiten – Text- und Bildtafeln für Menschen verschiedener Kulturen**

**Berrett S.**

1Bundeszentrale für gesundheitliche Aufklärung, AIDS-Prävention, Köln, Germany


**Schlussfolgerung:** Anhand des Mediums und seines Entstehungsprozesses wird ein praktikabler und erfolgreicher Weg aufgezeigt, im schwierigen Feld der Medienerstellung für heterogene Migrantengruppen übergreifende Medien zu entwickeln und unter Einbezug von Vertreterinnen und Vertretern der Zielgruppe Barrieren der Erreichbarkeit abzubauen.

**A.49 (Vortrag)**

**Patienten mit chronischen Infektionskrankheiten und Migrationshintergrund – Erste Auswertungen aus zwei Infektionsambulanzen in Unterfranken**

**Stich A.**

**Müller A.**

**Ziegler U.**

**Ludin D.**

**Heinz W.**

**Guhl C.**

**Langmann P.**

**Winzer R.**

**Napoles de Zlatic M.**

**Klinker H.**

1Missionsärztliche Klinik gGmbH, Tropenmedizinische Abteilung, Würzburg, Germany.

2Medizinische Klinik und Poliklinik II der Universität, Infektologie, Würzburg, Germany

**Hintergrund:** Mehr als 9 % aller in Deutschland lebenden Menschen haben einen Migrationshintergrund. In dieser Bevölkerungsgruppe bedingen unterschiedliche Ursachen eine Prävalenz chronischer Infektionskrankheiten, die höher als in der deutschen Bevölkerung ist. Andererseits wird die medizinische Versorgung von Flüchtlingen und Migranten im Vergleich zur deutschen Normalbevölkerung allgemein als schlechter eingestuft.

**Methodik:** Seit Juli 2006 werden in der Infektionsambulanz der Medizinischen Klinik und Poliklinik II der Universität und in der Tropenmedizinischen Abteilung der Missionärlichen Klinik in Würzburg systematisch Daten von Patienten mit Migrationshintergrund erfasst und anonymisiert ausgewertet

**Ergebnisse:** Auf Patienten mit Migrationshintergrund entfielen knapp 40 % (n = 472, Stand 1.2.2007) aller Arzt-Patient-Kontakte. Bei den chronischen Infektionskrankheiten waren die HIV-Infektion (n = 113) und die viralen Hepatitiden B (n = 76) und C (n = 123) von übergeordneter Bedeutung. 41 % der erfassten Patienten waren unter 40 Jahre alt, 76 % waren Männer. Die Hälfte der Patienten stammte aus Schwarzafrika, hier dominierte die HIV-Infektion. Ein weiteres Drittel hatte seine Heimat in Osteuropa und Zentralasien, bei diesen Patienten war die Hepatitis C die häufigste Diagnose. Ein höherer Schulabschluss (≥ 8 Schuljahre) war bei 77 % der Patienten vorhanden. Andererseits war bei 32 % der Patienten eine Kommunikation in deutscher, englischer oder französischer Sprache nicht ausreichend möglich. Bei der Betreuung waren grundsätzlich mehr Zeit aufwands sowie häufigere Einbestellungen für Kontrolluntersuchungen und weiterführende Gespräche notwendig, um eine ausreichende Einbindung in die Therapie zu gewährleisten.

**Schlussfolgerung:** Unsere Zahlen sind nicht repräsentativ für Menschen mit Migrationshintergrund in Deutschland. Dennoch lassen unsere Untersuchungen und Arbeitserfahrungen folgende Schlüsse zu:

1. In Infektionsambulanzen bestreiten Patienten mit Migrationshintergrund einen großen Anteil des Patientengutes,
2. Ein größerer personeller und zeitlicher Aufwand ist bei der Betreuung dieser Patientengruppe erforderlich,
Transferring intermediary training HIV/AIDS to Hamburg: Signs of early success

Robben K.1, Wiensold M.2, Brayer W.1, Salmann R.2, Migranten-Aids Projekt

1Kinder- und Familienzentrum Schnelsen, Hamburg, Germany, 2Ethno-medizinisches Zentrum Hannover, Hannover, Germany

Introduction: The number of newly diagnosed people with HIV-infection from high prevalence countries has doubled in Hamburg since 2000. There is evidence for migrants to be at a particularly high risk of infection and to delay the use of German institutions (e.g. AIDS-service organizations). A higher level of discrimination of migrants with HIV is found in their own communities. These issues have been addressed effectively by training transcultural intermediaries in HIV/AIDS prevention and care in Lower Saxony. Is a partnership able to establish training following this model elsewhere?

Method: A proven model for HIV/AIDS prevention in migrants was adapted and transferred to the site in Hamburg (11/05 to 02/07). Selected migrants were trained by experts (epidemiology, medicine, sexuality, policy and psychology). The project was evaluated through structured feedback during the training and by evaluating the group sessions.

Results: 30 bilingual, socially integrated and committed migrants were selected to participate in the training and campaign. A curriculum based on 50 hrs of training was applied and followed by supervised group session prepared and evaluated each by two of the intermediary trainees. 24 intermediaries completed the training and were certified as transcultural HIV/AIDS intermediaries. The training provided insights into the cultural background of HIV/AIDS in the countries of origin (e.g. AIDS as a punishment in Africa). The campaign highlighted the singular capacities of transcultural intermediaries to (1) identify target groups and (2) successfully conduct community group sessions in their respective ethnic communities. This observation remained valid throughout the project (18 sessions). Group sessions reached over 200 migrants in ten languages. The project elicited highest public interest and further demonstrated demand and opportunities for continuing the campaign through new funding.

Conclusions: Intermediaries successfully served as HIV/AIDS educators in their respective communities. Training transcultural HIV/AIDS intermediaries is now publicly recommended in Hamburg (Handlungsplan Integration des Hamburger Senats). In order to provide a perspective for a self-sustainable project in Hamburg further effort is needed.

Improved results of evaluation in intercultural settings: Participation of intermediaries in quality assurance and adaptation

Wienold M.1, Kimil A.1, Robben K.2, Menckhaus B.3, Sobiech C.1, Mönninghoff K.1, Salmon R.4

1Ethno-Medizinisches Zentrum, MAP-Team, Hannover, Germany, 2Kinder- und Familienzentrum, Hamburg, Germany, 3Ethno-Medizinisches Zentrum, MiMi-Projekt, Hannover, Germany, 4Ethno-Medizinisches Zentrum, Hannover, Germany

Question: The heterogeneous population of migrants in Germany (reflecting changing patterns in the history of immigration; first and second generation) appear to know less about health issues than the native German population. The Ethnomedical Centre in Hannover has established a model for evaluated health promotion by migrants for migrants. How can the tools be improved to better evaluate the impact of HIV/AIDS prevention in migrant communities?

Methods: Evaluation developed for health prevention campaigns in migrant communities in Germany (MiMi-Projekt) were adapted to the HIV/AIDS field following principles of continuous quality improvement and community orientation. The tools were developed in a multi-cultural and multi-professional team, followed by feedback from trained transcultural intermediaries and then translated (by intermediaries). The questionnaires for participants in community group sessions were bilingual. The validity of evaluation results was assessed. Data collected during a project in Hamburg (2006) were analysed using quantitative and qualitative methods.

Results: The materials were reviewed and adapted by trained intermediaries into e.g. Pigdin English. Questionnaires were successfully applied in six languages. The bilingual texts allowed evaluation in the team (German is the lingua franca of the project). A total of 21 community group session resulted in over 200 questionnaires returned reflecting ten different ethnicities (language groups). A preliminary evaluation of 115 questionnaires showed valid results relating to gender, recruitment, knowledge and feedback on quality of community group sessions and on information provided:

1Female migrants were in the majority,
2recruitment into community group sessions mostly worked through personal invitation,
3basic knowledge is highly variable with evidence for relevant deficits (e.g. homophobia),
4the feedback was highly positive. Open questions required translation into German for evaluation.

Conclusions: Evaluation tools can be improved by making use of intermediaries. Open questions remain to pose a particular obstacle for evaluation in this context. Standard criteria for community orientation in quality assurance may serve to further improve outcomes.

Intercultural Competence (IC) in the scope of outpatient medical care for migrants living with HIV/AIDS (MHA)

Jansen K.1, Kleiber D.1

1Free University Berlin, Institute for Public Health and psychosocial Health Research, Berlin, Germany

Objective: MHA are said to be underrepresented in practices specialised on HIV, but only few data are existent for the German situation. As barriers for access and containing diagnostics and treatment for MHA, culturally differing theories of sickness and social interaction, language problems as well as material and legitimate restrictions are considered. A study was carried out to clarify the extent and terms of outpatient medical care for MHA. Factors of good medical practice regarding MHA were surveyed, too.

Methods: In Berlin, all HIV specialised (N1=28) and a sample of regular (N2=841) practices were surveyed via a standardised questionnaire. Data were gained on structure of practices and composition of their migrated clientele, on communication and interaction problems (scale: 0 (no) - 9 (very high)) with MHA and on degree of IC within the practices. To

A.54 (Poster)

KABaSTI-study results: Demographic and behavioural characteristics of German men who have sex with men (MSM) who received their last HIV test by donating blood or plasma

Marcus U., Schmidt A.J., Hamouda O.

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: In western industrialised countries, men who have sex with men are excluded from donating blood due to an increased risk of HIV and other sexually transmitted infections. However, this exclusion based on sexual preference is challenged as discriminatory and the efficacy of a policy based on self disclosure of sexual preference is questionable.

Methods: We collected data on HIV testing sites of MSM in a large national survey on knowledge, attitudes and behaviour of German MSM as to sexually transmitted infections (KABaSTI-study). Participants (n=6,833) were recruited through MSM websites and through private medical practices with high proportions of MSM clients. We analysed demographic and behavioural characteristics of German MSM who received their last HIV test during a blood or plasma donation (BD) and compared them with MSM who used other sites (OS) for HIV testing.

Results: Seven percent of survey participants who gave information on their last HIV test (191/3,400) reported that their latest test was during a blood or plasma donation. Nine of the tests (4.7%) in BD had been positive. Most of the tests (67%) were recent (2005 or 2006). BD were more likely to be younger (57% vs. 38% <30 years), to live in smaller towns (52% vs. 32% <100.000), to have female sex partners (20% vs. 10%), to have less male sex partners (59% vs.42% with <6 partners in the previous 12 months), or to live in a monogamous relationship (27% vs. 20%). BD reported less unprotected anal intercourse (28% vs. 37% in the previous 12 months), and a lower incidence of sexually transmitted infections than OS (7% vs. 23% in the previous 12 months). BD had greater difficulties to talk to their doctor about sex or their sexual preferences.

Conclusions: MSM who donate blood have a lower sexual risk profile than MSM who do not donate blood. However, around 5% of BD report frequent unprotected anal intercourse, a crucial risk factor for HIV infection. The largest risk for the safety of the blood supply from BD seems to arise from (1) unrecognized and/or incident infections of stable partners, and from (2) men who seem to use blood donation as an HIV testing site.

The KABaSTI study was supported by a BMG grant.
A.55 (Vortrag)

Children and young people living or working on the streets: the missing face of the HIV epidemic in Ukraine. A research report published by UNICEF Ukraine and AIDS Foundation East-West (November 2006)

Teltschik A.1

1Free-lance public health consultant (Eastern Europe & Central Asia), Odessa, Ukraine

Objectives:
1. To close an existing gap in research and to systematically assess and present:
   a) Needs and demands of the target group;
   b) Rights violations;
   c) National policy and legal frameworks;
   d) Available resources;
   e) Service quality and levels of coordination and cooperation.
2. To provide recommendations and to guide the design, implementation and evaluation of an extended, comprehensive and multisectoral national response to prevention, treatment, care and support for this target group.

Methods: A comprehensive situation and comparative analysis and a quantitative and qualitative survey among 650 children and young people living or working on the streets in Kiev and Odessa.

Results:
1. The phenomenon of children and young people living or working on the streets has been steadily increasing over the past 16 years in Ukraine.
2. Most children run away from home, because of a dysfunctional family, abuse and the fact that there is no adequate social support system in place to address the problems at home and to prevent them from running away.
3. But once the children and young people are living or working on the streets, their needs are also not being adequately met.

Key research findings:
1. This is a group most likely to be exposed to violence, abuse, discrimination, exploitation, HIV and many other diseases.
2. They have a poor health status, very low education levels and their rights are being seriously violated.
3. The majority are engaging in risk behaviour.
4. They lack protection, as well as the means, skills, knowledge etc. to protect themselves.
5. The services provided to them are of low quality.
6. There is a lack of official, standardized and reliable data.

Conclusions: The target group represents only the ‘tip of the iceberg’. ‘Below the water’ is a large and growing number of vulnerable children and young people in Ukraine, who are also most-at-risk and most affected by the HIV epidemic, and should therefore be at the centre of policy-making. The research report provides detailed recommendations to the Ukrainian government in key strategic areas on how to extend and improve the national response based on the experience gained in addressing the HIV epidemic over the past years in the country.

A.56 (Poster)

Knowledge, attitudes and behaviour in regard to HIV and STI among MSM in Austria, Slovak Republic, Italy and Slovenia – a BORDERNET cross border survey

Amort F.1, Steffan E.2, Sokolowski S.2, Schnitzer S.2

1AIDS-Hilfe Wien, Prävention, Wien, Austria, 2SPI Forschung gGmbH, Berlin, Germany

Objectives: BORDERNET (EU funded) aims to enhance HIV/AIDS and STI-prevention, diagnostic and therapy in regions across the old and the current EC-outer borders. In Western Europe in general over one third (35%) of the HIV infection diagnosed in 2005 occurred through sex between men. The epidemics range in Central Europe remains still small in comparison, but also here sexual contacts between MSM are an important source of infection.

Methods: Two BORDERNET model regions (MR 3 – Austria/Slovakia, MR 4 – Italy/Slovenia) decided to make MSM to one of their target groups for a BORDERNET KAB survey with additional questions on mobility. Based on preliminary defined selection criteria of gay friendly venues, a total number of 371 MSM was questioned with a self-administration questionnaire.

Results: In regard to cross border mobility, the MSM respondents from Slovenia and Slovakia are the most frequent travellers to the neighbouring countries, whereas the Austrian men are moderate travellers and the Italian travel even more seldom. Leisure time is the most important reason for traveling across the borders.

Even though the respondents showed a very high basic knowledge of HIV/AIDS, there are also many insecurities as well as fears to get infected with HIV. A high percentage of MSM have been tested for HIV (Austria: more than 90%), and a high proportion of them stated to have received pre- and post test counselling.

Concerning condom use, different patterns of risk management, such as consequent safe sex, being faithful, decrease of number of partners, serosorting, seropositioning and avoidance of risky venues could be identified in all countries. More risky behaviour was stated with steady partners than with casual ones. Over 20% of the men reported an STI diagnosis in the last two years, Italian MSM showed the highest incidence here.

Discussion: A main challenge of the combined HIV and STI prevention among MSM is to handle the consequences of the “normalisation” process of HIV. Cross border prevention strategies for MSM might be a possibility to reach synergic effects and should particularly focus on irrational fears and risk management strategies and help to overcome still existing prejudices and misconceptions.

A.57 (Poster)

Ansatz der Bewertung einer HIV-Infektion bzw. AIDS-Erkrankung in Österreich, 2006

Schröck T.1

1Donauuniversität Krems, Wien, Austria


Schlussfolgerungen: Für HIV/AIDS-Erkrankungen kann es gesundheitsökonomisch nur folgende sinnvolle Vorgehensweise geben:
1. Prävention und damit Nicht-Ansteckung
2. Wenn eine Ansteckung erfolgt ist: frühzeitige Therapie und ein den Behandlungsrichtlinien des Arztes folgendes Patientenverhalten
3. Jede Verbesserung des Patientenverhaltens ist zu unterstützen und damit besonders der Einsatz von speziell geschulten Pflegekräften („Adherence Nurses“).

A.58 (Poster)

DAGN-AD improve project part II: National health economic cohort analysis (K3A)

Goetzenich A.1, Hanhoff N.1, Knechten H.2, Wasem J.3, Neumann A.3

1DAGNÄ e.V., Aachen, Germany, 2PZB, Aachen, Germany, 3Universität Duisburg-Essen, Lehrstuhl für Medizin-Management, Essen, Germany

Background: With ever increasing rates of HIV-infection in Germany, the impact of this condition is not only significant medically but also health economically. Recent nation-wide data on the costs of HIV/AIDS are lacking. Further, data on HIV-infection in Germany and its current management outside the clinical trials setting are needed.

Objectives: The objectives of this analysis are:
1) to gather data on the health economics of HIV-infection in Germany,
2) to sub-analyse these data according to stages of the condition,
3) to gather data on clinical parameters and antiretroviral treatment, including reasons for discontinuing or changing therapy.

Methods: The DAGN-AD Improve national health economic cohort analysis (K3A) is a prospective, multi-centre evaluation. Continuous health economical and clinical data pertaining to HIV-infection is gathered for each patient for 18 months. The health economical data include both direct (incurred through all HIV-related diagnostic and therapeutic procedures) and indirect costs (incurred through e.g. absence from employment due to illness, etc.). Clinical data include information on routine laboratory parameters (CD4 cell count, HIV-RNA), on AIDS-defining illnesses, on HIV-associated illnesses and co-infections and on antiretroviral therapy use. The latter also includes reasons for any treatment discontinuation or change. Data are obtained via health economic questionnaires and physician clinical documentation. The questionnaires are employed at every patient visit.

Results: Calculations based on a statistical power of 90% with a 5% confidence interval indicated that at least 528 cases need to be recruited. Nation-wide, 33 HIV-specialty and ambulatory care centres are participating in this evaluation and have recruited 668 patients. These are representative of the geographical distribution of all HIV-infected individuals in Germany according to epidemiological data published by the RKI. The evaluation is ongoing. A limitation to this study is that intangible costs (a monetary value assigned to pain, decreased quality of life, etc.) are not gathered.

A.59 (Poster)

Analysis of German costs of full virological suppression for treatment experienced, HIV infected patients in the POWER trials

Stoll M.1, Hill A.2

1Medizinische Hochschule Hannover, Zentrum Innere Medizin, Abt. Klinische Immunologie, Hannover, Germany, 2University of Liverpool, Pharmacology Research Laboratories, Liverpool, United Kingdom

Background: The aim of antiretroviral treatment is long-term suppression of HIV RNA below 50 HIV RNA copies/mL. The POWER 1 and 2 trials evaluated new protease inhibitor treatment – darunavir/ritonavir (DRV/r) 600/100 mg BID versus Control PI (CPI), in treatment experienced patients, where complex and expensive drug combinations are typically required.

Methods: Office based German 2007 costs (including tax) were used. Average costs of antiretroviral treatment were calculated from the percentage use of NRTIs, PIs and T-20 in the DRV/r and Control PI arms of the POWER 1 and 2 trials. Rates of HIV RNA suppression <50 cp/mL in different treatment groups were combined with drug costs to calculate the costs per patient with HIV RNA <50 copies/mL. This analysis does not account for differences in drug toxicity, or opportunistic infections of AIDS, which could also influence value assessments.

Results: For the POWER trials, the average per patient cost in the control PI arm was € 32,718/year, versus € 34,442 in the DRV/r arm. By Week 48, 10% of Control PI versus 44% of DRV/r patients had HIV RNA suppression <50cp/mL. The cost per patient with HIV RNA <50 was € 327,175 for the CPI arm, versus € 76,538 for the DRV/r arm. Assuming that the control PI used was only LPV/r, cost per patient with HIV RNA <50 cp/mL was € 310,901. Consistent improvements in cost-effectiveness for DRV/r versus control PI were shown using other endpoints (>1 log reduction, 25 cell rise in CD4 count, HIV RNA <400 cp/mL).

Conclusions: Treatment with DRV/r was associated with consistent reductions in the cost per patient with HIV
RNA $\leq$ 50 copies/ml, for treatment experienced patients, based on German antiretroviral drug prices.

A.60 (Poster)
Overall Quality of Life (QoL) and Health Related Quality of Life (HRQoL) in patients with HIV and cancer. Theoretical considerations and empirical results

Wulff W.1, Kofahl-Krause D.2, Stoll M.1, Schmidt R.E.1

1Medical School Hanover, Clinical Immunology, Hannover, Germany, 2Medical School Hanover, Haematology, Haemostaseology and Oncology, Hannover, Germany

Aims: Despite increasing advantages in QoL-research contradictory results lead to the formulation of "quality of life paradoxon"(1), which stated, that healthy impairments do not affect directly the perceived overall QoL, as shown by us in HIV-patients previously (2). With this statement the assumption is implied that health is the determining factor for subjectively perceived overall QoL. 50 HIV- and 54 Cancer-Patients were assessed for their overall and their health related QoL. It is supposed that health is not a determining factor in the overall QoL with differences between the groups in the total scores. Also it is hypothesized, that there are differences in the health related QoL between the groups.

Methods: 50 HIV- and 54 Cancer-Patients were assessed for their overall QoL with the SEIQoL-DW interview(3) and the MLDL questionnaire(4) and for their health related QoL with the SF-36 questionnaire(5).

Results: For the overall QoL the percentage of mentions for health reached 16.3 in the HIV- and 20.6% in the cancer group. The whole social environment reached significant higher percentages with 37.4% and 41.2% respectively(6). There are no significant differences in the total scores. In the health related QoL measurement the HIV-group scored mostly near the cancer standard while the cancer patients scored mostly under it. Cancer patients have lower physical scores and showed a significant better mental health at the same time, whereas the mental health of HIV-patients was significant worse compared to their physical status(7). Significant differences between the groups were found.

Conclusions: Health is an important, however, not the dominating factor of the overall QoL of people with HIV and cancer. The social environment plays a more important role. Healthy impairments may be balanced with supports from other fields of the social environment. Heathy impairments directly the perceived overall QoL as shown by us. Within the health related QoL the connection between HIV serostatus and employment status of the participants.

Remarks: (1) Herschbach, 2002; (2) Körner et.al. 1999; (3) O’Boyle et.al. 1993; (4) v. Steinbüchel 1993; (5) Bullinger, Kirchberger 1998; (6) p=.000, p=.000 (Wilcoxon related); (7) p=.000, p=.001 (Wilcoxon related)

A.61 (Poster)
Unemployment in a sample of German MSM (KABaSTI-Study) – relationship with age, HIV and educational status

Marcus U.1, Schmidt A.J.1, Hamouda O.1

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: HIV infection has evolved into a chronic manageable disease since the advent of highly active antiretroviral therapy (HAART) in 1996. Health status and especially chronic diseases may impact on employment opportunities and increase the risk of unemployment. In addition, disclosure of the HIV status may also increase the risk of unemployment because of the stigma, which is still attached to HIV/AIDS and because of unfounded fears of transmission risks associated with social contact at the workplace.

Methods: In a survey on knowledge, attitude and behaviour as to sexually transmitted infections in German men who have sex with men (n=6,833), we analyzed the relationship between HIV serostatus and employment status of the participants.

Results: The unemployment rate among the survey participants was 10% (684/6,822), which is comparable to the unemployment rate in the male general population. Unemployment was closely correlated with educational status (5.7% in men with university degree, 21% in men with lowest school degree) and with age (increasing from 8.4% for 20-29 years to 15.5 for 50-59 years). HIV status was not significantly correlated with employment status (OR=1.1, 95%CI:0.9-1.4), but HCV co-infection almost doubled the risk of unemployment (OR=1.9, 95%CI:1.2-3.1). The unemployment rate was increased for men who had received their positive HIV test result recently (24% for men with HIV diagnosis in 2005). The lifetime risk for STIs was increased for unemployed men (OR=1.3, 95%CI:1.1-1.6). Some indicators demonstrate financial barriers for accessing health care. Sexual risk behaviour in terms of partner numbers and unprotected anal intercourse as well as self-perceived risk for STIs and HIV was slightly higher in unemployed participants.

Conclusions: HIV infection does not seem to be associated with employment status, but selection biases, e.g. due to loss of resources necessary for internet access for long-term unemployed men cannot be ruled out. The high unemployment rate for men recently diagnosed with HIV may be an indicator of transient problems associated with HIV diagnosis, or of an increased risk of HIV infection in persons who just lost their job.

KABaSTI study was supported by BMG

A.62 (Poster)
Occupational stress reduces health related quality of life (HRQoL) in HIV infected individuals

Kroidl I.1, Oette M.2, Kaiser R.3, Siegrist J.1, Roedel A.1, Häußinger D.2, RESINA-Study-Team

1Heinrich-Heine-University, Medical Sociology, Düsseldorf, Germany, 2Heinrich-Heine University, Gastroenterology/Hepatology/Infectious Diseases, Düsseldorf, Germany, 3University of Köln, Institute of Virology, Köln, Germany

Background: Occupational stress has an important influence on the progress of several diseases, like cardiovascular disease, diabetes mellitus etc. The influence of infectious diseases like HIV is not well studied yet.

Methods: 216 patients from 34 places of a federal state of Germany answered a 40 items questionnaire. We included questions from evaluated questionnaires of HRQoL and the Effort-Reward-Imbalance questionnaire in addition to sociodemographic and clinical parameters. The patients were part of a study for primary viral resistance mutations against antiretrovirals in formerly untreated patients. (RESINA-Study 2003-2005)
Results: In this multicenter trial we found differences of the subgroups of patients enrolled in private practice or university ambulance. Patients treated in private practices are significantly better educated, are more often employed, have less likely advanced HIV disease and more CD4 cells. These findings emphasize the importance of multicenter studies, which involve different treatment settings for representative results. In regression analysis we found that HRQoL has significantly lower scores in people who have high scores of occupational stress (p<0.01), are unemployed or premature retired (p<0.001), have advanced HIV disease (p<0.02), or wish more social support (p<0.01). Other factors like gender, way of transmission, age or partnership had no significant influence on HRQoL, neither had parameters defining the social ranking like education, current position, social acceptance of the job. We found primary drug resistance in 11.1% of the studied population, with no significant differences between subgroups regarding CDC Status, ethnic groups, longevity of the HIV infection, or others factors.

Conclusions: Occupational stress and employment status influences HRQoL in HIV-infected individuals significantly. Whether this has an impact on the progression of the disease, mediated for example by compliance will be shown in follow up of the cohort.

A.63 (Poster)

Experienced discrimination and strategies of information of patients with chronic diseases in Germany - preliminary data

Kittner J.M.1, Wulf W.1, Jäger B.2, Schmidt R.E.1

1 Hannover Medical School, Clinical Immunology, Hannover, Germany, 2 Hannover Medical School, Psychosomatic Medicine and Psychotherapy, Hannover, Germany

Objective: Although HIV infection has become a manageable condition and transmission is very unlikely to occur in daily life, HIV patients report of ongoing social discrimination which may augment personal difficulties in coping with the disease. However, for Germany neither is known whom HIV patients tell about their diagnosis, nor is reliable data available about reactions patients encounter after disclosure. This information is also lacking for patients with other chronic diseases like diabetes or chronic viral hepatitis.

Methods: Patients with diagnosis more than 1 year, but less than 6 years ago are asked to fill in a self-developed questionnaire in order to reveal which persons they have informed about their disease, and how they have perceived these persons’ responses. In addition, the HADS, a widely used anxiety and depression scale, is performed. For comparison, patients with diabetes or with chronic viral hepatitis will be recruited. Each group is planned to comprise 100 patients.

Results: Up to now, 26 questionnaires from HIV infected patients could be analyzed. Patients had told a median of seven persons (range 1-28) about their disease. They report to have informed 95% of current and recent partners, and have experienced an immediate supportive feedback from 78% and a long-term support from 84% of their partners. Patients have informed 51% of close family members and friends, and had experienced immediate supportive reactions in 87% of disclosures and a long-term support from 88% of informed family members and friends. After disclosing to public persons like medical doctors, dentists, health insurance employees etc., patients experienced a supportive feedback in 78% of cases, whereas long-term support was perceived in 62%. Overall, patients rated ongoing discrimination in Germany due to HIV with 2.73 ± 1.08 on a 1 to 4 point Likert scale.

Conclusions: The majority of HIV patients perceives significant ongoing discrimination and is rather restrictive with the information. However, most disclosures are followed by supportive reactions, which is especially true for disclosure to family members and friends. More patients’ data will be available, and more detailed analyses and correlation with HADS depression score will be presented.

A.65 (Poster)

Increased life expectancy of HIV-infected patients in the industrialized countries: The case for case management on the example of the city of Essen, Germany

von der Crone K.1, Gieseler R.K.2

1 University of Duisburg-Essen, Faculty of Educational Sciences, Essen, Germany, 2 Rodos BioTarget GmbH, Div. of Research & Development, Hannover, Germany

Objective: To evaluate the potential value of case management (CM) for ageing patients infected with HIV-1.

Methods: HIV-1+ patients in the industrialized countries enjoy an increasingly prolonged life expectancy. This goes along with HIV-1- and treatment-related sequelae and side effects, e.g., accelerated ageing and an increased risk to develop more rare diseases and malignant tumors. The peculiar sociomedical needs of growing numbers of ageing HIV+ people thus pose a challenge to society. Current status and goals of HIV/AIDS-related support networks/organizations were evaluated on the example of the city of Essen. Combined with the relevant general societal and legal contexts, this exploration may offer first clues as to the usefulness of CM for the ageing HIV-positive clientele.

Results: Germany is a progressively ageing society. The increasing life expectancy of HIV-positive patients thus needs to be regarded in the context of this demographic change. According to AIDS-Hilfe Essen e.V. (a metropolitan key support association for HIV+ people), the city is home to >2,000 people living with HIV/AIDS. Essen’s Arbeitskreis Versorgung (AV: Working Committee Logistcs) is the central hub for planning and implementing the chaperonage of these patients, and supports and coordinates all efforts of the city’s HIV-related confessional and non-confessional helplines, information centers, support agencies, and University Hospital. In a joint and generally accepted effort, the AV has developed a catalog specifying approaches for action, as well as a network coordinating all organized HIV/AIDS work. The City of Essen has established a Coordinating Office and defined certain standards of quality assurance. More recently, CM gains increasing importance within this framework. The legal frame to further proceed in this direction is in existence.

Conclusions: CM may be the method of choice to address specific requirements of HIV-1+ long-term survivors. Combined with an analysis of the general societal and legal frames, this exemplary survey highlights various points of (potential) synergy that offer the chance to focus on the interest of the target group, while concomitantly sparing social and health-care resources to enable both cost-reduction and sustainability.
A.66 (Poster)

Psycho-social aspects and the reality of live of HIV-positive patients in the Ukraine

Traute A.1

1Connect plus, Berlin, Germany

An Ukrainian-German working group (Lavra Clinic Kiev, NGO “Time of Life plus” Kiev, Institute for Political Psychology at the Paedagogical Academy Ukraine and Connect plus e.V. Berlin) surveyed 1.245 HIV-positive patients (770 male, 467 female) between July and December 2006 in one of the large AIDS Clinics of the Ukraine. Patients were interviewed per paper and pencil questionnaire about personal living situation and emotional condition, patient satisfaction, drug use, sexual behaviour, incarceration experience, STDs and about medical and care needs. Another aim of the survey was to verify the official figure that less than 1% of Ukrainian people with HIV and AIDS belong to the group of MSM.

32% of respondents say that they are often in an irritated or aggressive state of mood, only 16.8% often in a depressive mood (64.3%: sometimes). About half of the respondents consumes larger amounts of alcohol, almost 30% say they are frequently intoxicated by alcohol use (58%: often). 14% have IVDU experience. Both applies more often for men than for women. Hepatitis, gonorrhoea and syphilis are relevant STDs.

The quality of medical treatment and care at the place of residence is considered significantly worse than at Lavra Clinic. Reasons for treatment at the clinic is a need for solid analysis of medical condition and for ART treatment (only approx. 6,000 PLWHA out of estimated 350,000 to 500,00 in the Ukraine -UNAIDS estimation- have access to ART).

More than half of the respondents do not rule out same sex contacts. 15.7% of interviewed men have a same sex partner outside the regular partnership, 14.1% of the women. 19% of men had sexual contacts with a man within the last half year, 15% of the women. This supports our assumption that same sex behaviour is a widespread phenomenon in the Ukraine, while at the same time highly tabooed within Ukraine society.

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A.67 (Poster)

Das neue Sozialhilferecht

Exner-Freisfeld H.1

1Universitätsklinikum Frankfurt am Main, HIVCENTER, Oberursel, Germany

Fragestellung: Bringt die neue Sozialhilfe im SGB XII vom 01.01.2005 grundsätzliche Änderungen gegenüber dem früheren Bundessozialhilfegesetz (BSHG)?

Methodik: Anhand vorgegebener Gesetzes texte und ausführlicher Kommentare wird auf die Leistungspflicht der Sozialhilfe träger eingegangen.


Schlussfolgerungen: Sozialhilfeleistungen sollen nicht nur Armut verhindern, sondern dem Leistungsberechtigten eine Lebensführung auf gesellschaftlich akzeptablem Niveau ermöglichen, das der Würde des Menschen entspricht.

B. Klinik der HIV-Infektion

B.1 (Poster)

Pneumokokkenisolat von HIV-positiven und -negativen Patienten: vergleichbare Antibiotika-Resistenzprofile

Stephan C.1, Just-Nübling G.2, Shah P.M.2, Babacan E.1, Bickel M.1, Staszewski S.1

1HIVCENTER - Schwerpunkt HIV, Frankfurt, Germany, 2Infektionslaboratorium, Zentrum der Inneren Medizin am Klinikum der Johann Wolfgang Goethe-Universität Frankfurt, Frankfurt, Germany


B.2 (Poster)
Sehverschlechterung als Leitsymptom der Lues


1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany, 2Universitätsaugenklinik, Würzburg, Germany, 3Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany


B.3 (Poster)
Regionale Unterschiede in der Inzidenz von atypischen Mykobakteriosen
Salzberger B.1, Heindel B.1, Hartmann P.1, Ehrenstein B.1, Fäktenheuer G.2
1Universitätsklinikum Regensburg, Klinik I für Innere Medizin, Regensburg, Germany, 2Universitätsklinikum Köln, Klinik I für Innere Medizin, Köln, Germany

Ziel: Untersuchung der regionalen Unterschiede in der Inzidenz disseminierter Infektionen mit Mykobakterium avium intracellulare-complex (MAI).


Ergebnisse: In der analysierten Studie (n=682) zeigten sich erhebliche regionale Unterschiede in der Inzidenz von MAI-Infektionen. Die Inzidenz insgesamt in den USA war 19%, Frankreich 10% und Deutschland 8%, mit jeweils höheren Werten in der Placebo- und niedrigeren Werten in der Verum-Gruppe. Adjustiert für CD4-Zellzahl bei Baseline war das Risiko der Entwicklung einer MAI-Infektion in Deutschland und Frankreich etwa 0.25 des Risikos in den USA (p=0.001). In allen Regionen zeigte sich eine Wirksamkeit der Prophylaxe in einer Verminderung des Risikos einer MAI-Infektion um ca. 50%. Die niedrigere Inzidenz bewirkt eine andere Bewertung der medikamentösen Prophylaxe (NNT 8 in den USA bei Reduktion des Risikos von 26 auf 13%, ca. 33 in Deutschland und Frankreich bei Reduktion von 7 auf 4%).

Zusammenfassung: Es existieren deutliche regionale Unterschiede in der Inzidenz von atypischen Mykobakteriosen mit einem deutlich niedrigeren Risiko in Deutschland und Frankreich im Vergleich zu den USA. Das hat erhebliche Auswirkungen auf Prophylaxestrategien.

B.4 (Poster)
Pulmonary cryptococcal infection in acquired immunodeficiency syndrome
Mylius E.1, Träder C.1, Arastéh K.1
1Vivantes Auguste-Viktoria-Klinikum, Abteilung Infektiologie, Berlin, Germany

Cryptococcal infection in AIDS Patients is a systemic infection with generalized clinical symptoms and nearly always a manifestation in the cerebrospinal fluid (CSF). We report the history of four patients with generalised cryptococcal infection or cryptococcal pneumonia in combination with other fungal and bacterial infections but no isolated cryptococcal meningitis.

All of them showed up with the clinical signs of a severe pneumocystis jirovecii-pneumonia such as fever and coughing for a couple of days or weeks and increasing respiratory distress and weakness. They were HIV-positive in the state of AIDS with less than 100 CD4-cells/ml. Two of them were highly active antiretroviral therapy (HAART) naïve, two were already on antiretroviral medication. All were diagnosed by bronchoalveolar lavage (BAL). Patient A: Cryptococcus neoformans was isolated out of BAL, Aspergillus fumigatus and Pseudomonas aeruginosa were also present, no Pneumocystis jirovecii despite the interstitial infiltrates in Chest XR. Systemic cryptococcal infection could also be detected (antigen titre). In the CSF was neither the pathogen nor Cryptococcus-Ag detectable. Patient B, HIV-Infection and intestinal B-cell Lymphoma and Kaposi-Sarkom, had Cryptococcus neoformans, Pneumocystis jirovecii and Haemophilus influenza in his bronchial system. In this case Cryptococcus neoformans was found in CSF. Patient C had a pneumonia caused by Pneumocystis jirovecii in combination with Steptococcus pneumonia and Neisseria pneumonia (isolated from bronchial system). As we proved Cryptococcus neoformans-Ag in the blood without any signs for a cerebral cryptococcal infection this patient seemed to have also a cryptococcal-pneumonia. In Patient D we could prove a Pneumocystis jirovecii pneumonia and a systemic cryptococcal infection. All patients were treated for underlying disease and got in addition antimycotic treatment.

These reports show the possibility of a single pulmonary cryptococcal infection or the coinfection with different pathogens, i.e. pneumocystis and cryptococcus. As a consequence all HIV patients presenting with clinical signs for PCP or severe impairment of lung function should also be evaluated for cryptococcal infection.

B.5 (Vortrag)
Treatment of HIV-associated Hodgkin’s disease (HIV-HD): Interim analysis of a prospective multicenter trial
Henrich M.1, Kreckel P.2, Weyn C.3, Schürmann D.4, Kloenne U.5, Mosthaf F.6, Buch T.7, Fong D.8, Meyer R.9, Arastéh K.2, Engert A.1, Fäktenheuer G.3, Mitrou P.10, Hoffmann C.11
1Klinikum Harlaching, München, Germany, 2Auguste-Victoria-Krankenhaus, Berlin, Germany, 3Universitätsklinik Köln, Köln, Germany, 4Charité Universitätmedizin, Berlin, Germany, 5Universitätsklinik Münster, Germany, 6Schwerpunktpraxis, Karlsruhe, Germany, 7Schwerpunktpraxis, Hamburg, Germany, 8Universitätsklinik, Innsbruck, Austria, 9Diakonie Krankenhaus, Bremen, Germany, 10Universitätsklinik, Frankfurt, Germany, 11ifi, Hamburg, Germany

Objective: Hodgkin’s disease (HD) is one of the most common non-AIDS defining malignancies. Before the introduction of highly active antiretroviral therapy (HAART) the median survival of patients (pts) with HIV-HD was < 20 months. Recent data indicate an improved outcome of pts with HIV-HD treated in the HAART-era. The current trial was initiated to investigate a risk adapted treatment strategy in pts with HIV-HD in accordance with standard treatment procedures established for HIV-negative pts with HD.

Methods: Pts with HIV-infection and histologically proven HD are included in the ongoing study. Pts are planned to receive 2x ABVD + 30 Gy involved field (IF) radiation for early stage (ES) favourable HD, 4x BEACOPP baseline + 30 Gy IF for ES unfavourable HD (extranodal involvement, large mediastinal mass, ≥ 3 lymph node areas involved), and 6-8 x BEACOPP baseline for advanced stage HD. BEACOPP may be replaced by ABVD at the physicians choice. HAART is given to all patients in parallel to chemotherapy (CT).

Results: Since March 2004, 33 patients (median age 44 yrs, range 30 – 58) were included in (n=28) or treated according to the ongoing trial (n=5). To date baseline characteristics are available in 30 pts. Pts were diagnosed with stage I (n=1), stage II (n=7), stage III (n=11) and stage IV disease (n=11). B-symptoms were present in 14 of 28 cases (50%). In 23 of
28 pts (82%) HAART was given prior to HD and 6/26 pts (23%) had a prior AIDS defining illness. The median CD4 counts at HD diagnosis was 300/µL. Pts received/are receiving ABVD (n=11), BEACOPP baseline-21 (n=18) or BEACOPP-14 (n=1). Grade 3/4 peripheral neuropathy and grade 3/4 infections occurred in 6 of 21 pts each. To date response data are available in 15 pts (CR in 10 pts, PR in 4, SD in 1). 3 pts have died, all of them diagnosed with stage IVB HD. Causes of death were treatment related sepsis during the 1st months on ART. The high mortality and the relatively low rates of complete remission observed in this cohort underline the need for intensive efforts to improve treatment concepts of pts with ARL.

### B.6 (Vortrag)

**Current trends in AIDS-Related Lymphoma (ARL) – preliminary results of the German ARL Cohort Study**


1ifi Institut, Hamburg, Germany, 2Universität Köln, Köln, Germany, 3Arztforum Seestrasse, Berlin, Germany, 4Universität Düsseldorf, Düsseldorf, Germany, 5Universitätsklinikum Eppendorf, Hamburg, Germany, 6Universität Bonn, Bonn, Germany, 7Universität Essen, Essen, Germany, 8MacResearch GmbH, München, Germany, 9Universitätsklinikum Schleswig-Holstein, Kiel, Germany, 10Klinikum Harlaching, München, Germany, 11Schwerpunktpraxis, Karlsruhe, Germany, 12Klinikum Krefeld, Krefeld, Germany, 13Klinikum Augsburg, Augsburg, Germany

**Background:** The incidence of ARL has decreased less profoundly than that of other AIDS-defining illnesses. Chemotherapy is hampered by toxicity and infectious complications. The German ARL Cohort Study was initiated in order to analyze the characteristics and outcome of patients (pts.) with ARL with respect to potential risk factors and to the use of specific polychemotherapy (PCT) and antiretroviral therapy (ART).

**Methods:** This prospective multicenter cohort study includes pts with new or recurrent ARL (including Hodgkin’s Disease, HD) diagnosed since January 2005. After enrolment, pts are followed every six months.

**Results:** As of January 2007, 103 patients (93 males, 10 females) from 16 centers were included in the cohort. The most common histological diagnosis was diffuse large B-cell lymphoma (40 %), followed by Burkitt lymphoma (19 %) and HD (15 %). Mean age at ARL diagnosis was 44.5 years (range, 23.0–72.5). Median CD4 count was 211 cells/µl and 35 % of the patients had a prior AIDS-defining illness. In 30 %, HIV was diagnosed at the time of ARL diagnosis. Only 51 % were treated with HAART, and 22 % had a plasma viremia below 50 copies/ml. There were more HD cases in virologically suppressed pts. than in pts with detectable viremia (30 % vs 10 %, p=0.03). Sixty-two pts (60%) received a CHOP-based PCT while 11 pts (11%) received a protocol of short and intensified PCT which was adapted from the German multici-ter study group for adult acute lymphoblastic leukemia. The remaining 30 pts received other or no PCT. In 41 %, immunotherapy with rituximab was added to PCT. Of the 48 pts with available staging after completion of PCT, 29 (60 %) pts achieved complete remission of ARL. After a median follow-up of 5.9 months, 27 pts had died, among them 13 from progressive lymphoma. There were 6 treatment-related deaths (bloodstream infections) which were not related to specific PCT
timers.

**Conclusions:** Preliminary data of this ongoing, prospective study suggest that many of ARL pts. do not receive ART at the time of diagnosis. HD seems to be more frequent in patients on ART. The high mortality and the relatively low rates of complete remission observed in this cohort underline the need for intensive efforts to improve treatment concepts of pts with ARL.

### B.7 (Vortrag)

**Second line chemotherapy with IMVP16 after failure of CHOP in patients with HIV-related Non-Hodgkin-Lymphomas**

_Müller M^1_, Kölsche F^1_, Marretta L^1_, Träder C^1_, Weiss R^2_, Zwingers T^3_, Kowol S^1_, Arasteh K^1_

1Vivantes Auguste-Viktoria-Klinikum Berlin, Department of Gastroenterology / Infectious Diseases, Berlin, Germany, 2Private Praxis, Bremen, Germany, 3Estimate GmbH, Augsburg, Germany

**Objective:** Since decades the CHOP regimen is a well established first line therapy for NHL. In former days HIV-patients with NHL had a poor prognosis. The introduction of HAART improved the overall survival. The impact of immunotherapy (Rituximab) in HIV-related NHL is under investigation. However, it is not clear as to how non-responders should be managed further.

**Method:** Retrospective analysis of a single centre cohort of 140 HIV-patients with NHL, between 1/1989 and 10/2005. After failure of standard CHOP regimen (relapse or insufficient response) some patients received IMVP-16, a second line regimen, which is used in HIV-negative patients with lymphomas.

**Results:** 29 patients with at least one cycle of IMVP-16 were identified with a median follow up of 26.2 months. Characteristics at NHL diagnosis: Median age: 41.9 years (range: 31–75 years), median CD4: 180/µL (range 20–560), HIV-stage (CDC) “C”: 15 patients “B”: 10 patients “A”: 4 patients. NHL-stage (Ann-Arbor) I+II: 7 patients, III+IV: 22 patients. NHL-histology: DLBCL: 18 patients, Burkitt/Burkitt-like lymphomas: 5 patients, others: 6 patients. 2 patients were treated before 1997, 27 patients after 1997 (HAART era), 9 patients are still alive with a median follow up of 52 months (range 35–92 months), 20 patients died after a median survival-time of 11 months (range 4-22 months).

**Conclusion:** There is no standard second line chemotherapy in patients with relapsed or progressive HIV-related NHL’s. High dose chemotherapy and autologous stem-cell transplantation should be discussed in all patients. IMVP-16 might be a less invasive option.
Introduction: We report 58 (56 male, 2 female) HIV-infected patients who presented with an isolated cervical mass lesion at the Department of Infectious Diseases of the Vivantes Auguste-Viktoria-Klinikum, Berlin from 2001 through 2006. None of the patients was an IVDU, all of the males were MSM, and the two females had acquired HIV infection heterosexually.

Methods: All patients were registered in the electronic medical database and data were retrospectively analysed for demographic, clinical, immunological and microbiological characteristics. Diagnosis was achieved by ultrasound guided biopsy in all patients. Biopsy material was evaluated after staining and immunohistology preparation.

Results: The mean time between diagnosis of HIV infection and presentation for a cervical mass lesion was 6.5 years (range 1-20 yrs.). In 23 cases the histopathological findings showed a lymphoproliferative disease, 11 patients had Hodgkin’s disease, 10 had Non-Hodgkin’s lymphoma and two patients had lymph node metastasis of a solid carcinoma. Ten patients had acid-fast bacteria identified, 7 of them had mycobacterium tuberculosis and 3 had atypical mycobacteria on culture. Twenty-two patients were diagnosed with non-specific lymphadenopathy, two patients had parotid cyst, and one had parotid pleomorphic adenoma. Patients with malignant, non-malignant, or infectious neck mass lesions showed no significant differences for age, duration of HIV infection and CDC staging.

Conclusion: Biopsy revealed a diagnosis with an urgent need for treatment in almost two-third of the patients. Based on these findings, biopsy of HIV-infected patients with a neck mass lesion is strongly recommended regardless of constitutional signs and symptoms.

B.9 (Vortrag)

Retrospektive Analyse von Symptomatik und Therapieverlauf bei neun HIV-positiven Patienten mit multizentrischem Morbus Castleman

Teutsch C.1, Träder C.1, Masuhr A.1, Arasteh K.1, Kowol S.1

1Vivantes Augustine-Ludwig-Klinik, Innere Medizin, Internistische Gastroenterologie, Berlin, Germany


B.10 (Poster)

Gastrointestinal spindle cell tumor in a young HIV1-infected African woman

Zoufaly A.1, Schmiedel S.1, Lohse A.W.2, van Lunzen J.2

1Universitätsklinikum Hamburg-Eppendorf, 1. Medizinische Klinik, Hamburg, Germany, 2Universitätsklinikum Hamburg-Eppendorf, Ambulanzzentrum Infektiologie, Hamburg, Germany

None of the patients was an IVDU, all of the males were MSM, and the two females had acquired HIV infection heterosexually.
rapid remission of intestinal lesions. On the background of HIV infection the presence of HHV8 as the causative agent of Kaposi sarcoma should be sought after as distinct treatment is indicated.

B.11 (Vortrag)

Muster neuropsychologischer Defizite bei klinisch asymptomatischen, HIV-1-positiven Patienten

Arendt G.1, Noitilng T.1, Husstedt I.-W.2, Koutsilieri E.3, Maschke M.4, Obermann M.4, Sopper S.5, Riederer P.6, ter Meulen V.3, Kompetenznetz HIV/AIDS

1Universitätsklinikum Düsseldorf, Neurologie, Düsseldorf, Germany, 2Universitätsklinikum Münster, Neurologie, Münster, Germany, 3Universität Würzburg, Virologie, Würzburg, Germany, 4Universitätsklinikum Düsseldorf-Essen, Neurologie, Essen, Germany, 5Deutsches Primatenzentrum, Virologie und Immunologie, Göttingen, Germany, 6Universitätsklinikum Würzburg, Psychiatrie und Psychotherapie, Würzburg, Germany

Einleitung: Die Bedeutung der HI-Viruslast (VL) im Liquor für cerebrale Funktionseinbußen HIV-1-positiver Patienten ist nach wie vor unklar. In der vorliegenden Studie wurden bei klinisch asymptomatischen Patienten die Ergebnisse rein motorischer Tests, von Tests, die cognitive, motorische und visuelle Fähigkeiten in Kombination erfassen sowie rein cognitiver Tests mit der HI-Viruslast im Liquor korreliert. Die These war die sog. „Störungsmuster“.

Methodik: Es wurden konsekutiv 142 Patienten rekrutiert, 111 von ihnen hatten eine höhere Plasma als Liquorviruslast, 33 ein umgekehrtes Verhältnis. Beide Gruppen wurden in 6 Untergruppen gegliedert: Gruppe 1+2: CDC-Frühstadienpatienten (A1+2, B1+2) +/-HAART, Gruppe 3+4: CDC-Spätstadienpatienten (A3, B3, C1-3) +/-HAART, Gruppe 5+6 Drogen-gebrauchende Patienten +/-HAART. Folgende Tests wurden angewendet:
- rein motorischer Test
- motorische Testbatterie nach Arendt et al., (1990)
- motorisch/cognitive Tests
- Trail Making Test Form A+B (TMT A + B)
- Digit Symbol Test (DST)
- Motorisch/cognitiv/visuelle Tests Grooved Pegboard Test (GPT)
- rein cognitive Tests
- Aids Dementia Scale (ADS)
- Syndrome Short Test (SKT)
- Digit Span Test (DSpT)
- Logical Memory Test I + II
- Mosaik Test

Ergebnisse: Siehe Tabelle 1

Die übrigen Tests waren unauffällig.

B.12 (Vortrag)

Neurodysfunction in immunodeficiency virus-infected subjects is due to disruption of the glutamatergic synapse

Meisner F.1, Scheller C.1, Neuen-Jacob E.2, Sopper S.3, Vosswinkel D.2, ter Meulen V.1, Koutsilieri E.1, (for the German Competence Network HIV/AIDS)

1University of Würzburg, Institute of Virology and Immunobiology, Würzburg, Germany, 2University of Düsseldorf, Institute of Neuropathology, Düsseldorf, Germany, 3German Primate Center, Göttingen, Germany

Glutamate-mediated neurodysfunction in HIV infection has been primarily suggested by in vitro studies. The regulation of glutamatergic neurotransmission in inflammation is a complex interaction between activation of immune mediators and adaptive changes of the functional elements of the glutamatergic synapse. We have used the most relevant animal model for HIV infection, the simian immunodeficiency virus (SIV)-infected macaques, to answer the questions
whether perturbation of glutamate neurotransmission is evident during progression of immunodeficiency disease, b) what are the mechanisms underlying this impairment and c) what are the consequences on neuronal function.

Disease progression both in the periphery and in the brain was documented by clinical and general pathological examination, plasma and CSF viral RNA load, T-cell analysis and brain histopathology. We report for the first time disruption of amino acid transporters (EAATs) during SIV infection and a break down of EAATs associated with development of rapid AIDS. This great impairment is accompanied by increases in glutamate levels and changes in the expression of NMDA subunits during disease progression. In accordance to a recent study reporting that TNF-alpha downregulates EAAT2, we found higher TNF-alpha production in microglia isolated from these animals. TNF-alpha production was correlated with activation status of microglia. In these settings, we found dramatic decrease in function of cholinergic neurons without an effect on GABA neurons in the putamen of animals with AIDS. Our data on SIV-infected macaques support the glutamate hypothesis for HIV dementia and suggest that the pathogenetic mechanism for the neurodysfunction is the break down of glutamate clearing which occurs in the stage of AIDS and which is associated with high levels of TNF-alpha produced by activated microglia.

**B.13 (Poster)**

**Impairment of sexual well-being in HIV-positive women**

*Sonnenberg-Schwan U. 1, Müller M. 2, Kästner R. 2, Gingenmaier A. 2*

1German AIDS Society (DAIG e.V.), Section ALL AROUND WOMEN special, Munich, Germany, 2Gynecological Hospital, University Ludwig - Maximilian, Munich, Germany

**Objectives:** Sexual dysfunctions (SD) or impairment of sexual well-being are often reported by HIV positive men and women. Studies in male patients show associations of SD with HAART, but also with psychosocial factors. In women, impairment of sexual well-being is especially pronounced after HIV diagnosis. Data on the prevalence or variety of SD in HIV positive women is scarce. We assume that SD is associated with multiple bio-medical and psychosocial factors. The study is aiming at identifying factors influencing sexual well-being in HIV-positive women.

**Methods:** In a cross-sectional approach, from 09.2002 – 04.2006 77 HIV-positive and a control group of 63 HIV-negative women were examined using a set of semi-standardised and standardised questionnaires comprising socio-demographics, partnership, reproduction, physical and psychological symptoms, impairment of sexual well-being, body image, QoL, and gynaecological and laboratory parameters.

**Results:** Mean age of the study group was 37.9 years (range 22-63), of the control group 33.4 (range 19-64). 77% were taking ARVs. 14% vs. 3% were migrant women, 62% vs. 76% were living in a partnership, 44% vs. 34% had children. 40% vs. 24% reported their sexual well-being as being often or always impaired. Sexual abuse had occurred in 35% vs. 24%. Complete withdrawal from sexual activities after HIV diagnosis occurred in 31% of the study group. Although sexual well-being improves over time, HIV-positive women reported a wide range of psychological and physical symptoms: mainly peripheral fat loss (26%) fatigue (26%), mood disorders (22%) and lack of sexual desire (21%) (only symptoms marked as “severe”). 23% felt their sexual life was impaired by side-effects of HAART.

**Discussion:** HIV-positive women showed a greater impairment of sexual well-being than HIV-negative women. Findings stress the variety of factors associated with sexual health and identify a range of physical and psychological symptoms. Due to the small study population, associations with HAART could not be analysed. Health practitioners should include the assessment of sexual well-being of HIV-positive women and intervention strategies as important factors of living and coping with HIV/AIDS. Attributing SD to HAART might interfere with adherence.

**B.14 (Poster)**

**Dysphagia and cervical lymphadenopathy in homosexual men**

*Karcher H. 1, Halleck P. 2, Loddenkemper C. 3, Zeitz M. 1, Schneider T. 1*

1Charité-University Medicine, Campus Benjamin-Franklin, Department of Gastroenterology, Rheumatology and Infectiology, Medical Clinic I, Berlin, Germany, 2Charité-University Medicine, Campus Benjamin-Franklin, Department of Otorhinolaryngology and Head and Neck Surgery, Berlin, Germany, 3Charité-University Medicine, Campus Benjamin-Franklin, Department of Pathology, Berlin, Germany

Two homosexual male patients (32 and 48 years old) presented after 3-4 weeks of recurrent fever, fatigue, painless left cervical swelling and dysphagia. One patient was HIV-infected (CDC stage B3). Cervical computed tomography revealed left pharyngeal wall swelling and enlarged lymph nodes in both patients (figure, A, arrow). One patient also had an enlarged left tonsil. Further exploration was performed to exclude a malignant lymphoma. In one patient, fiberoptic panendoscopy showed a mucosal ulcer extending from the left pharyngeal base of the epiglottis into the false vocal fold (figure, B); biopsies were taken from the ulcer. An ulcer was detected in the left tonsil of the other patient after a bilateral tonsillectomy. Histopathology showed follicular hyperplasia and ulcerated tonsilar epithelium as well as endothelial cell swelling and a chronic inflammatory infiltrate containing many plasma cells (figure, C; hematoxylin-eosin x 100). The Warthin-Starkey silver stain disclosed numerous coiled spirochetes (figure, inset, oil x 1000). Both patients had similar histopathologic findings. The diagnosis of primary syphilis was serologically confirmed. Both patients recovered completely after penicillin treatment. Cervical lymphadenopathy with recurrent fever for several weeks is indicative for a malignant lymphoma and this life-threatening disease must be excluded by histopathologic examinations. A Warthin-Starkey stain and serologic examinations may be helpful in differential diagnosis. A throat ulcer combined with cervical lymphadenopathy is a relatively untypical oral manifestation of primary syphilis since ulcers are usually seen in the lips, tongue, palate or in the buccal mucosa. Moreover, oral ulcers occur more frequently in the secondary disease stage. Due to increasing rates of syphilis infections especially in homosexual men and the popular practice of unsafe oral-genital sex untypical manifestations as described here will probably increase. Clinicians should be aware of this important differential diagnosis in cervical lymph node swelling (Figure 1A-C).
with HIV infection is unknown. We aimed to investigate about 10% in the general population. The association of RLS
The life-time prevalence of restless legs syndrome (RLS) is
The diagnosis of RLS in HIV infected patients.

A standardized questionnaire was presented to 228 HIV infected patients of the HIV outpatient clinic at the Department of Neurology, University of Münster, Germany. 129 patients (57% recall; 15% female, 44 ± 9 years; mean CD4+ cell count 333 ± 274/µl, 82% under highly active antiretroviral treatment) were included in the statistical analysis. 100 age- and sex-matched controls (20% female, 42 ± 13 years) were recruited from waiting relatives of surgical patients. Beside demographic and disease-specific data, the questionnaire included the diagnostic questions for RLS and the RLS severity scale by the International RLS Study Group. Diagnosis of RLS was confirmed by experienced neurologists.

33.3% of the HIV infected patients and 7.0% of the controls (p<0.001) fulfilled the diagnostic criteria for RLS. The mean RLS severity score was higher in HIV infected patients (19.5±7.2) than in controls (7.3±1.5; p<0.001) and correlated inversely with the CD4+ cell count (r=-0.381; p=0.024) and the BMI (r=-0.548; p<0.001) but not with other disease-specific factors. HIV infected patients show a significantly higher prevalence rate for RLS than the general population. The HIV infection itself with its immunological changes and involvement of the central nervous system may predispose for a risk of RLS in HIV infected patients.

B.16 (Poster)
Epilepsy in HIV infected patients – diagnostic value of EEG changes

Methods: The patient charts of all HIV infected patients admitted to the neurological inpatient clinic of the University of Münster, Germany, between 2004 and 2006 were analysed concerning the following items: demographic data, HIV related data, epileptic seizures, EEG abnormalities, and cerebral imaging data.

Results: In this population, 11/40 HIV infected patients (28%) had at least one epileptic seizure. Seizure aetiology was cerebral opportunistic infection in six patients (55%), HIV associated encephalopathy in one patient (9%), concurrent aetiology in three patients (27%), and seizures of unknown origin in one patient (9%). 7/11 HIV infected patients with epilepsy (64%) had interictal EEG abnormalities: Seven patients (64%) had focal slowing, two patients (18%) had generalized slowing, and one patient (9%) had focal spiking. Only four patients (36%) showed a good correlation between the localization of HIV related brain lesions and the localization of EEG changes. All patients with subcortical brain lesions due to progressive multifocal leukoencephalopathy (PML) (4/11) had temporal slowing.

Conclusion: EEG is a sensitive tool in HIV infected patients with epilepsy. However, our data suggest that EEG changes due to HIV associated brain lesions are non-specific and of low prognostic value concerning the localization of the epileptogenic lesion. Temporal slowing may indicate a subcortical lesion.

B.17 (Poster)
Neuropsychologische Defizite und zentralnervöse Zytokinspiegel bei HIV-Patienten

and a antiretroviral treatment was seen (viral load 2600 cp/ml, CD4 510 cells/µl). In the 19+2 week of gestation a pronounced TTTS with pathological color duplex sonography of the donor (195g) and the acceptor (326g) with a massive polyhydramnion was established. Concerning the wack prognosis the indication for a laser photocoagulation was set. To reduce the risk of a vertical HIV transmission a antiretroviral therapy with Kalerta and Tru-

**Ergebnisse:** Alle Patienten unterschieden sich nicht hinsichtlich ihres Alters und der CD4-Zellzahl. Die Viruslast war hoch in Spiegeln von ALCAM (CD166), Fas (CD95) und IL-

**Diskussion:** Die Studie konnte einen schwachen Zusammenhang zwischen entzündlichen Reaktionen und neuropsychologischen Defiziten im Zentralnervensystem von HIV-Patienten mit oder ohne antiretrovirale Therapie feststellen. Interessant ist, dass es offensichtlich einen frühzeitigen, direkt virusvermittelten Schaden bei hoher Virusreplikation gibt, der durch eine antiretrovirale Therapie nur unvollständig positive beeinflussbar ist. In späten Stadien ist eine Virusreplikation unterhalb der derzeitigen Nachweisbarkeitsgrenze in Zusammenhang mit einer autoimmunologischen Dysfunktion des Immunsystems als Mediator der fortschreitenden neuropsychologischen Defizite wahrscheinlich.

**B.18 (Vortrag)**

**Impact of depression on overall and health related Quality of Life (QoL) in HIV- and cancer-patients**

Wolff W.1, Kofahl-Krause D.2, Stoll M.1, Schmidt R.E.1

1Medical School Hanover, Clinical Immunology, Hannover, Germany, 2Medical School Hanover, Haematology, Haemostaseology and Oncology, Hannover, Germany

**Aims:** The estimates for lifetime prevalence of depression in HIV patients differ between 22 and 45% compared to appr. 15% in non HIV infected people (1). Also in cancer patients published prevalences of depression range between 15 and 53% (2). The impact of depression on overall or health related QoL in these groups is very plausible but not well established. HIV- and cancer-Patients were assessed by different tools for QoL and depression personality.

**Methods:** 50 HIV- and 54 cancer-Patients were assessed for their overall QoL with the SEIQoL-DW interview (3) and the MLDL questionnaire (4) and for their health related QoL with the SF-36 questionnaire (5). Depression was assessed with the BDI questionnaire (6) and personality with the FPI-R inventory (7). Stepwise regression analyses were performed.

**Results:** (See Table 1)

Referring to the health related QoL depression is the first factor for both HIV and cancer patients in the subscale health perception explaining 40.6% of variance (HIV patients) and 39.8% (cancer patients). In the category mental health depression is the first factor for the HIV group explaining 52.5% of variance, but for the cancer group BDI-depression is only the second factor explaining 12.2% of variance behind the first factor FPI-emotionality with 49.0%. The models for all other subscales do not include BDI-depression or show it only as the second or third factor explaining minor percentages of variance.

**Conclusions:** Depression substantially influences QoL in both HIV and cancer patients. The overall QoL seemed to be even more affected than health related QoL. Regarding their mental health HIV patients are more affected by depression than cancer patients.


**B.19 (Poster)**

**Management of a HIV-exposed pregnancy with twin-to-twin transfusion syndrome (TTTS)**

Kost B.P.1, Kästner R.1, Sovric M.1, Kainer F.1, Gingeimaier A.1

1UFK, LMU München, Frauenklinik-Innenstadt, München, Germany

**Objectives:** Options and risks of an invasive intervention (laser photocoagulation) in twin-to-twin transfusion syndrome (TTTS) and HIV-infection in pregnancy.

**Method:** A case report

**Results:** HIV infection of a 27 year old III-para I-para with monozygotic, diamniotic twins was diagnosed external in the 9th week of gestation. At that time no indication for antiretroviral treatment was made. Concerning the wack prognosis the indication for a laser photocoagulation was set. To reduce the risk of a vertical HIV transmission a antiretroviral therapy with Kalerta and Tru-
vada was started. The laser photoagulation and a drainage of the amniotic fluid (3.5l) was carried out in the 19+6 week of gestation (viral load of the mother 500 copies/ml, HIV-PCR of the amniotic fluid was negative). Due to a zero growth of the second fetus (alumnum donor), pathological color duplex sonography and suspicious CTG delivery was carried out via section caesarea in the 28+4 week of gestation. At the 20th of november 2006 childbirth of two male newborns (1215g and 570g) without any evidence for an HIV-infection so far.

Case report: The medical care of HIV-infected pregnant women is according to standardized rules. Increasing more complex cases are in need for individual and interdisciplinary care.

**B.20 (Poster)**

**Polymyositis - differential diagnosis in HIV-associated myopathy**

**Kaup R.¹, Schlottmann R.¹, Ellrichmann G.², Ellrichmann M.¹, Banasch M.¹, Potthoff A.³, Brockmeyer N.³, Schmidt W.¹**

¹St. Josef-Hospital, Ruhr-Universität Bochum, Innere Medizin, Medizinische Klinik I, Bochum, Germany,
²St. Josef-Hospital, Ruhr-Universität Bochum, Neuropsychische Klinik, Bochum, Germany,
³St. Josef-Hospital, Ruhr-Universität Bochum, Dermatologische Klinik, Bochum, Germany

**Case report:** Elevation of muscular creatinine phosphokinase is often seen in HIV-infected patients.

We describe a 31 year old HIV infected male from kamerun with WHO stadium CDC B2, presented with muscle pain, proximal muscle weakness, weight loss and markedly elevated creatinine phosphokinase (>3000 U/l) which was originally ascribed to nucleoside induced mitochondrial toxicity. Despite withdrawal of antiretroviral therapy he developed progressive disease. Further investigation excluded malignancy.

Electromyographie and muscle biopsy were performed and polymyositis was diagnosed. The patient recovered quickly and creatinine phosphokinase markedly reduced after initiation of oral prednisolone therapy.

**Conclusion:** This case demonstrates the importance of muscle biopsy in HIV infected patients with unclear myopathy. Musculoskeletal manifestations are common in HIV infected patients and can occur in any stage of disease. Myopathies may be caused by infection (e.g. viral, bacterial, parasitic), drug effect (e.g. AZT myopathy), neoplasic processes (e.g. lymphoma) or rheumatic disease (e.g. polymyositis).

Knowledge of the conditions affecting muscle in HIV infected patients is essential for successful management. Muscle biopsy is important for diagnosis since there are many reasons for myopathy in HIV infected patients and accurate diagnosis is essential for effective therapy.

**B.21 (Poster)**

**Anfälle und Epilepsie bei HIV-Infektion – Untersuchung zur Häufigkeit bei Patienten einer neurologischen Universitätsklinik**

**Kovac S.¹, Kellinghaus C.¹, Engbring C.¹, Möddel G.¹, Evers S.¹, Husstedt I.W.¹**

¹Universitätsklinikum Münster, Klinik für Neurologie, Münster, Germany

**Ziele:** Erhebung von systematischen Daten zur Inzidenz und Prävalenz von epileptischen Anfällen bei HIV-infizierten Patienten einer neurologischen Universitätsklinik.

**Methodik:** In der Patientenbank der Klinik für Neurologie der Universitätsklinik Münster wurde nach Patienten HIV-positiven Patienten identifiziert, die zwischen 1992 und 2004 stationär oder ambulant behandelt wurden. Die Krankenakten dieser Patienten wurden nach Hinweisen auf akute epileptische Anfälle oder Epilepsie durchsucht. Dabei wurden alle verfügbar angeamnestischen und klinischen Daten sowie Angaben zur Therapie und Outcome erfasst.

**Ergebnis:** Wir identifizierten 831 HIV-infizierte ambulante und stationäre Patienten im Untersuchungszeitraum. Von diesen hatten 51 (6,2%) epileptische Anfälle. Elf Patienten (22%) erlitten einzelne Anfälle als Begleitsymptom akuter ZNS-Erkrankungen, Alkohol- oder Drogenzusatz bzw. Schlafenzug, oder ungeklärter Ätiologie. Bei der Mehrheit der Patienten (n=32, 63%) traten die Anfälle rezidivierend und im Verlauf der Infektion auch ohne akuten Anlass auf. Bei acht der 51 Patienten (16%) war eine Epilepsie schon vor Beginn der HIV-Infektion bekannt. Die Anfallssymologie war generalisiert bei 40 Patienten, einfach-fokal bei 8 Patienten und komplex-fokal bei 3 Patienten. Siebenundzwanzig Patienten (53%) wurden längerfristig antikonvulsiv behandelt, davon 14 mit Gabapentin und 9 mit Carbamazepin.

**Schlussfolgerung:** Epileptische Anfälle sind ein wichtiges neurologische Symptom im Verlauf der HIV-Infektion. Obwohl das Auftreten der Anfälle in manchen Patienten auf eine akute Krankheitsphase beschränkt bleibt, entwickelt die Mehrheit eine Epilepsie und benötigt antikonvulsive Therapie. Trotz der Verfügbarkeit alternativer Präparate werden viele Patienten immer noch mit pharmakokinetisch ungünstigen Antikonvulsiva behandelt.

**B.22 (Poster)**

**Allergic diathesis in HIV-infection**

**Potthoff A.¹, Tigges C.¹, Doerler M.¹, Brockmeyer N.H.¹, Kompetenznetz HIV/AIDS**

¹St. Josef Hospital, Dermatologie, Bochum, Germany

**Introduction:** In the course of HIV infection multiple skin reactions can be observed. Itching and dry skin (xerosis cutis) has been reported repeatedly in association with antiretroviral therapy (HAART). In HIV infection IgE is an unreliable marker for allergic diathesis, since it is commonly elevated in these patients. Primary manifestation and worsening of allergic diathesis has been linked to HIV-infection.

**Materials and methods:** In this study allergic diathesis was determined with the “Erlanger Atopic Score” (EAS). It includes 24 items with a maximum of 42.5 points. Itching was monitored by a visual analog scale (VAS) from 0 to 10 and xerosis cutis was evaluated by a dermatologist.

**Results:** 195 caucasian patients (173 male and 22 female, mean age 42.5 years) were examined. 44 had no HAART, 64 a PI containing regimen and 87 an NNRTI containing regimen. CD4 cell count was >500/µl in 99 patients, between 200 and 499/µl in 75 patients and <200/µl in 21 patients. The EAS was negative in 65 patients, questionable in 90 patients and positive in 40 patients. Itching grade 1-3 was seen in 32 patients, grade 4-6 in 23 patients and grade 7-10 was seen in 22 patients. 118 patients had no pruritus. 106 patients had xerosis cutis. 23 of 53 patients treated with an NRTI/PI containing regimen had pruritus (43%) and 33 dry skin (62%). 31 of 79 patients treated with an NRTI/NNRTI containing regimen had pruritus (39%) and 43 dry skin (54%). 17 of 44 patients with...
out HAART had pruritus (38%) and 18 dry skin (40.9%). IgE was elevated in 43 patients, 8 of those had a CD4 cell count <200. In total 21 patients with elevated IgE levels had a positive EAS.

**Discussion:** A lot of HIV positive patients suffer from itchy, dry skin. In 20.5% of the patients an allergic diathesis could be seen in the EAS. Dry skin seems to be more common in PI containing regimens, which was expected since e.g. indinavir is known for its retinoid-like effects. The prevalence of pruritus is high in all groups and much higher than in other populations.

**Conclusion:** The EAS can be helpful to distinguish between xerosis cutis with pruritus and atopic eczema. The prevalence of dry and itchy skin in HIV positive patients is very high and should be addressed competently by the HIV specialist.

**B.23 (Poster)**

**Oral manifestations in correlation with highly-active antiretroviral therapy in adult hiv-seropositive patients**

**Jordan R.¹, Gängler P.², Raetzke P.³**

¹Universität Witten/Herdecke, Fakultät für Zahn-, Mund- und Kieferheilkunde, Abteilung für Konservierende Zahnheilkunde, Bereich Community Oral Health, Witten, Germany, ²Universität Witten/Herdecke, Fakultät für Zahn-, Mund- und Kieferheilkunde, Abteilung für Konservierende Zahnheilkunde, Witten, Germany, ³Johann Wolfgang Goethe-Universität, Zentrum für Zahn-, Mund- und Kieferheilkunde (Carolinum), Poliklinik für Parodontologie, Frankfurt, Germany

**Aims:** Declining prevalences of opportunistic infections and oral manifestations have been noticed since inauguration of highly-active antiretroviral therapy without evidence regarding specific therapeutics. The aim of this study was to evaluate correlations between the epidemiology of oral manifestations and key drugs of antiretroviral therapy (nnrti vs. pi) in the contemporary haart-era.

**Methods:** 92 HIV-1-seropositive patients on a medium age of 36 years have been examined for oral manifestations according to the EC-Clearinghouse Classification of Oral Lesion in HIV-Infection during dental routine check up. After building subgroups of antiretroviral therapy and non-therapy the signs of disease were analyzed statistically for smoking behaviour, CD4-counts, viral load and antiretroviral composition.

**Results:** Acute periodontal diseases (p=0.008), esp. necrotizing ulcerative periodontitis (p<0.005), erythematous candidiasis (p=0.01) and oral hairy leukoplakia (p<0.05) have been statistically associated with a high vial load above 10,000 rna-copies/ml plasma and antiretroviral non-therapy. The comparison of key drugs of a highly-active antiretroviral therapy include various inflammatory reactions due

**Conclusions:** Highly-active antiretroviral therapy and a low viral load below 10,000 copies/ml plasma are negatively associated with oral manifestations in HIV-infection. A manifestation triad consisting of candidiasis, oral hairy leukoplakia and necrotizing ulcerative periodontitis could be a reliable prognostic marker for an existing and progressive hiv-infection or failing antiretroviral therapy.

**B.24 (Poster)**

**Development of an IRIS-like syndrome of the CNS after HAART initiation in a patient with listeriosis and advanced immune-deficiency**

**Herlitzy S.¹, Schmiedel S.², Kreuzberg C.², Degen O.², van Lunzen J.¹**

¹Ambulanzzentrum des UKE GmbH, Infektiologie, Hamburg, Germany, ²Universitätsklinikum Hamburg Eppendorf, Medizinische Klinik 1, Hamburg, Germany

**Background:** HAART-induced immune restoration may induce a paradoxical clinical deterioration due to an immune reconstitution inflammatory syndrome (IRIS) in rare cases with advanced immune-deficiency. This syndrome can manifest with a wide range of symptoms and is mostly associated with systemic inflammatory responses to subclinical opportunistic infections. Recently an increasing frequency of IRIS of the CNS after HAART initiation was discussed.

**Case presentation:** A 41-year-old man, was firstly diagnosed with HIV-1 infection in November 2006, during a septicemia with Listeria monocytogenes without detection of Listeria in the CSF. He responded rapidly to an antibiotic treatment with i.v. ampicillin for 3 weeks. At this time his CD4 T cell count was 3 cells/µl and the plasma HIV RNA load 970,000 copies/ml. Following a four week HAART with Lopinavir/r, Tenofovir and Emtricitabin the viral load decreased to 70 copies/ml and the CD4 cell count increased to 25 cells/µl. One week later the patient presented with an impaired vision and an up-beat-nystagmus. Brain magnetic resonance imaging (MRI) demonstrated multiple small lesions in brain stem and cortex compatible with encephalitis. The CSF showed an inflammatory response with a pleocytosis of 63 cells/ml, common pathogens including L. monocytogenes were ruled out by CSF culture and PCR. The toxoplasma serology was negative as well as PCR for Tbc, CMV and Cryptococcus antigen in the CSF. So we suspected that the rapid response to HAART induced an IRIS on the basis of a pre-existing HIV-encephalitis. The clinical signs and symptoms improved rapidly after an immunosuppressive therapy with prednisolon in a dose of 1 mg/kg/bodyweight.

**Discussion:** Rarely the development of cerebritis in the course of an infection with L. monocytogenes is described. There was no proof of L. monocytogenes in the CSF of this patient and the neurological symptoms started more than six weeks after a successful antibiotic therapy with ampicillin and a good clinical restoration. Thus, the development of cerebral IRIS in association with an underlying HIV-encephalitis is likely in this patient and might be of increasing importance in patients starting HAART in advanced stages of immunodeficiency.

**B.25 (Poster)**

**Lopinavir-associated tenosynovitis resembling lipomatosis cured by switch to atazanavir plus saquinavir: An immune reconstitution inflammatory phenomenon?**

**Behrens G.¹, Moebius U.², Ulbricht K.², Heiken H.², Stoll M.², Schmidt R.E.²**

¹Hannover Medical School, Clinical Immunology, Hannover, Germany

**Background:** Side effects after initiation or switch of antiretroviral therapy include various inflammatory reactions due to...
to immune reconstitution frequently presenting with atypical clinical signs and symptoms.

**Results:** A 62 year old HIV-infected patient reported development of a focal swelling of the dorsum of the left hand resembling lipomatosis 2 weeks after switching to an antiretroviral therapy regimen consisting of AZT, 3TC, and lopinavir. At that time CD4 cell count was 247/µl and viral load below the limit of detection. Four months later therapy was changed to lopinavir monotherapy because of toxicity (anemia) and further two months later the patient realised a similar swelling of the dorsum of his right hand with progress over two months. The tumor of the left hand was then diagnosed as tenosynovitis based on magnetic resonance tomography (MRT) revealing a non-infiltrating fluidlike process with a size of 7x16x25 mm and peripheral vascularisation consistent with an inflammatory process. He complained about no pain or other signs and symptoms. He had been on different combination therapies including non-nucleoside and nucleoside analogue reverse transcriptase inhibitors for three years with good immunological response (CD4 cells 8/µl, > 750,000 copies HIV-RNA copies/ml plasma before therapy). He had never had lipomas before in his live nor did any of his family members. After initiation of lopinavir therapy increase of C-reactive protein (CRP) to 46.9 mg/l was observed. Because of the close time relation of the hand swelling and start of lopinavir treatment, the therapy was switch to atazanavir 300mg QD, ritonavir 100mg BID, and saquinavir 500mg BID. This was followed by immediate and complete disappearance of the left and significant reduction of the right dorsal hand lipomas within a few weeks. Six weeks after the last therapy switch CRP had declined to 27.3 mg/l.

**Conclusion:** Tenosynovitis associated with protease inhibitor therapy can be misdiagnosed as lipomatosis. Whether this patient suffered from either immune reconstitution syndrome or rather drug related toxicity remains unclear. Replacement of lopinavir led to complete clinical resolution and drop of inflammatory parameters.

**B.26 (Vortrag)**

**Untreated HIV patients with undetectable virus – What happens to the CD4 cells?**


**1HIV Research and Clinical Care Centre Munich, Munich, Germany, 2MUC Research, Munich, Germany, 3HIV Outpatient Practice Kaiserdamm, Berlin, Germany, 4Private Practice for Internal Medicine, Hematology and Oncology, Mannheim, Germany, 5HIV Outpatient Practice, Stuttgart, Germany, 6Private Practice for Hematology, Oncology and Infectious Diseases, Karlsruhe, Germany, 7University Hospital of Bonn, Bonn, Germany, 8Ärzteforum Seestraße, Berlin, Germany, 9HIV Outpatient Practice, Berlin, Germany**

**Background:** To evaluate whether low level viral replication in untreated HIV-1 patients will persistently prevent immunological deterioration and disease progression.

**Methods:** Ongoing multi-centre cohort study in untreated HIV-1 patients with low virus replication. Entry criteria were a persistent viral load (VL) level <500 copies/ml without any treatment (transient VL-blips allowed), an observation time of ≥1.5 years, and the availability of ≥3 VL-measurements <500 copies/ml.

**Results:** So far, N=56 of 64 reported patients fulfilled the criteria: 27 females (8/27 pattern II), 29 males. Median age at time of HIV-diagnosis was 29 years (range 17–56). At the latest documented time point (LOCF), median time since HIV-diagnosis was 8.7 years; median observation time was 6.5 years. Median CD4 cell counts at the first and latest documented time points were 780/µl and 720/µl (p=n.s.). In 89%, VL was <500 copies/ml; in 57%, VL was <50 copies/ml (LOCF). Two patients had >1,000 copies/ml (5,704 and 1,288 copies/ml). In the 1st patient, VL was undetectable for 8 years (with few exceptions) and then gradually increased to 5,704 copies/ml. Since 1996, CD4 count declined from >1,500/µl to ≤400/µl. In the 2nd patient, CD4 count declined from >600/µl to ≤400/µl. Recently, this patient was started on ART. Two further patients (HIV-diagnosis in 1997 and 1986) were started on ART despite persistent VL-suppression: one case due to a CD4 decline from >600/µl to <200/µl, and the 2nd case due to persistently low CD4 cells and a decline in relative CD4 count (268/µl, 8%).

**Conclusions:** In this specific cohort of untreated HIV patients with low level virus replication, we saw significantly more females than expected according to epidemiological data from Germany. In most of the patients CD4 counts remained stable. But in few patients, persistent viral load levels <500 copies/ml did not preclude a gradual CD4 cell decline.

**B.27 (Poster)**

**Assoziation von HIV-Serostatus mit nasaler Kolonisation durch Methicillin - resistenten Staphylococcus aureus (MRSA) oder Methicillin - sensiblen Staphylococcus aureus (MSSA) bei ambulanten Patienten**

**Boynern J.1, Suphth-Schröder B.1, Greiser J.1, Sternfeld T.1, Seybold U.2, Hogardt M.3**

1Klinikum der Universität München, Med. Poliklinik, München, Germany, 2Emory University School of Medicine, Division of Infectious Diseases, Atlanta, United States of America, 3Max von Pettenkofer Institut, Lehrstuhl Bakteriologie, München, Germany

**Hintergrund:** In den letzten Jahren beobachteten wir mehrfach Fälle schwerer S. aureus – Infektionen, auch unter HAART. Die Kolonisation mit S. aureus (SA) ist ein Risikofaktor für eine spätere Infektion. Die Prävalenz der nasalen SA Kolonisation bei HIV infizierten Patienten wurde in Deutschland bisher nicht untersucht.


**Ergebnisse:** Zwischen 10/06 und 2/07 wurden 84 HIV-Infizierte und bisher 30 Kontrollpatienten untersucht. Das mediane Alter der Pt betrug 45 Jahre (24 - 67), 93% waren Männer. Bei 43 Pt (51%) fand sich eine Kolonisation der Nase mit SA: bei 41 (49%) mit MSSA und bei 2 (2,4%) mit MRSA. In der Kontrollgruppe mit nicht HIV-Infizierten wurde eine nasale Kolonisation mit MSSA bei 6 Pt (20%) gefunden (p<0,003), bei keinem der Kontrollpatienten MRSA. Nur 4
der positiv getesteten Pt (9,3%) hatten in den letzten 12 Monaten einen Krankenhausaufenthalt mit systemischer Antibiotikagabe. Vier Pt (9,3 %) hatten CD4 Helferzellen < 200/µl. 5 (11,6%) erhielten keine ART, darunter waren 3 (7,0%) therapienaiv. Die Viruslast war bei allen 79 therapierten Pt < 400 cp/ml.


B.28 (Vortrag)

CD4 cell reconstitution is impaired in patients with toxoplasma encephalitis as an AIDS indicator disease as compared to patients with pneumocystosis in the ClinSurv cohort

Kastenbauer U, Kollan C, Hamouda O, Bögner JR, ClinSurv Studiengruppe

1Klinikum der LMU, Infektionsabteilung, München, Germany, 2Robert Koch Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: Toxoplasma encephalitis is still a relatively frequent AIDS indicating disease in Germany. Unlike in other opportunistische infections (OI), guidelines regarding the duration of secondary prophylaxis and treatment continuation are not available, probably due to the fact that this disease is less frequent in North America. There is no data on immune reconstitution in antiretroviral naive patients with toxoplasmosis. The observation of several cases with a very slow increase of CD4 cells upon start of antiretroviral treatment (ART) prompted us to investigate the topic in the ClinSurv cohort.

Methods: ClinSurv is an open multicentre observational cohort coordinated by the Robert Koch Institute collecting anonymised patient data on diagnoses, treatment, and laboratory items from 17 centres in a standardised format. Patients who met the following criteria were selected: diagnosis of toxoplasmosis (TOXO) or pneumocystosis (PJP) between 1999 and 2005, no ART prior to OI diagnosis, sufficient documentation of ART, CD4, viral load for at least 12 months. Descriptive analysis and group comparisons were performed using SPSS statistical package.

Results: A total of 269 patients were eligible for analysis. 64 patients were in the TOXO – and 205 in the PJP group. Demographic baseline data did not show significant differences with regard to gender, age (40.4 years), ethnicity, and baseline CD4 counts (71.8 vs 57.9 /µl, p = 0.219). After six months and 12 months CD4 cells increased less rapidly in the TOXO versus the PJP group (99.2 vs 136.7 /µl, p = 0.026; 12 months: 154.1 vs 211.0 /µl, p = 0.003). Viral load was higher in the PJP group at baseline (168641 vs 336684 /µl, p = 0.062), but the percentage of patients with VL below detection limit did not differ after 6 (74.2% vs. 78.1%, p = 0.458) and 12 months (80.7% vs 83.1%, p = 0.682).

Conclusion: Our data shows for the first time that the average CD4 increase of patients with TOXO is slower as compared to PJP. This is important because most clinicians would not be prepared to discontinue follow up TOXO-therapy unless CD4 counts of 200 are reached. Explanations for our finding might be the myelosuppressive effect of pyrimethamine or not yet known interactions of TOXO therapy with ART.

B.29 (Poster)

Therapieunterschiede bei HIV-infizierten Frauen und Männern in einer monozentrischen deutschen HIV-Kohorte

Balogh A, Mueck B, Koegl C, Wolf E, Jaegel-Guedes E, Jaeger H

1MUC Research, München, Germany, 2Gemeinschaftspraxis Dr. Jaegel-Guedes - Dr. Jaeger, München, Germany

Fragenstellung: Sind innerhalb einer monozentrischen Kohorte von 1056 HIV-infizierten Patienten geschlechtsspezifische Unterschiede in der HIV-Therapie und im virologischen und immunologischen Ansprechen auf eine antiretrovirale Therapie zu erkennen?


Ergebnisse: 21% der Frauen bzw. 15% der Männer waren therapienaiv. In Therapiepause befanden sich 1% der Frauen und 2% der Männer. 77% der Frauen und 83% der Männer wurden z.Zt. mit antiretroviralen Medikamenten behandelt, davon 37% der Frauen und 32% der Männer mit NRTI/PI-Kombinationen. 35% der Frauen und 32% der Männer wurden mit NRTI/NNRTI-Regimen behandelt. Frauen wurden signifikant häufiger mit dem NNRTI Nevirapin behandelt (Frauen: 25% NVP, 10% EFV; Männer: 14% NVP, 18% EFV; p<0,001). Ein NRTI-Regime aus AZT+3TC+ABC

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Table 1.
B.30 (Vortrag)

Opportunistic infections 1995 -2006: A retrospective analysis of the AVK cohort

Traeder C.1, Kowol S.1, Masuhr A.1, Arastéh K.1

1Vivantes Auguste-Viktoria-Klinikum Berlin, Infektionologie, Berlin, Germany

HIV patients have been treated at Vivantes Auguste Viktoria Klinikum Berlin since 1985. In total, the number of episodes of treatment were 15228 until end of 2006, the number of different patients has been 5368 and constant with 750 – 850 patients / year.

All HIV positive patients in the AVK are registered with the electronic data base of the department of infectiology. The analysis was done by a retrospective analysis of this data.

From 15228 patients treated in 20 years 10523 showed an AIDS defining condition. Numbers peaked between 1991 – 1995 with 768 AIDS defining conditions (1991) minimum and 1086 AIDS defining conditions (1994) maximum. Since 1996 the absolute number of AIDS defining conditions decreased to 286 (2006) – 366 (2002) AIDS defining conditions. Most Opportunistic infections have decreased since 1996. However, candida esophagitis and recurrent pneumonia have shown constant numbers. Especially candida esophagitis seems to increase (maximum in 1994 with 94 CE, and again 2005 with 99 CE, total number 1206 CE 1985 - 2006). The OI with Cryptococcus neoformans remained constant over the years with 2 – 9 cases / year. Kaposi sarcoma has decreased dramatically. Non Hodgkin Lymphoma has also decreased. However, this is mainly due to the changed practice of treating NHL Patients in the out patient department.

An extensive table shows absolute numbers and percent-ages.

The age of patients has increased from 35 to 43 years. Furthermore the age of patients being first admitted to hospital has changed from 34 to 42 in 2005 (41 years in 2006) The duration of a hospital stay has steadily changed from 34 days in 1985 to 13.5 days in 2006. The number of patient’s repetitive stays in hospital were highest with 1.9 stays in 1993. Since 1996 stays have varied between 1.4 and 1.6 stays/patient.

The mortality has dramatically changed. A maximum of 263 deaths was reached in 1994. Since 2001 numbers have varied between 28 and 39 death/year.

B.31 (Vortrag)

Gender differences on demographics, disease stage, antiretroviral therapy, and response to therapy in the cohort of the German Competence Network HIV/AIDS

Kuemper H.1, Sonnenberg-Schwan U.1, Hahn M.2, Jaeger H.3, Plettenberg A.4, Göl; J.5, Moll A.5

Fäktenheuer G.6, Esser S.7, Skoetz N.8, Brockmeyer N.9, for the German Competence Network HIV/AIDS

1German AIDS Society, All Around Women Special, Bochum, Germany, 2University of Cologne, Institute for Medical Statistics, Informatics, and Epidemiology (IMSMIE), Cologne, Germany, 3MUC Research, Munich, Germany, 4Biological Institute for Interdisciplinary Medicine, Hamburg, Germany, 5Praxiszentrum Kaiserdammm, Berlin, Germany, 6University of Cologne, 7University Hospital of Essen, Dep. of Dermatology, 8Venerology and Allergology, Essen, Germany, 9Coordinating Center for Clinical Trials, Cologne, Germany, 10Ruhr-University, Clinic for Dermatology, Bochum, Germany

Objective: We examined differences between HIV+ women and men on demographics, disease stage, antiretroviral therapy (ART), and response to ART.

Method: Baseline and 6-month follow-up of a nationally representative patient cohort of the German Competence Network HIV/AIDS (n = 13435, 15% female, 85% male) was analyzed.

Results: Gender differences (p <.0001) were found on age, socioeconomic status, ethnicity, risk of infection, and disease stage. Women were more likely than men to be younger (41.37 ±10.41 vs. 44.77 ±10.21), African (22% vs. 3%) or Asian (6% vs. 1%) and less likely Caucasian (65% vs. 91%), employed (45% vs. 59%) or baccalaurean (26% vs. 40%) . Heterosexual contact, IV-drugs, blood products, work accident, and vertical transmission were more prominent in women, and homo-/bisexual contact in men. Despite time since diagnosis and initiation of ART did not differ at entry, women were more likely than men to have asymptomatic CDC-stage (40% vs. 35%), lower viral load (VL) log (2.76 ±2.0 vs. 2.92 ±1.22, n = 6854), and lower CD4 cells (472.72 ±264.00 vs. 490.21 ±261.30, p = .0422, n = 6854). Further, men were twice as likely as women to develop AIDS symptoms within 6 months (OR = 2.07, 95% CI 1.00 - 4.27, p = .0221, n = 824). Controlling for baseline gender differences on CD4 and VL changes over 6 months were no longer significant. Women were more likely than men to take NRTIs only (13% vs. 10%, p = .0026), while PI or NNRTI based regimens did not differ on gender. Controlled for baseline, there were no significant gender differences on viro-immunological response when stratifying for ART (PI, NRTI, NRTI/NNRTI, NRTI/PI, NRTI/NNRTI/PI, T-20 based regimen), except for NRTI/PI regimens: women had less VL reduction over 6 months than men (-0.01 ±1.13 vs. -0.25 ±1.05, p = .0221, n = 824).

Conclusions: Gender differences in the German cohort of HIV+ people comprise psychosocial factors, disease progression, ART regimen, and response to ART. Despite lower socioeconomic status, women may have a slower disease progression, or may be diagnosed at an earlier stage of disease (e.g., during pregnancy), take less potent ART with fewer side effects, and may show less virological response than men to PI based regimens. Underlying factors need to be unraveled.
B.32 (Vortrag)

Clinical correlates and consequences of discordant immuno-/virological response in patients initiating HAART at severe immunodeficiency

Kreuzberg C.1, Lüchters G.2, Hertling S.3, Degen O.3, van Lanzen J.3

1Universitätsklinikum Hamburg Eppendorf, Medizinische Klinik I/Ambulanzzentrum Infektiologie, Hamburg, Germany, 2Robert Koch Institut, Infektionsepidemiologie, Berlin, Germany, 3Universitätsklinikum Hamburg Eppendorf, Ambulanzzentrum Infektiologie, Hamburg, Germany

Background: Discordant immuno-/virological response has been described in HIV infected patients following initiation of HAART. However, the clinical consequences of such discordant response remain to be elucidated especially in patients starting HAART in advanced stages of immunodeficiency.

Methods: A cohort of 39 HAART naïve patients with severe immunodeficiency (CD4 counts below start of HAART < 100 cells/µl) but adequate antiviral treatment response (sustained virological suppression <400 copies/ml after 6 months of HAART) was followed for a mean observation period of 5.8 years (range 2.2 – 10.3). The occurrence of AIDS defining events and baseline parameters were compared between patients who showed cellular immune reconstitution (sustained rise in CD4 counts > 200 cells/µl on two subsequent occasions) after 1 and 2 years of HAART versus those with discordant response (suppressed viral load but no rise in CD4 > 200 cells/µl).

Results: At initiation of HAART 30/39 (76.9%) of the patients had at least one AIDS defining diagnosis. One third of the patients (12/39) developed a rise in CD4 count to > 200 cells/µl in the first year of therapy. There was no difference in mean initial CD4 counts and viral load (49 versus 28 CD4 cells/µl and 5.5 versus 5.6 log HIV RNA copies/ml) in patients with or without immunoreconstitution after year one. Five patients (12.8%) experienced at least one AIDS defining event during the first year of HAART, 4.80% of the events occurred in the discordant group. The overall incidence rate was higher (5/148 versus 1/71.5 person years) in this group. In the second year of HAART 26 (66.7%) reached CD4 counts above 200 cells/µl. Again mean CD4 counts and viral loads at initiation of HAART (39 versus 25; 5.6 versus 5.2 log) did not differ clinically significantly. Interestingly the overall incidence of AIDS defining events in long-term discordant patients was even lower (0/ 72.5 versus 6/146 person years).

Conclusion: Severely immunocompromised patients with discordant immuno-/virological response are at special risk to develop disease progression in the first year after initiating HAART but not thereafter. Long term inadequate rise in CD4 count does not seem to have clinical relevance in patients with sustained viral suppression.

B.33 (Poster)

CD4 cell count at initiation of HAART over time - An approach by using German ClinSurv multicenter cohort data

Kollan C.1, Kühne A.1, Hamouda O.1, for the ClinSurv Study Group

1Robert Koch Institut, Infektionsepidemiologie, Berlin, Germany

Objectives: Since introducing HAART the “philosophy” when to initiate therapy changed several times. The “hit ear-ly” era was followed by the paradigm to start late which meant at CD4 levels £200. The optimal time point to begin ART is still uncertain. This study aims to highlight the actual clinical reality in Germany in the past 10 years. Comparison of CD4-counts at ART onset in 21 HIV treatment centres between 1997 and 2006.

Methods: Analysis of CD4 counts at start of first-line ART by period of clinical observation. CD4 values closest to start-date were chosen in a range of 30 days before and 10 days after initial treatment. Patients where stratified into: (a) having been observed >45 days before ART and (b) £45 days of observation. CD4 counts were compared by the Kruskall-Wallis test.

Results: 1.552 patients were eligible, 578 for (a) and 974 for (b). The trend over time of median CD4 counts for both groups show a parallel course with a peak in the year 1998, 438 and 224 for (a) and (b) and a minimum in 2000, 93 and 221 for (a) and (b) respectively. The overall median is 171 and group medians are 252 (a) and 105 (b) (<p<0.001). Median number of days of observation before ART-start are 242 (a) and 14 (b), median time between CD4-date and ART-start are 11 (a) and 8 (b) days. In (a) 19% suffered an AIDS-defining disease compared to 35% in (b).

Conclusions: Patients first presenting at specialised centres briefly before initial ART are characterized by progressed HIV disease and higher morbidity. In this group the decision to start ART is not primarily guided by CD4 counts. Whereas longer previous observation might allow a CD4 guided decision to initiate ART. Our data suggest that after an era of early treatment at the end of the last decade ART is now initiated at CD4 ranging from 220 to 250. The low CD4 counts at initial treatment around the year 2000 was caused predominantly by the “latecomers”.

B.34 (Poster)

CAT – a treatment strategy in heavily pre-treated patients with multi-drug resistant HIV-1

Weber C.1, Stocker H.1, Tschochner M.2, Walter H.2, Sopper S.3, Arasteh K.1

1Auguste-Viktoria-Klinikum, Klinik für Infektiologie/Gastroenterologie, Berlin, Germany, 2Universität Erlangen, Institut für klinische Virologie, Erlangen, Germany, 3Deutsches Primatenzentrum, Göttingen, Germany

Background: Heavily pre-treated patients with multi-drug resistant HIV-1 (MDR) strains left with whether or a few options only for further HIV treatment, although there are a few new drugs with activity against MDR. Since it is common sense that at least two drugs of full activity plus optimized background are needed to reduce viral replication safely in MDR patients, there are a few studies only providing patients with more than one new drug at a time. It is still of high interest to find strategies to bridge time till more than one new drug is available. This study was intended to investigate the efficacy of a new strategy.

Method: We conducted a single armed, prospective study with heavily pre-treated patients. Patients were excluded if results in genotyping showed sensitivity to more than 2 drugs. Pt started on a regimen with at least 3 NRTI. Whenever the VL increased by at least 0.5 log a viral genotype was obtained. According to the change in the mutational pattern 2 PIs were chosen and administered to the patient. This regimen was prescribed until VL rose by at least 0.5 log. At this time another genotype was ob-
B.35 (Poster)
Frequency and reasons for ARV switch in heavily pretreated patients in a 24 months observation period. Results of the Radata-cohort


1ifi-Institut für interdisziplinäre Medizin, Hamburg, Germany, 2Universität Frankfurt, HIV-Center, Frankfurt, Germany, 3Klinikum der Universität zu Köln, Klinik I für Innere Medizin, Köln, Germany, 4Medizinische Poliklinik, Klinikum der Universität München Innenstadt, Infektionsambulanz, München, Germany, 5Universitätsklinikum Hamburg-Eppendorf, Ambulanzzentrum Infektiologie, Hamburg, Germany, 6Klinikum Osnabrück, Infektionsambulanz, Osnabrück, Germany, 7HIV-Schwerpunktpraxis, Frankfurt, Germany, 8Praxis für Allgemeinmedizin, Krefeld, Germany

**Objective:** Radata is an internet-based system which provides planning of antiretroviral therapy (ART), according to resistance analysis, adherence questionnaire, therapeutic drug monitoring and external expert advice.

**Methods:** Of 637 patients included in the radata database, 224 patients with a follow-up of at least 24 months were selected and were analysed according to frequency and reasons for switches of ART. All patients were put on a new ART at the time of enrolment.

**Results:** Within the 24 months period of follow-up, 317 ART switches in 146/224 patients (1.4 switches per patient, range 0-7) were observed. The main reason for switch was therapeutic failure (n = 180, 50.4 %). Within this subgroup, elevated viral load was the main reason in 117, CD4-T-cell decline in 17 and clinical progression in 7 cases. For 39 cases, the detailed reason for switch due to therapeutic failure was not stated by treating physician. Besides therapeutic failure, switches due to drug related side effects were noted in 75 cases (21.0 %). In 27 cases (7.6 %) simplification of regimen was the primary reason for therapeutic change, 25 cases (7.0 %) were switched due to inadequate adherence of patients and for 13 cases (3.6 %) study related conditions (protocol requirement) were responsible. In 12 cases (3.4 %), comorbidities such as acute illnesses or newly diagnosed gravity led to the switch. In 6 cases (1.7 %) physicians assumed unfavourable drug interactions. In 19 cases (5.3 %) physicians did not state a specific reason for change of therapy.

**Conclusions:** Despite intensive pre-treatment of the patients, only half of the therapy switches over a period of 24 months in this cohort were due to therapeutic failure. Other predominant reasons were side effects, treatment simplification and inadequate patient adherence.

B.36 (Vortrag)
Sexually transmitted infections in men having sex with men with primary HIV infection

**Lenz J.C.C.,** **Jessen H.,** **Jessen A.B.**

1Praxis Jessen/Jessen/Stein, Berlin, Germany

**Objective:** In the very early stage of HIV infection high levels of HIV virus are measured. Also at this stage individuals with HIV are often not aware of their infection. Both may contribute to the high proportions of HIV transmission in this phase. Sexually transmitted infections (STI) are known to increase both the risk to acquire HIV as well as to transmit HIV to sex partners. Co-infections of HIV and STI in patients with primary HIV infection (PHI) may represent an individual risk factor that facilitated acquiring the new HIV infection as well as a risk factor to transmit HIV to other sex partners. In this study we want identify the rate of STI in patients with primary HIV infection.

**Methods:** We performed a retrospective analysis of all men having sex with men (MSM) with PHI in the years 2005 and 2006 in the database of a single center (Praxis Jessen, Berlin) an HIV and STI practice. PHI was defined as presence of HIV (measured by PCR) and three or less HIV specific bands in the western blot. For these patients the charts were reviewed for clinical signs and laboratory test (Syphilis, Gonorrhea, Chlamydia, Hepatitis B and C) results indicative of symptomatic STI.

**Results:** We identified 22 individuals with PHI. In 4 (18%) active infection with syphilis, chlamydia or gonorrhea was found. In two other possibly sexually transmitted diseases were present (campylobacter, unspecified urethritis). Over all 1/3 of the patients with PHI had infections that are possibly sexually transmitted.

**Conclusions:** The presence of STI in about 1/3 of patients with PHI in this center may represent an individual risk that led to the HIV infection. It may also indicate that HIV and STI have been acquired at the same time. This finding leads us to conclude that screening for STI should be performed in PHI. The identification and subsequent treatment of STI will not only prevent negative consequences of STI, but also may help to reduce the additional risk for onward transmission of HIV caused by an active STI.

B.37 (Poster)
Antiretroviral (AR) treatment (ART) in the German ClinSurv multicenter cohort - An overview of HAART in Germany over the last ten years

**Kollan C.,** **Kühne A.,** **Hamouda O.**, for the ClinSurv Study Group

1Robert Koch Institut, Infektionsepideimiologie, Berlin, Germany

**Objective:** With the available number of different AR-substances (S) the number of drugs (ARV) and AR-regimen (R)
increase. However, factors such as tolerance, pill count and drug-resistance determine the use of AR-drugs. Determination and specification of (ART)-strategies in HIV treating centres between 1996 and 2006.

Methods: Analysis of high-grade ART data from 21 ClinSurv centers. Daily R were generated using documented start and stop dates for each drug. Ongoing R were censored at the last known clinical event or the end of the observation period. The analysis is focused on the main class-regimens (MR) representing at least 1% of entire R-time.

Results: The assessment of daily ART was based on 15.2 mill. S-days or 4.6 mill. R-days, respectively. Overall 3,757 patients NUC-combinations achieved in 2003 9% and decreased to 4%. NUC-R held 46% of R-time in 1996 and lost rapidly impact. 3-quarterly used S increased from 11 to 24 over time. 12 MR have been treated with 30 S in six S-classes. The number of presenting at least 1% of entire R-time.

Conclusions: ART-strategies documented in ClinSurv changed lasting. With the appearance of TDF and FTC increased by 23% in the last five years. The frequency of PI-containing R decreased since 1998 from 60% to 27% in 2003 and currently increased up to 35%. The frequency of NNRTI-containing R increased to a stable rate of 44% over the last six years. At the end of study period 57% of boosted PI-R were based on LPV and 16% on ATV, whereas in 1999 IDV or SQV were the predominant S.

Prevalence and characteristics of HIV-2 infection in Germany

B.38 (Poster)


1University of Bonn, Department of Medicine I, Bonn, Germany, 2Coordinating Centre for clinical trials, Cologne, Germany, 3University of Bonn, Institute for Medical Microbiology, Immunology, and Parasitology, Bonn, Germany, 4Private Practice, Hamburg, Germany, 5Hannover Medical School, Dept. of Clinical Immunology, Hannover, Germany, 6Private Practice, Munich, Germany, 7MUC Research, Munich, Germany, 8Ruhr-University Bochum, Department of Dermatology, Bochum, Germany

Background: While infection with HIV-2 is predominantly found in West Africa, HIV-2 infections are rare elsewhere. It is known that clinical course and clinical picture of HIV-1 and HIV-2 infection differ. Little is known about HIV-2 infection in Germany. Therefore we investigated prevalence and clinical characteristics of HIV-2 infection in Germany.

Methods: Since 2002 13995 HIV positive patients have been enrolled in the Competence Network for HIV/AIDS. Clinical data (CD4 cell count, CDC stage) of these patients were collected every 6 months.

Results: HIV-2 infection was detected in 29/13995 (0.2%) of HIV infected subjects. In these individuals no co-infection with HIV-1 was found. Interestingly, only 8/29 (28%) were of African origin. 85% of HIV-1 infected subjects were men, while only 65% of HIV-2 infected subjects were male. MSM was found to be the predominant risk factor of HIV-2 transmission in 17/29 (51%). There was no difference in CD4 cell count in HIV-2 infected patients (491.9 vs 498.9, respectively).

Conclusions: HIV-2 infection is not common in Germany. Interestingly, risk of HIV-2 infection is not restricted to people from high prevalence countries. Despite comparable CD4 cell counts AIDS is less frequent in HIV-2 infected in cohort participants.
B.40 (Poster)

Incidence of gastritis in patients presenting before and after 1996 and the role of ART. A retrospective analysis of the AVK cohort

Traeder C.E. 1, Kowol S. 1, Masuhr A. 1, Arastéh K. 1
Kompetenznetz HIV/AIDS Deutschland

1Vivantes Auguste-Viktoria-Klinikum Berlin, Infektiologie, Berlin, Germany

HIV patients have been treated in the Vivantes Auguste-Viktoria-Klinikum (AVK) Berlin since 1985. The total number of episodes of treatment amounts to 15228 until the end of 2006, with 5368 different patients and a constant number of 750-850 patients/years. Gastritis is a constant problem in patients presenting with HIV infection. The reason for this is not clear and the role of HAART is discussed controversially.

Methods: We compared the number of gastritis found in endoscopic examinations and correlated these results to the HIV therapy taken by the investigated patients. The analysis was done by a retrospective analysis of the electronic data base of the department of infectiology. Data were analysed for the years 1994–1996 (853 gastroscopies) and the years 2004 – 2006 (1159 gastroscopies). Gastritis, which in this presentation is not being differentiated into gastritis a, b or c, was diagnosed endoscopically or histopathologically. Recurrent patients were counted.

Results: 1994 – 1996: 853 gastroscopies, gastritis 327/38.3% (included 71 patients with CMV gastritis). These 327 patients could be divided in the group with NRTI (42, 12.8%) and the group without NRTI (285, 87.2%). None of the patients got PI or NNRTI, study medication not detected.

2004 – 2006: 1159 gastroscopies, gastritis 422/36.4% (included 36 patients with CMV gastritis). These 422 patients could be divided in the group of combination therapy with NNRTI or PI (249, 59.0%) and without combination therapy (173, 41.0%). ART in the years 2004 – 2006: 2764 stays, 1549 (56.0%) on HAART, 1215 (44.0%) without HAART. NNRTI or PI / all patients with use of NNRTI or PI / gastritis: total number of episodes of treatment amounts to 15228 until the end of 2006.

Discussion: We did not observe an increase in gastritis since 1996. The percentage of 38% in the first period is comparable with 36% of the second period. The use of HAART in the second period is much higher (60% versus 12%) and reflects the availability of combination therapy. There is no difference between NNRTI or PI combination therapy (compared use of NNRTI or PI / all patients with use of NNRTI or PI / gastritis patients).

### Table 1

<table>
<thead>
<tr>
<th>Duration of treatment (n)</th>
<th>On treatment &lt;400 copies/ml</th>
<th>Intent to treat &lt;400 copies/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year (n= 20)</td>
<td>78.9% (15/19)</td>
<td>75% (15/20)</td>
</tr>
<tr>
<td>2 years (n= 18)</td>
<td>66.7% (12/18)</td>
<td>63% (12/19)</td>
</tr>
<tr>
<td>3 years (n= 17)</td>
<td>70.6% (12/17)</td>
<td>63.2% (12/19)</td>
</tr>
<tr>
<td>4 years (n= 16)</td>
<td>61.5% (6/13)</td>
<td>63.6% (7/11)</td>
</tr>
<tr>
<td>5 years (n= 16)</td>
<td>63.6% (7/11)</td>
<td>43.6% (7/16)</td>
</tr>
<tr>
<td>6 years (n= 14)</td>
<td>83.3 (5/6)</td>
<td>35.7% (5/14)</td>
</tr>
</tbody>
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B.41 (Vortrag)

Die Primäre HIV-Infektion: Grundlagen, Diagnostik und Behandlung

Jessen H. 1

1Gemeinschaftspraxis Jessen/Jessen/Stein, Berlin, Germany


B.42 (Vortrag)

6 year-outcome in 20 HIV-1 positive children treated with 2 nucleoside reverse transcriptase inhibitors + Nelfinavir as first line protease inhibitor

Hien S. 1, Buchholz B. 1, Beichert M. 2, Duerken M. 1, Schäible T. 1

1Universitätskinderklinik Mannheim, Mannheim, Germany, 2Universitätsfrauenklinik Mannheim, Mannheim, Germany

Purpose: Because only few data about long term outcome of HIV-1-infected children treated with Nelfinavir (NFV) as first line protease inhibitor (PI) exist, a retrospective analysis of antiviral activity and safety in these children was performed.

Methods: 20 PI-naive children, who were treated with 2 nucleoside reverse transcriptase inhibitors (NRTI) + NFV between Oct 1997 – Jan 2007 were analysed. According to CDC-classification 7 children were classified as stage A1-2, 6 as B1-2, 3 as B3 and 4 as C3 at start of NFV. 10 had a HIV-1 viral load (VL) <100.000 - 5 a VL 100.000-1Mio. - and 5 >1Mio. copies/ml. All children received NFV as whole, halved or crushed tablets (dissolved in water) in a dosage of initially 3x 30mg/kg and after 1999 of 2x 60-65mg/kg.

Results: In the table the proportions of patients with HIV1-VL less than 400 copies/ml by on-treatment - versus intent-to-treat analysis are shown (Table 1).
In one girl under concomitant tuberculostatic therapy and in one boy therapy was temporally interrupted for one week because of grade 4 elevation of CK and continued thereafter. With the exception of mild diarrhoea and mild elevations of CK there were no other adverse effects.

Conclusions: Anti-retroviral therapy with NFV as first line PI in combination with 2NRTI was well tolerated and the antiviral activity was excellent for 3 years, but decreased thereafter.

B.43 (Poster)
Irreführende Interpretation der HIV-Diagnostik bei einem HIV-infizierten Neugeborenen
Englert C.1, Schmitt D.1, Ganschow R.1
1Kinderklinik, Universitätsklinikum Hamburg-Eppendorf, Pädiatrische Immunologie, Hamburg, Germany

We report about an HIV-infected newborn, who was prematurely born due to a non-compliance of the patient during her pregnancy. The mother was HIV-positive, and the newborn was not diagnosed serologically at birth. During routine checks, HIV was non-detectable at the PCR-diagnostik. We found that the infant was HIV-positive at the 2nd week of life when all maternal HIV-antibodies had disappeared and HIV was not detected in the peripheral blood. Newborns were treated with zidovudine and lamivudine. The treatment was well tolerated, and the antiviral activity was excellent for 3 years, but decreased there after.

B.44 (Poster)
Humoral immunity in HIV-exposed children
Scheuplein M.1, Linde R.1, Königs C.1, Köhl U.2, Klingebiel T.1, Kreuz W.1
1JW Goethe University, Department for Pediatrics, Hemostasis and Immunodeficiency Treatment and Research Unit, Frankfurt, Germany, 2JW Goethe University, Department for Pediatrics, Immunology Lab, Frankfurt, Germany

Newborns of HIV-positive mothers receive antiretroviral drugs as part of a regimen to prevent mother-to-child-transmission. This protocol has reduced the rate of transmission drastically, but possible acute and long-term side effects of these drugs in the neonate are being discussed.

HIV-exposed children are checked regularly to monitor the transmission status. In the Frankfurt cohort of HIV-exposed children, immunological parameters were also monitored during routine checks.

HIV-exposed children showed some differences in their humoral immune response in comparison to age-matched unexposed controls. Mean humoral antibody-levels of IgG and IgA were in the lower normal range or pathologically low in comparison to an age-matched control. There were no differences in other immunological parameters as IgM, leucocytes, lymphocytes or lymphocyte subpopulations (CD4, CD19). Only HIV-exposed but HIV-negative children were included in this analysis. HIV-infection was excluded at the age of 2 years when all maternal HIV-antibodies had disappeared and HIV-PCR had been repetitively negative. In addition, HIV-exposed children seemed to have more respiratory and gastrointestinal infections than unexposed children of the same age group. For the abnormal immunological parameters, HIV-exposed children showed a delay in maturation of the immune system. Whether this delayed is due to the HIV-exposure or the antiretroviral prophylaxis is unclear and needs to be investigated.

C. Koinfektionen / Komorbidität
C.1 (Poster)
Seroprevalence of other antibodies (herpes, CMV, rubella, varicella, hepatitis B, hepatitis C, syphilis, chlamydia, mumps, toxoplasmosis) in HIV positive patients
Ajayi G.1, Omilabu S.1, Alamu D.1, Balogun Y.1, Badaru S.1
1Prenatal Diagnosis and Therapy Center, Tertiary Hospital, Lagos, Nigeria

Objective: To determine the seropositive of HIV positive patients to other antibodies (herpes, CMV, rubella, varicella, hepatitis B, hepatitis C, syphilis, chlamydia, mumps, toxoplasmosis).

Setting: Prenatal Diagnosis and Therapy Centre of a Tertiary Hospital in Lagos.

Materials and method: In a total of n=70(50 females and 20 males) attending the prenatal Diagnosis and Therapy Centre between June 1997-December 2005 who were screened and found to be HIV-seropositive were further screened for Herpes Simplex IgG/IgM, CMV IgG/IgM, Rubella IgG/IgM, Varicella IgG/IgM, Mumps IgG/IgM, Toxoplasmosis IgG/IgM, Chlamydia IgG/IgM, Hepatitis B and Hepatitis C IgG/IgM using ELISA kits and Syphilis (TPHA) using HAE method.
Result: 41 (82%) out of 50 females were positive to Herpes IgG out of which 28 (68.3%) were positive to IgM. 20 out of 12 (93.3%) were positive to Herpes IgG out of which 7 (63.6%) were positive to IgM. 37 (94.9%) out of 39 females were positive to CMV IgG out of which 21 (56.8%) were positive to IgM. 12 (93.3%) out of 13 males were positive to CMV IgG out of which 7 (58.3%) were positive to CMV IgM. 30 (76.9%) out of 39 females were positive to Rubella IgG out of which 9 (26.5%) were positive to Rubella IgM. 11 (91.7%) out of 12 males were positive to Rubella IgG out of which 10 (90.9%) were positive to IgM. 14 (58.3%) out of 24 females were positive to Varicella IgG out of which 5 (20.8%) were positive to Varicella IgM. 8 (72.7%) out of 11 males were positive to Varicella IgG out of which 1 (12.5%) was positive to Varicella IgM. 25 (65.8%) out of 38 females were positive to Mumps IgG out of which 17 (53.1%) were positive to the IgM. 24 (71.4%) out of 33 females were positive to Syphilis IgG out of which 11 (33.3%) were positive to Syphilis IgM. 31 (72.1%) out of 43 females were tested positive to Chlamydia IgG out of which 22 (61.1%) were positive to the IgM. 8 (57.4%) out of 14 males were positive to Chlamydia IgG, 2 (40%) out of 5 IgG positive tested positive to the IgM. None (0%) out of 38 females tested positive to Hepatitis B and Hepatitis C. 2 (16.7%) out of 12 males were positive to Hepatitis and none was positive to Hepatitis C. 4 (10.3%) out of 39 females were positive to Syphilis. 3 (7.3%) out of 11 males were positive to Syphilis

Conclusion: Our study shows that HIV positive patients are carriers of other antibodies and should be screened for them before therapy.

C.2 (Vortrag)

GBV-C co-infection in HIV patients downregulates CCR5 and CXCR4 surface expression on CD4 cells


1Medizinische Klinik und Poliklinik I, Universität Bonn, Bonn, Germany, 2Universitätsklinikum Bonn, Bonn, Germany, 3Medizinische Klinik und Poliklinik I, Universität Bochum, Bochum, Germany

Background: The flavivirus GB virus-C (GBV-C), thus far not known to cause any disease, has been shown to be associated with delayed progression of HIV disease. Recently, in vitro studies demonstrated down-regulation of CCR5 as a potential mechanism of GBV-C to modulate HIV disease progression. We therefore studied surface expression of the two major HIV co-receptors, CCR5 and CXCR4, on CD4+ and CD8+ T-cells in 110 HIV patients stratified with respect to their GBV-C status and immune function.

Methods: GBV-C infection was studied in 110 HIV patients by RT-PCR. CCR5D32 mutation was analyzed by real time PCR. FACS analysis was used to measure CCR5 and CXCR4 surface expression on CD4+ and CD8+ T-cells. Results: GBV-C RNA replication was detected in 31% (34/110) of patients. Fourteen patients were excluded from the analysis because of reduced CCR5 surface expression due to a heterozygous CCR5D32 mutation. In the remaining HIV/GBV-C co-infected patients with CD4 <350/µl CCR5 and CXCR4 expression on CD4+ T-cells was significantly reduced to 77% and 80%, respectively, of the levels measured in HIV mono-infected patients (p<0.05). In contrast, HIV-monoinfected and HIV/GBV-C co-infected patients did not differ with respect to CCR5 and CXCR4 expression on CD4+ T-cells in the subgroup with preserved immune function (CD4>350/µl) and on CD8+ T cells independent of immune function. Of note, we also found significant downregulation of CXCR4 (78%; p<0.05), but not CCR5 expression on CD4+ T-cells in HIV/GBV-C co-infected patients with detectable HIV replication compared to HIV mono-infected patients.

Conclusions: GBV-C co-infection is common in HIV infected patients and is associated with reduced expression of both major HIV co-receptors on CD4+ T-cells in the subset of HIV patients with poor antiretroviral therapy response to HIV replication and advanced immunodeficiency. Therefore, the molecular and cellular mechanisms underlying down-regulation of HIV co-receptors by GBV-C merit further investigation.

C.3 (Vortrag)

Effect of the IL-6 C174G gene polymorphism on treatment of acute and chronic hepatitis C in HIV co-infected patients


1Uni-Klinikum Bonn, Medizinische Klinik I, Bonn, Germany, 2Universitätsklinikum Charité, Campus-Virchow-Klinikum, Universitätsmedizin, Medizinische Klinik mit Schwerpunkt Hepatologie und Gastroenterologie, Berlin, Germany, 3St Vincent’s Clinical School, Faculty of Medicine, Sydney, Australia, 4Practice Dupke / Carganico / Baumgarten, Berlin, Germany, 5Practice Ärztetforum Seestraße, Berlin, Germany, 6San Matteo Hospital, Division of Infectious and Tropical Diseases, Hepatology outpatient Unit, University of Pavia - IRCCS, Pavia, Italy, 7University Hospital Germans Trias i Pujol, Universitat Autonoma de Barcelona (UAB), HIV Clinical Unit Department, Barcelona, Spain, 8Praxiszentrum Kaisersdamm, Berlin, Germany, 9HIV-cohort, Frankfurt, Germany, 10Practice Freiwill/Rausch, Berlin, Germany, 11Practice St. Georg, Hamburg, Germany, 12Practice Bieniek / Cordes, Berlin, Germany, 13University Hospital and Medical Center, Division of Infectious Diseases, Department of Internal Medicine, Ulm, Germany

Background and aims: HCV/HIV co-infection poses a difficult therapeutic problem. Response to HCV-specific therapy is variable but might be influenced by host genetic factors, including polymorphisms of cytokine genes. Here, we studied whether interleukin-6 (IL-6) C174G gene polymorphism affects the response to antiviral treatment in HIV-infected HIV-positive subjects.

Methods: We determined IL-6 genotypes in HIV-positive patients with acute (N=52) and chronic (N=60) hepatitis C treated with pegylated interferon-α. 210 HCV mono-infected, 197 HIV mono-infected, and 100 healthy individuals were studied as controls. Patients were classified into high and low producers according to IL-6 genotypes. Rates of sustained virological responses (SVRs) were compared between the IL-6 genotypes. STAT3 phosphorylation was analyzed by Westernblot in HCV core-transfected Huh7 cells.

Results: Distribution of IL-6 genotypes did not differ significantly between the study groups. SVR was achieved in 63%
of HIV/HCV co-infected patients. Carriers of the IL6 high producer (HP) genotype had significantly higher SVR rates than patients with a IL6 low producer genotype (70.1% vs. 52%; P<0.002). This effect was seen in both HIV-positive patients with acute (74% vs. 33%; p<0.05) and chronic (66% vs. 33%; p<0.05) hepatitis C. Multivariate analysis confirmed IL6 HP carriage as an independent positive predictor for SVR patients with acute (74% vs. 33%; p<0.05) and chronic (66% vs. 52%; P<0.002). This effect was seen in both HIV-positive patients. Carriers of the IL6 high producer genotype, which might be due to IL-6 mediated STAT3 activation.

**Conclusions:** Response rates to HCV-specific treatment are higher in HCV/HIV-positive patients carrying the IL6 HP genotype, which might be due to IL-6 mediated STAT3 activation.

**C.4 (Vortrag)**

**Comparison of Chlamydia trachomatis strains identified in HIV-infected patients with Lymphogranuloma venereum of Hamburg and Vienna**

Meyer T.1, Noah C.1, Stary G.2, Geusau A.2, Steilbrink H.-J.3, Plettenberg A.4

1IPM (Institute for Immunology, Clinical Pathology, Molecular Medicine), Virology, Hamburg, Germany, 2Medical University of Vienna, Dept. Dermatology, Vienna, Austria, 3ICH (Infekionsmedizinisches Centrum Hamburg), Hamburg, Germany, 4 IFI (Institut für Interdisziplinäre Medizin), Hamburg, Germany

**Objective:** An outbreak of lymphogranuloma venereum (LGV) among men having sex with men (MSM) was recognized recently in European countries and in North America. First cases were described in Rotterdam in 2003 and were found to be associated with a Chlamydia trachomatis L2 variant, named L2b. The same variant has also been detected 20 years earlier in an LGV outbreak in San Francisco.

In order to verify whether one or multiple C. trachomatis strains are involved in the current LGV outbreak in Europe, we compared LGV-associated strains identified in Hamburg and Vienna with the L2b strain from Rotterdam.

**Methods:** C. trachomatis infections were diagnosed by detection of bacterial DNA using PCR (TaqMan, Roche) and SDA (ProbeTec, Becton-Dickinson). C. trachomatis genotypes (serotypes) were identified by sequence analysis of the VS4 region of outer membrane protein (Omp) 1. To characterize different strains of LGV genotypes, the VS1 and VS2 region of Omp1 were also analyzed in 27 cases (15 from Vienna and 12 from Hamburg).

**Results:** 21 of the 27 L2-strains were identical to L2b based on omp1 sequence analysis. In addition, we identified four L2-sequences (3 in Vienna, one in Hamburg) with distinct point mutations in addition to those differentiating L2b from L2, putatively named L2c, L2d, L2e and L2f. One of them (L2c) was identified in two different patients.

**Conclusion:** Our findings indicate C. trachomatis strain L2b to be responsible for the current LGV-outbreak in Europe. Probably, L2b was imported into Europe some time ago and since then has undergone some sequential changes resulting in different regional variants.

**C.5 (Poster)**

**GBV-C coinfection decreases Fas expression and Fas-mediated apoptosis in HIV-1 infected patients**

Moen kemeyer M.1, Hong H.2, Bhattacharyya N.1, Schmidt R.E.1, Heiken H.1

1 Medizinische Hochschule Hannover, MHH, Klinische Immunologie, Hannover, Germany

**Objective:** Induction of Fas (CD95/Apo-1) expression on virus-infected cells plays a role in the control of infection by eliminating the infected cells. Lymphocytes of HIV-1 infected patients show increased expression of membrane-bound Fas and higher sensitivity to Fas-mediated apoptosis (FMA) compared to healthy individuals. Fas expression has been reported to increase during disease progression, and FMA is one of the mechanisms responsible for CD4+ cell depletion in HIV-1 infection.

Persistent coinfection with the apathogenic GB virus C (GBV-C) leads to slower disease progression in human immunodeficiency virus (HIV)-1 infected patients. The exact mechanisms underlying this beneficial effect in the course of HIV infection in vivo remain unclear. Aim of this study was to investigate whether Fas might be involved in this beneficial effect.

**Design:** Fas expression was evaluated in 42 GBV-C co-infected and 101 non-coinfected HIV-1 patients. 12 healthy and 11 Hepatitis C virus (HCV)-infected individuals were analyzed as controls.

**Methods:** PBMCs were isolated by Ficoll-Hypaque centrifugation. Cell surface Fas expression was determined by flow cytometry and Fas-mediated apoptosis was evaluated by staining with Annexin V and propidium iodide followed by multiparameter flow cytometry analysis.

**Results:** In untreated HIV-1 patients GBV-C coinfection was associated with significantly lower percentage of Fas+ cells as compared to GBV-C non-coinfected individuals. PBMCs of patients receiving highly active antiretroviral therapy (HAART) did not show such a difference. Functional analysis revealed a direct correlation between expression of Fas and Fas-mediated apoptosis. Sensitivity to FMA was unchanged in GBV-C coinfected patients.

**Conclusion:** Untreated HIV-1 patients GBV-C coinfection have reduced cell surface Fas expression. This correlates with reduced response to Fas-mediated apoptosis in vitro without affecting on sensitivity to FMA. This effect might contribute to prolonged survival of GBV-C coinfected HIV-1 patients.

**C.6 (Poster)**

**Safety of Atazanavir (ATV) and Atazanavir/ritonavir (ATV/r) in patients co-infected with HIV and hepatitis B and/or C: 1100 subject-years of treatment exposure**

Witek J.1, Mc Callister S.2, Reeb I.3, Nakons T.3, Odesho L.4, Thiiry A.4, Frederick D.4, Ledesma E.4, Hammond J.4

1 Bristol-Myers Squibb, Plainsboro, United States of America, 2Bristol-Myers Squibb, Lawrenceville, United States of America, 3Bristol-Myers Squibb GmbH&Co.KGaA, Munich, Germany, 4Bristol-Myers Squibb, PRI, Wallingford, United States of America

**Background:** HIV co-infection with hepatitis B or C is common and up to 45% of co-infected patients receiving ARV therapy develop grade 3-4 ALT/AST elevations. ATV is a po-
tent, generally well-tolerated, QD protease inhib or with a relatively low rate of ALT/AST elevations similar to comparators. Patients with co-infection from 4 ATV clinical development studies were analyzed.

Methods: This post-hoc analysis of studies in ARV-naïve (BMS 034, 089) and experienced (BMS 043, 045) patients using ATV, with/without RTV, was performed to assess the rate of ALT, AST, total bilirubin elevations and AEs in the presence or absence of hepatitis co-infection.

Results: 866 subjects received ATV-based regimens (214 ATV/r; 652 ATV) for a median of 48 to 95 weeks (110 subject-years of treatment exposure). 134 (15%) had baseline HBV and/or HCV co-infection (Table 1).

Grade 3/4 total bilirubin elevation rates were comparable in subjects with/without co-infection. Subjects who received ATV/r or ATV, with/without co-infection, had similar rates of Grade 2-4 treatment-related AEs (including jaundice and scleral icterus) and liver-related AEs.

Conclusions: Similar to other ARVs, patients with HBV and/or HCV co-infection had a higher rate of G3/4 ALT/AST elevations. In contrast, G3/4 bilirubin elevations, overall AEs and liver-related AEs, had a comparable frequency in patients with/without co-infection, suggesting that ATV and ATV/r are safe treatment alternatives in this population.

C.7 (Poster)

Ocular syphilis prefers different anatomical structures in HIV-negative and -positive patients

Kunkel J.1, Schirrmann D.2, Kneifel C.3, Zeitz M.1, Pleyer U.4, Krause L.3, Schneider T.1

1Charité Campus Benjamin Franklin, Med. Klinik I, Gastroenterologie, Infektiologie, Rheumatologie, Berlin, Germany, 2Charité Campus Virchow Klinikum, Med. Klinik m. S. Infektiologie, Berlin, Germany, 3Charité Campus Benjamin Franklin, Klinik für Augenheilkunde, Berlin, Germany, 4Charité Campus Virchow Klinikum, Klinik für Augenheilkunde, Berlin, Germany

Objective: To evaluate differences in ocular syphilis between HIV-negative and –positive patients.

Methods: All patients with ocular syphilis treated in our institutions at the Charité between 1998 and 2006 were reviewed. The diagnosis of ocular syphilis was made on the criteria:

1) inflammatory or noninflammatory ocular disease;
2) serological evidence for syphilis with a positive Treponema pallidum particle agglutination (TPPA) titer and fluorescent treponemal antibody absorption test (FTA-Abs) result or positive venereal disease research laboratory (VDRL) titer;
3) improvement following antimicrobial therapy. Major ophthalmological finding, patients’ characteristics, laboratory features including HIV status, CSF examination and data on treatment were collected.

Results: We identified 22 cases (37 eyes) of ocular syphilis nine of which were HIV-positive. One patient’s HIV status remained unknown because testing was refused, the patient (1 eye) was therefore excluded from the study. The mean case load was 2.75 cases/year. Presenting complaints were generally similar, comprising loss of vision, foggy vision, feeling of pressure and ocular pain (data not shown). 8 of 12 HIV-negative patients (67%) and 7 of 9 HIV-positive patients (78%) had a bilateral manifestation. Optic neuritis was most common in HIV-negative patients (6 of 12 patients/ 9 of 20 eyes), panuveitis was most common in HIV-positive patients (6 of 12 patients/ 9 of 20 eyes), panuveitis was most common in HIV-positive patients (6 of 9 patients/ 8 of 16 eyes). For six patients the ocular symptoms led to the diagnosis of a previously undetected HIV-infection. Age, CRP, TPPA and VDRL titers, CSF-cells and -VDRL titers and intrathecal Treponema pallidum antibody index (ITPA) were not different in the two groups. 13 of 21 patients had skin or mucosa alterations like palmoplantar exanthema or enoral ulcerations (9 of 12 HIV-negative and 4 of 9 HIV-positive). After treatment with iv betalactame antibiotics for at least 10 days all patients improved except one patient who had concomitant vitreous opacity not connected to syphilis infection (Table 1).

Conclusions: Ocular syphilis prefers optic nerve in HIV-negative patients and uvea in HIV-positive patients. It should be considered in any patient with unclear ocular lesions and screening for HIV-coinfection is essential.

Table 1 (C.6).

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Table 1 (C.7).
C.8 (Vortrag)

NRTI-freie HAART bei pegliert er Interferon / Ribavirin Therapie der chronischen Hepatitis C – ein Behandlungs vorteil?

Vogel M.1, Ahlenstielh G.1, Ummard K.2, Lutz T.3, Schürmann D.4, Khaykin P.5, Mayr C.6, Carganico A.7, Buggisch P.8, Kliner H.9, John C.10, Götz J.2, Staszewski S.5, Rockstroh J.K.1, German Hepatitis Group

1Universität Bonn, Bonn, Germany, 2Praxiszentrum Kaiserdamm, Berlin, Germany, 3Praxis Gute / Locher / Lutz, Frankfurt / Main, Germany, 4Charité, Berlin, Germany, 5Universität Frankfurt, Frankfurt / Main, Germany, 6Ärzteforum Seestrasse, Berlin, Germany, 7Praxis Dupke / Baumgarten / Carganico, Berlin, Germany, 8Universität Hamburg, Hamburg, Germany, 9Universität Würzburg, Würzburg, Germany, 10Praxis John, Berlin, Germany


Ergebnis: 115 Patienten (Arm A = 48, B = 36, C1 = 20, C2 = 11), 79 Männer, mittleres Alter 40 Jahre. Überwiegendes Transmissionsrisiko war intravenöser Drogenabusus (60%). Die HCV-Genotypverteilung zeigte Typ 1 in 51%, Typ 2 in 4% der Fälle. In der Intent to Treat Analyse zeigte sich eine SVR bei 54% aller Patienten (Arm A 54%, B 58%, C1 40%, C2 64%). In der binären logistischen Regressionsanalyse zeigte sich ein Einfluss des HCV-Genotyps (1 oder 4) auf das Behandlungsergebnis (p < 0.0001) ohne H- Trägerstatus ohne Einfluss war (p = 0.936). Eine Subanalyse HIV-positiver Patienten zeigte keinen signifikanten Einfluss von HAART (p=0.468) oder NRTI-freier HAART (p=0.273) auf das Behandlungsergebnis.

Schlussfolgerung: Hohe SVR-Raten wurden bei 54% aller HIV-positiven Patienten beobachtet. Wenngleich sich in der Untersuchung kein signikanter Vorteil für eine NRTI-freie HAART zeigte, so erreichten im NRTI-freien Behand lungsarm mehr Patienten eine SVR als im NRTI-haltigen Be handlungssarm.

C.9 (Poster)

Treatment outcome and virus specific immune responses following antiviral treatment in concomitant acute HCV/HIV co-infection

Pieper D.1, Schulze zur Wiesch J.2, Mohn J.1, Jordan S.2, Eiermann T.3, Degen O.4, Hauber J.1, Stahmer I.1, Lohse A.2, van Lunzen J.3

1Heinrich Pette Institut, Hamburg, Germany, 2Universitätsklinikum Eppendorf, Medizinische Klinik I, Hamburg, Germany, 3Universitätsklinikum Eppendorf, Institut für Transfusionsmedizin, Hamburg, Germany, 4Universitätsklinikum Eppendorf, MVZ Infektiologie, Hamburg, Germany

Background: Early treatment of acute HCV infection results in sustained virological response (SVR) in the majority of monoinfected patients. Few data exist for treatment of concomitantly acquired acute HCV/HIV co-infection, or the immunologic events following acute HCV infection of the immunocompromised host. Here, we present detailed clinical and immunologic analysis of three individuals following concomitant acute HCV/HIV infection.

Methods: PBMC were collected and viral loads were determined during the course of acute infection. Responses against HIV were tracked by ELISPOT and proliferative assays. Additionally, HCV specific CD4+ responses were determined in T cell lines from each patient.

Results: In all three patients anti-HCV treatment was started with PEG-IFN-alpha for a mean of 32 wks and antiretroviral treatment (ART) was co-administered during primary infection. Subject A had a nadir CD4 count of 316 cells/mm3, with a peak HIV VL 127.000 c/ml and a peak HCV VL of 40.000 (GT1b). Subject B had a nadir CD4 count of 323 cells/mm3, with a peak HIV VL 2.770.000 c/ml and a peak HCV VL of 393.000 (GT3). Subject C had a nadir CD4 count of 178 cells/mm3, with a peak HIV VL 160.000 c/ml and a peak HCV VL of 2.000.000 (GT3). All patients achieved a HIV VL <50 c/ml during ART. After cessation of ART subject A had a median HIV VL of 1.317 (420-4.1000 copies/ml) and a median CD4 counts of 429 cells/µl. Subject B had a HIV VL re-bound to a median of 946 copies/ml and a median of 479 CD4 cells/µl. Both subjects did not receive ART again. Subject C was started on ART again after the HIV VL had increased to 150.000 copies/ml. All three subjects achieved a SVR for HCV. We were able to recover multispecific HCV CD4 responses in subject A and B but not in subject C who had a CD4 nadir lower than 300 cells/µl.

Conclusions: Our data indicate that HCV therapy should be administered early in the setting of concomitant acute HCV/HIV co-infection and that clearance of HCV is possible even during primary HIV infection. Larger trials have to determine the best HCV treatment and whether adjuvant ART is needed to achieve a favorable outcome. Our study shows that HCV-specific T cell immunity is generated during the acute phase in HIV+ individuals and can be preserved by HCV treatment.
Risk factors for hepatitis C in HIV positive MSM. 
A preliminary evaluation of a case control study

Schmidt A.1, Vogel M.2, Rockstroh J.K.2, Radun D.1, Study Group on Sexual Risk Factors for Hepatitis C

1Robert Koch-Institut, Infektionsepidemiologie, Berlin, Germany, 2Universitätsklinikum Bonn, Medizinische Klinik und Poliklinik I, Bonn, Germany

Objectives: Since 2001, clinicians in Europe have been reporting increasing numbers of infections with the hepatitis C virus (HCV) in HIV positive men who have sex with men (MSM). The possible routes of HCV transmission are still uncertain and controversial. Despite biological plausibility, major longitudinal studies in HIV negative MSM showed no evidence for an epidemiologically relevant sexual transmission. Therefore, the aim of this study is to explore social, behavioural/sexual, or nosocomial risk factors for hepatitis C in HIV positive MSM.

Methods: In 2006, we conducted a case control study embedded in a survey on knowledge, attitudes and behaviour in German MSM as to sexually transmitted infections. Cases consisted of HIV positive MSM with known HCV infection and no history of injecting drug use (IDU), as IDU and related sharing of equipment is the leading risk factor for HCV infection in industrialised countries. HIV positive MSM without known HCV infection, matched for age group, served as controls. The HCV serostatus of controls was confirmed by an anti-HCV-antibody test from dried blot spots.

Results: So far, 22 cases and 44 controls were included for preliminary evaluation. In the bivariate analysis, significant risk factors were

(1) consumption of nasally applicable drugs like cocaine (OR=10.5; 95%CI:2.2-52.8),
(2) history of major surgery (OR=9.1; 95%CI:1.7-48.9),
(3) ”gangbanging” or group sex (OR=7.7; 95%CI:2.0-29.1),
(4) a history of more than 5 episodes of unprotected anal intercourse within the last 12 months (OR=7.5; 95%CI:2.1-26.2),
(5) bleeding anal injuries from any sexual intercourse (OR=7.13; 95%CI:1.3-39.1),
(6) "fisting" (OR=5.9; 95%CI:1.4-25.9), or
(7) use of sildenafil (OR=4; 95%CI:1.3-13.0).

In logistic regression, (1) and (5) remained in the model (OR=13.2; 95%CI:2.3-74.9 and OR=7.7; 95%CI:1.0-60.3).

Conclusion: There is evidence that in HIV positive MSM, a complex interaction between certain sexual practices and associated behaviour like consumption of cocaine are relevant risk factors for HCV transmission. However, a history of major surgery might be a non-sexual risk factor, and clinical studies should be implemented to further focus on nosocomial risks. More cases and controls are needed to fit adequate power.
C-) for CD40 (p=0.0018), and 5.37 ± 0.88% (n=7 GBV-C+) vs. 1.58 ± 0.51% (n=7 GBV-C-) for CD83 (p=0.0041). The mean fluorescence intensity (MFI) of CD40 and CD86 was higher in GBV-C coinfected HIV-1 patients after 24hrs. IFN-γ production was comparable between the two groups.

Conclusion: HIV-1 patients coinfected with GBV-C have a higher percentage of pDCs expressing CD40 and CD83. This significant difference suggests that certain phenotypic characteristics of pDCs are influenced by GBV-C coinfection in HIV-1 infection.

C.13 (Poster)

Hepatitis B virus markers in HIV-infected pregnant women

Weizsaecker K.1, Castelyn S.1, Siedentopf J.-P.1, Feiernma-Sperling C.2

1Charité Universitätsmedizin, Klinik für Geburtsmedizin, Berlin, Germany, 2Charité Universitätsmedizin, Klinik für pädiatrische Pneumologie und Immunologie, Berlin, Germany

Objective: Hepatitis B virus (HBV) coinfection is common in HIV-infected individuals. According to current German prenatal care guidelines only HBsAg-status is determined during the third trimester of pregnancy. Newborns of HBsAg-positive mothers receive active and passive immunization immediately after delivery in order to prevent vertical transmission of HBV. There is little data about the seroprevalence of HBV-markers in HIV-infected pregnant women.

Methods: HIV-infected women were cared for at our center during a total of 245 consecutive pregnancies from January 1998 to February 2006. HBsAg, anti-HBs, anti-HBc (IgG and IgM) as well as HCV-antibodies and HCV-PCR were determined.

Results: 38.7% of women showed evidence of past or present HBV-infection; HBsAg was positive in 5.3%. The seroprevalence of hepatitis B markers in HBsAg-negative women was as follows: Both anti-HBs and anti-HBc positive 22.4%, only anti-HBc positive 12.9%, only anti-HBs positive 9.1%, all markers were negative in 49.6% of women, data were incomplete in 6.0%. Anti-HBc as the only positive marker was found more frequently among women from high-prevalence regions (20/119 or 16.8%) and especially among HIV-infected patients (12/45 or 26.7%).

Conclusions: Markers of HBV-infection were detected in a high proportion of HIV-infected pregnant women at our center. Especially anti-HBc-only positive women may be potentially infectious in spite of negative HBsAg-status, and the risk of vertical transmission of HBV cannot be completely ruled out in this group. Therefore complete HBV-serology should be part of routine prenatal care for all HIV-infected women. Furthermore, only 15.4% of all eligible patients showed serological evidence of HBV-vaccination, a rate that could be greatly improved.

C.14 (Poster)

Relapse of HCV viremia in two patients with spontaneous HCV-clearance after restarting HAART

Sauter F.1, Wojcik K.2, Kupfer B.3, Schwarze-Zander C.2, Bliesener N.2, Rockstroh J.K.2

1Universität Bonn, Medizinische Klinik 1, Köln, Germany, 2Universität Bonn, Medizinische Klinik 1, Bonn, Germany, 3Universität Bonn, Virologie, Bonn, Germany

Overall, in the natural course of HIV/HCV coinfection, higher HCV-RNA levels are found in HIV seropositive patients as compared to HIV seronegative patients with hepatitis C. Indeed, analysis of HCV-RNA levels in haemophiliacs showed that mean HCV-RNA levels increased by 1 log over the first 2 years after HIV-seroconversion. Which impact HAART has on HCV kinetics so far is still discussed controversially.

Here we describe 2 rare cases of patients, in which after having experienced spontaneous HCV-RNA clearance after developing severe CD4-depletion, reappearance of HCV occurred when CD4 counts started rising again after initiation or ongoing HAART. Acute reinfection during the observation period was ruled out. In one case a new HAART regimen (TDV, FTC, LPV/r) was started after CD4-counts had fallen down to 14 cells/µl. HIV viral load was then above 500.000 copies/ml. At the same time HCV-RNA became undetectable after having continuously fallen during the last years. In the other patient HCV-RNA clearance was documented 6 months after HAART (LPV/r, ABC,3TC) was initiated but here, due to compliance problems, HIV-RNA remained detectable. Indeed HCV clearance was documented at 20.000 HIV-RNA copies and progredient CD4 count loss with CD4-levels between 14 and 40 cells/µl. Subsequently, compliance was improved and HCV-RNA became undetectable (<400 copies/ml). Both patients remained HCV-RNA negative even by highly sensitive TMA assay (lower limit of detection is 10 IU/ml) over a period of approximately three months before HCV-RNA reappeared in their sera after successful HAART and CD4 count recovery up to 60 cells/µl in the first and 113 cells/µl in the second patient.

Reappearance of HCV may be an important complication of HAART induced immune restoration. This warrants a close surveillance of serum HCV-RNA levels in patients with low CD4-counts and HCV-antibodies but negative HCV-RNA.

C.15 (Poster)

Therapeutic drug monitoring of Lopinavir in a HIV-patient with visceral leishmaniasis, chronic hemodialysis and continuous therapy with miltefosine

Heinz W.1, Guhl C.1, Weissbrich B.2, Winzer R.1, Langmann P.1, Klinker H.1

1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany, 2Institut für Virologie und Immunobiologie der Universität Würzburg, Würzburg, Germany, 3Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany

Objective: Successful antiretroviral therapy (ART) in HIV patients is not only jeopardized by incomplete compliance, but also by interaction with concomitant medication or impaired organ function. Although lopinavir (LPV) is mainly metabolized in the liver by cytochrom P450, renal elimination might also play a role and data to therapy in case of renal insufficiency are rare. Miltefosine is used for therapy of leishmaniasis and is mainly renal eliminated. To our knowledge interactions with LPV have not been investigated, although HIV has a high prevalence in most African countries with endemic leishmaniasis. Here we describe case of ART in a HIV patient with chronic haemodialysis and concomitant medication of miltefosine.

Methods: LPV plasma levels were determined via HPLC before and after haemodialysis, and CD4 cell count and viral load have been correlated to ART and kidney impairment.

Results: A 40 year old HIV patient suffered from visceral
leishmaniasis and after courses of liposomal amphotericin B and short term miltefosine for up to 4 weeks a long-term therapy with miltefosine was started. Based on chronic damage of the kidneys, which might have been impaired by previous indinavir administration, terminal renal insufficiency developed as a typical side effect of therapy with the polyene amphotericin B. Independent of the renal function and miltefosine ART was continued with a combination of LPV-ritonavir (RTV) (dosage 2 cps bid, than 1 tbl. bid) and a 2-NRTI backbone including abacavir and lamivudin. After 8 months of follow up a continuous complete suppression of viral replication (viral load < 50 copies/μl) could be documented and CD4 cell count remained stable (165 - 232 copies/μl). 20 trough levels before haemodialysis have been determined, revealing sufficient antiviral activity with a mean of 5979 ng/ml (standard deviation (SD) 2339 ng/ml). A mean peak concentration after medication and haemodialysis in 12 samples has been 12177 ng/ml, SD 2470 ng/ml. The results were analyzed in correlation to possible HIV-coinfection and comedication of HAART.

Conclusions: Here we report of a case of VL with multiple manifestations, relapsing after L-AmB therapy and secondary prophylaxis, which could be successfully treated with continuous miltefosine administration, despite persisting HIV related immunosuppression.

C.17 (Poster)
Comparison of Ribavirin plasma concentrations in HCV-monoinfected and HCV/HIV coinfected patients with or without concomitant HAART

Guhl C.1, Rasche S.1, Kubisch A.1, Schirmer D.1, Heinz W.1, Winzer R.1, Langmann P.2, Klinker H.1
1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany, 2Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany

Objective: Patients coinfected with Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) taking HAART are on higher risk to die of liver-related problems than of HIV-related illnesses. Therefore, treatment of HCV in HIV-patients is important but difficult, especially due to a higher risk of toxicities and pharmacological interactions with HAART. Ribavirin (RBV) drug levels might play a crucial role not only in deteriorating drug addicted side effects like hemolytic anemia but also in effectiveness of treatment and early virological response. Orally taken, RBV is quickly sorbed. Maximal plasma concentration (PC) can be reached after 1.5 hours and a steady state is reached after 4 weeks of treatment. Measuring PC of RBV can help optimizing the HCV-treatment. Here we investigated the RBV PC in HIV/HCV-coinfected patients regarding a comedication with HAART.

Methods: A high performance liquid chromatography (HPLC) was established to determine PC of RBV after solid phase extraction. Plasma samples from patients treated for HCV have been collected and PC have been determined. The results were analyzed in correlation to possible HIV-coinfection and comedication of HAART.

Results: A total of 178 samples of 78 patients has been collected and PC have been measured during steady-state, i.e. after 4 weeks of treatment and 8 to 16 hours after having taken the pills. 67 patients (n=136 samples) had HCV only (group 1) and 11 patients (n=42 samples) have been coinfected with HIV and HCV. 7 of the HCV/HIV-coinfected patients were treated only against HCV (group 2, 20 samples) and 4 received concomitant HAART, respectively (group 3, 22 samples). The plasma trough level for RBV in all samples was 1702 ± 582.5 ng/mL. In group 1 (HCV) the trough level was 1724 ± 590 ng/mL, in group 2 (HCV/HIV without HAART) 1721 ± 623 ng/mL and in group 3 (concomitant d HAART) 1302 ± 225 ng/mL. Due to the small number of patients in group 2 and 3 significances testing has not been performed.

Conclusions: In this retrospective analysis we could show a trend that HAART reduces PC of RBV whereas the HIV-in-
fection itself seems to have no influence. Concerning changes in RBV daily dosing in patients with concomitant HAART, further investigations have to follow.

**C.18 (Poster)**

**Zungenbeteiligung bei Syphilis und HIV-Koinfektion: 2 Fallberichte**

*Sornprat-Ragaller P.*

1 Klinik und Poliklinik für Dermatologie, Universitätsklinikum Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany

Einleitung: Bei HIV-Koinfektion sind häufig ungewöhnliche Stadienverläufe und Senoreaktionen der Syphilis zu beobachten. Im Folgenden werden 2 Patienten beschrieben, bei denen zunächst tumoröse Zungenveränderungen im Vordergrund standen, bevor anhand begleitender bzw. später auftretender Hautveränderungen eine Syphilis diagnostiziert wurde.


**Fall 2:** MSM, 44 J, bekannte HIV-Infektion unter antiretroviraltherapie. Über 2 Monate unklare indurierte Schwellung der Zungenmitte; aufgetreten im Rahmen eines fieberhaften Infekts, danach jedoch keine Abheilung. Durch HNO-Arzt Zungenbiopsie; histologisch polypöses Plattenepithel mit entzündlichem plasmazellreichen Infiltrat, keine Granulome; gedeutet als Granuloma pyogenicum. Bei Vorstellung auch exanthematische Herde an Handflächen und perigenital sowie Condylomata lata, klinisch eher spätsekundäre Veränderungen; zudem kleiner ulcusverdächtiger Herd am Gaumen; zudem kleiner ulcusverdächtiger Herd am Gaumen, Histologie: Granuloma pyogenicum. Bei Vorstellung auch exanthematische Herde an Handflächen und perigenital sowie Condylomata lata, klinisch eher spätsekundäre Veränderungen; zudem kleiner ulcusverdächtiger Herd am Gaumen. Nach der Therapie mit Penicillin 3x 10 Mio IE i.v. an Tag 1, 8 und 15.

**Schlussfolgerung:** Eine Zungenbeteiligung der Syphilis kann in allen Stadien (als Primäraffekt, verschiedene Manifestationen im Sekundärstadium, Zungengumma) auftreten und ggf. auch einzige Manifestation der Syphilis sein. Isolierte Zungenherde sollten daher, gerade bei atypischen Verläufen bei HIV-Koinfektion, auch an eine Syphilis denken lassen. Als Screening ist eine Bestimmung des TPHA bzw. TPPA-Tests allein nicht ausreichend.

**C.19 (Poster)**

**HIV und Hepatitis Koinfektion in Deutschland: werden koinfizierte Patienten unterschiedlich behandelt?**


1 Universität Bonn, Medizinische Klinik und Poliklinik I, Bonn, Germany, 2 Universität Bonn, Bonn, Germany, 3 KSK, Köln, Germany, 4 Universität Bochum, Bochum, Germany, 5 MUC-Research GmbH, München, Germany, 6 Universität Essen, Essen, Germany, 7 Praxisszentrum Kaiserdamm, Berlin, Germany


Ergebnis: 6259 Patienten, 66% Männer. Eine chronische Hepatitis B Infektion lag bei 359 Patienten (5,7%), eine chronische Hepatitis C Infektion bei 687 (11,0%) vor. Während bei HIV-monoinfizierten und HIV/HBV koinfizierten homosexuellen Geschlechtsverkehr das wesentliche Transmissionssrisiko darstellte (65% bzw. 71%), so überwog bei Hepatitis C intravenöser Drogennahverbrauch (45%). Hepatitis B Koinfizierte nahmen signifikant häufiger eine HAART ein als HIV-Monoinfizierte (86% vs. 79%, p < 0.001). Keine Unterschiede fanden sich zwischen Patienten mit Hepatitis C (81%) und Hepatitis B Koinfektion oder mit HIV-Monoinfektion.

Method: In this cross sectional study, 701 patients were tested with the QFT. In case of QFT reactivity, tuberculin skin testing was performed and TB related clinical, socio-epidemiologic and microbiological data were gained. The mean follow up time was 6 months.

Results: The QFT was reactive in 39/701 patients (5.6%). An indeterminate result was obtained in 33 patients (4.7%). QFT indeterminate patients had significantly lower CD4 cells as compared to patients with positive or negative test results (p=0.001 and p<0.001, respectively). Active TB was found in 3/39 QFT+ individuals, but not in patients with negative or indeterminate test results. In 2 of the patients a reactive QFT revealed otherwise undiagnosed TB. Among the 39 QFT+ patients, 16 originated from Western Europe, 14 were from Africa, 5 from Central Europe, 3 from Eastern Europe and 1 from South America. Six patients had been previously diagnosed with TB. Eight QFT+ patients reported recent exposure to a patient with active TB, 18 recently travelled to a high-prevalence country. In 77% (29/39) at least one of these risk factors was identified. Eight patients had pulmonary symptoms, 14 reported moderate weight loss, night sweats, or fever but no microbiological or radiological evidence of active TB was found. Two patients with positive QFTs died during the follow up period, one of them due to TB. Concordance for TB at baseline developed active TB during the follow up period, one of them due to TB. Concordance for QFTs and tuberculin skin tests was found in 64% of patients tested. None of the QFT+ patients without evidence of active TB at baseline developed active TB during the follow up period.

Conclusion: The QFT appears to be highly sensitive and may reveal sub- or preclinical TB even in moderately immunocompromised HIV patients. However, prolonged observation is needed to unravel the positive or negative predictive values of QFT in patients with HIV.

C.21 (Poster)
Tuberculosis in HIV patients: Diagnosis and management in a low-prevalence country

Kowar M.1, Voigt E.1, Ahlenstiel G.1, Nattermann J.1, Vogel M.1, Rockstroh J.K.1

1Medical Department I, University of Bonn, Bonn, Germany

Background: Tuberculosis (Tb) is common and the main cause of death among HIV patients worldwide. With increasing migration Tб becomes more prevalent in low-prevalence countries.

Methods: We retrospectively analyzed a cohort of 29 HIV patients suffering from Tb between 1988-2005 at a single large HIV care center in western Germany, regarding clinical presentation, diagnostic procedures and treatment outcome.

Results: In recent years the number of HIV patients with active Tb increased at our site with 16 cases before and 13 cases since 2000. Patients’ median age was 34 years (range 21-47). 52% of patients were female, 42% originated from high prevalence countries. Tb mainly involved lymph nodes (n=16) and lung (n=11) without differences in CD4 counts between the two entities, however, patients with both entities were more profoundly immunosuppressed. Main symptoms were fever, weight loss and cough in 66, 52 and 41% of patients, respectively. Only 55% of patients with pulmonary Tb had a cough. 20% of patients with negative chest X-ray revealed pulmonary involvement by computer tomography. 79% of patients received Tb and antiretroviral treatment (ART) concomitantly (NNRTI-based 21%, PI-based 24%, NRTIs only 31%). 28% were already on ART and 52% initiated ART when Tb was diagnosed. Median duration of Tb treatment was 14 months (range 6-26). 25% of patients developed isoniazide-induced hepatitis, all of them were on ART. HIV RNA declined significantly and CD4 count increased by a median of 113 cells/μl until the end of Tb treatment. Three patients (10%) died. We observed higher rates of class I Human leukocyte antigens (HLA) A1, A2, B1, and B2 among coinfected patients (n=11) compared with HIV patients without Tb (n=22).

Conclusions: Even in a low-prevalence region Tb becomes increasingly important in HIV patients. Diagnosis can be hampered by unspecific symptoms and false negative results of examinations. ART appears feasible and effective with concomitant Tb-treatment. The influence of HLA types on susceptibility to Tb deserves further study.

D. Therapie der HIV-Infektion

D.1 (Vortrag)
It’s the study, stupid: A systematic review of randomized clinical trials using zidovudine (ZDV), lamivudine (3TC) and efavirenz (EFV) in treatment naive HIV infected patients

Hoffmann C.1, Wolf E.2

1ifi Institut, Hamburg, Germany, 2MucResearch GmbH, München, Germany

Background: The combination of ZDV+3TC+EFV is one of the most recommended antiretroviral therapies (ART) which has been used as the standard-of-care arm in numerous clinical trials.

Design: Systematic review, evaluating outcome of all large randomized trials examining ZDV+3TC+EFV in at least one treatment arm in ART naive HIV-infected patients (pts), published by the end of 2006. Outcome variable was the viral load (VL) response at week 48 (ITTMissing=failure).

Results: In total, 7 trials enrolling 2.225 pts in 8 ZDV+3TC+EFV arms met the criteria for analysis. One study (ACTG 384) was excluded due to its specific design. In the remaining 7 study arms, a high variation in response rates was observed. The rates of pts achieving a VL < 50 copies/ml differed significantly from 36.9 to 70.4 % (p<0.0001). Even after exclusion of the AA424-034 trial in which specimen processing errors had effected the results, outcomes differed significantly, ranging from 59.4 to 70.4 % (p=0.03). Differences were still marked when analysing only pts with a baseline VL > 100,000 copies/ml (47.5-66.7 %, p=0.04) and were also found in VL response rates of < 400 copies/ml (63.0-72.8 %, p=0.04). Response discrepancies could neither be explained by significant differences in tolerability of ZDV+3TC+EFV reflected by the rates of pts discontinuing ART due to adverse events (in total: 6.5-12.3 %, p=0.20; grade III-IV anemia: 0.6-5.5 %, p<0.001) nor by the rates of pts lost to FU or with consent withdrawal (6.0-13.7 %, p<0.01). Possible confounding factors such as pill burden due to study design, race, gender, CD4 cells or the percentages of pts with a baseline VL > 100,000 copies/ml (27.3-50.0 %, p<0.0001) did not show a clear association with overall VL response. I. e., the trial with the highest percentage of highly viremic pts had the best response rate.

Conclusion: The heterogeneity in efficacy and tolerability of the same antiretroviral regimen in different studies strongly
sugest that cross-trial comparisons between different regimens should be discouraged. In the light of intensive marketing strategies focussing on assumed (and often minor) advantages of antiretroviral agents, more data on confounding factors with possible impact on treatment response is needed.

D.2 (Vortrag)
Results of LORAN trial: double-protease-inhibitor, RTI-sparing regimen in therapy-naive HIV-1-infected patients
Ulbricht K.U.1, Stoll M.1, Behrens G.M.1, Salberge B.2, Jessen H.3, Jessen A.B.3, Kuhlmann B.4, Trein A.5, Heinen H.1, Schmidt R.E.1

1Medizinische Hochschule Hannover, Klinische Immunologie, Hannover, Germany, 2University of Regensburg, Regensburg, Germany, 3Praxis Motzstr., Berlin, Germany, 4Praxis Georgstr., Hannover, Germany, 5Praxis Schwabstr., Stuttgart, Germany

Background: Double-PI regimens are a reliable therapeutic option in salvage therapy. However, first-line therapy demands combinations including RTI. Apart from resistance and toxicity, common problems in RTI-therapy, triple RTI therapies are less efficient, whereas boosted PI-based regimens postpone the incidence of resistance for years. In the LORAN study, a 72-week, randomized trial among HAART-naive patients, LPV/r is combined with either CBV (ATZ+3TC) or ATV. Primary endpoints are metabolic side effects and QOL, secondary endpoints are virological and immunological response. The relevance of this study approach is emphasized by recently published data on Mono-PI-therapy.

Methods: Treatment-naive HIV-1-infected patients with need for HAART were randomly assigned to either treatment arm. In this substudy, we analysed virological failure in both groups, defined as VL >50 copies/mL at week 24. Comparisons between treatment arms were performed using Fisher’s exact test. Plasma HIV-1 from patients at baseline and at virological failure was analysed genotypically.

Results: In this substudy, we present 24-week data of 67 patients focusing on virological response. 24/30 patients in the CBV-LPV/r arm show virological response (6 discharged before week 24) vs. 15/37 in the ATV-LPV/r arm (14 discharged, 6 of them due to virological failure). Referring to non completion equals failure, the intent-to-treat analysis revealed significant differences for virological failure in the LPV/r-ATV arm compared to the control group: Chi-Q p=0.015, Fisher’s Exact Test p=0.021. With regard to 47 on-study subjects in week 24, there are 14 failures observed in the ATV-LPV/r arm vs. no failure in the CBV-LPV/r arm (Chi-Q and Fisher’s Exact test: p<0.001). ATV-LPV/r failures were on low level (9/10 virological failures <700 copies/mL). Pharmacokinetic measuring showed reduced LPV concentrations in 1/7 tested subjects.

Conclusions: This substudy of the LORAN trial is the first report of a Double-PI first line therapy showing low level virological failure. In this setting, ATV and LPV/r are less effective than the conventional RTI-based regimens. Further exploration of early RTI-sparing therapy with regard to metabolic side effects and QOL is warranted.

D.3 (Vortrag)
Effective MTCT-prophylaxis with AZT/TDF plus FTC or 3TC
Haberl A.1, Linde R.2, Reitter A.3, Knecht G.4, Staszewski S.1

1Johann-Wolfgang-Goethe-Universitätsklinikum, Innere Medizin, Frankfurt am Main, Germany, 2Johann-Wolfgang-Goethe-Universitätsklinikum, Kinderklinik, Frankfurt am Main, Germany, 3Johann-Wolfgang-Goethe-Universitätsklinikum, Frauenklinik, Frankfurt am Main, Germany, 4IFS, Frankfurt am Main, Germany

Background: Current MTCT-recommendations have their limitations in the antiretroviral transmission prophylaxis. Nevirapine implies an aggravated risk for hepatotoxicity in women with CD4 > 250 and also involves the risk of fast resistance development. Efavirenz has been classified FDA-categori D recently and PI-containing regimens require adherence of a large extent.

The combination of AZT and TDF plus FTC or 3TC offers a favourable resistance profile and a low pill burden. For the use in pregnant women TDF and FTC are categorized B by the FDA. AZT and 3TC are already recommended for MTCT-prophylaxis. Objectives and methods: We investigated the effectiveness, tolerance and safety of AZT plus TDF in combination with either FTC or 3TC in pregnant women with CD4 > 250 or adherence problems in history. We used the fixed combinations CBV (AZT/3TC) and TIVD (TDF/FTC) as well as the single substances. The analysis started in January 2005 and is still ongoing. So far we observed 28 pregnancies of HIV-positive women treated with the regimens mentioned above.

Baseline characteristics: 22 (80%) of the 28 pregnant women were migrants, mostly from African countries. The mean age was 32 years. 12 (43%) patients were ART-naive. Median CD4-count at baseline: 338/µl; median viral load at baseline: 46.000 copies/ml. Mean time of starting antiretroviral treatment during pregnancy: 32. week of pregnancy.

Results: The mean time of delivery was the 38. week of pregnancy. The mode of delivery was an elective caesarean section. Median CD4-count at delivery: 465/µl; median viral load at delivery: < 50 copies/ml. The mean birth weight was 2.800 g. The antiretroviral transmission prophylaxis was tolerated well. There were no discontinuations due to any side effects or adherence problems. No case of vertical transmission has been observed in the 28 born children.

Conclusions: Since MTCT-prophylaxis with AZT/TDF plus FTC or 3TC was effective and safe in our analysis it could be considered as a new option for the treatment of pregnant women.
D.4 (Poster)

What experts anticipate: Predictability of virological response in the RADATA cohort

Platenberg A.1, van Lunen J.2, Rockstroh J.3, Knechten H.1, Mauss S.3, Salzberger B.5, Stoll M.7, Stoehr A.1, Hoffmann C.1, Lorenzen T.1, for the Radata-studygroup

1ifi-Institut für interdisziplinäre Medizin, Hamburg, Germany, 2Universitätsklinikum Hamburg-Eppendorf, Ambulanzzentrum Infektiologie, Hamburg, Germany, 3Universitätsklinikum Bonn, Medizinische Klinik und Poliklinik I, Bonn, Germany, 4HIV-Schwerpunktpraxis Aachen, Germany, 5HIV-Schwerpunktpraxis, Düsseldorf, Germany, 6Universitätsklinikum Regensburg, Klinik I für Innere Medizin, Regensburg, Germany, 7Medizinische Hochschule Hannover, Abteilung Klinische Immunologie, Hannover, Germany

Objective: Recent studies suggested that virological response in HIV-infected patients is better when expert advice for new antiretroviral therapy (ART) is available. However, data on predictability of virological outcome after expert-guided switch of ART is limited.

Methods: RADATA is an internet-based system which provides external expert advice for ART-switch. After external experts had given advice on ART switch which based on pre-treatment, resistance analysis, drug monitoring, compliance questionnaire and demographic parameters, experts were requested to provide their opinion on virological outcome of the patients after three and twelve months. Prognoses were grouped into “good virological outcome” (at least a viral load decline > 1 log copies/ml) and “poor virological outcome” (viral load decline < 1 log copies/ml). Prognoses were correlated with virological outcome which was grouped in the same way. For analysis, only cases in which the treating physicians followed expert advice where selected.

Results: Of 187 expert prognoses for 64 patients, 67 for 37 patients were eligible for further analysis. Compared to actual outcome, virological outcome (good or poor) was predicted correctly in 40 (60 %) of the cases. A good virological outcome was predicted in 38 cases (57 %). Of these, 31/38 prognoses (82 %) were correct. In 29 cases (43 %) experts assumed poor virological outcome. Of these, only 9/29 prognoses (31 %) were accurately predicted. Comparing these two groups p-value is 0.04 in Chi-Square-Test. Of note, 19 patients achieved a viral load of < 50 copies/ml although the external experts anticipated either an unchanged viral load or a decline < 1 log copies/ml.

Conclusions: In this cohort of pretreated patients, preliminary data suggest that virological outcome is predicted accurately in most cases. However, there remains a considerable number of cases in which the virological response is underestimated by external experts.

D.5 (Poster)

The rainbow cohort: Saquinavir/r is effective and well tolerated in antiretroviral therapy (ART)-naïve patients initiating treatment with saquinavir

500mg film-coated tablets - 24 week interim results from Germany


1Praxen Zentrum Blondelstrasse (PZB), Aachen, Germany, 2HIV treating physician, Berlin, Germany, 3HIV treating physician, Munich, Germany, 4HIV Research and Clinical Care Center, Munich, Germany, 5HIV treating physician, Frankfurt a.M., Germany, 6HIV treating physician, Karlsruhe, Germany, 7HIV treating physician, Hamburg, Germany, 8Klinikum der Johann-Wolfgang-Goethe Universität, Frankfurt a.M., Germany, 9Roche Pharma AG, Grenzach-Wyhlen, Germany

Objective: The aim of the Rainbow Cohort – an international observational study - is to assess the efficacy and tolerability of initiating treatment with, or switching treatment to the new saquinavir (SQV) Invirase® 500 mg film-coated tablet (FCT) formulation. We present an interim 24-week subgroup analysis of antiretroviral therapy (ART)-naïve patients in Germany participating in the Rainbow Cohort.

Methods: Multicenter, prospective, open label, observational study. Efficacy assessments include changes in viral load (VL) and CD4 count, tolerability assessments include changes in liver enzymes and lipid levels from baseline.

Results: 24-week interim analysis of n=142 ART-naïve patients from the German cohort. Baseline characteristics: 85% male, median age 39 years, median time since first diagnosis 1 year (IQR 0 - 4), median baseline viral load (VL) 111,204 HIV RNA copies/mL (IQR 19,000 – 306,000), median CD4 count 198 cells/mm3 (IQR 107 - 204). In week 24 the proportion of patients achieving a VL < 400 copies/mL was 92.7% in the as treated (AT) and 85.2% in the intent-to-treat (non completers=failures) [ITT (NC=F)] population. 73.4 % (AT) and 67.4% [ITT (NC=F)] of patients respectively, had undetectable VL < 50 copies/mL in week 24. Median increase in CD4 cell count was + 147 cells/mm3 (IQR 70 - 237). Median changes in triglycerides, total cholesterol, ALT, AST and g-GT were +12 mg/dL (IQR -39 - 85), +26 mg/dL (8 - 46), -6 U/L (-21 - 3), -3 U/L (-13 - 1), -2 U/L (-25 - 5), respectively. There were no clinical grade 3 and 4 adverse events. SQV treatment was stopped in 7.7 % of the patients (1 patient due to virological failure, 3 pts due to side effects, 3 pts were lost to follow up, 4 pts due to other reasons).

Conclusions: These data confirm that SQV/r is effective and well tolerated in ART-naïve patients in the real-life clinical setting. The results of this observational cohort of treatment with the new 500 mg tablet formulation of SQV are consistent with high efficacy and tolerability results seen in controlled studies with SQV/r.
D.6 (Vortrag)

Recovery of CD4+ T-cells after switch to a nucleoside free regimen in patients with poor immunologic response despite complete HIV-RNA suppression

Lehmann C.1, Hoffmann A.1, Corneley O.1, Jung N.1, Hartmann P.1, Norbert S.1, Wyen C.1, Fäkenheuer G.1

1Medizinische Klinik I, Klinische Infektiologie, Universität zu Köln, Köln, Germany

Background: Antiretroviral Therapy (ART) usually leads to suppression of HIV load and rapid rise of CD4+ T-cell count. However, in some patients poor recovery of CD4+ T-cell despite optimal viral suppression on ART is observed. As some combinations of nucleoside analogues (NA) have been associated with paradoxical depletion of CD4+ T-cells, we postulated that the change from a NA containing to a NA free regimen could improve quantitative immunological parameters.

Methods: 15 HIV-1 infected patients on NA containing ART with undetectable HIV load and CD4+ T-cells < 250/μL for at least 6 months were included in this study after informed consent. Treatment was switched to Atazanavir (ATV) (300mg qd), Saquinavir (SQV, 1000mg bid) and Ritonavir (RTV, 100mg qd)

Results: Median [IQR], age [yrs.]: 46 [38-62]; gender: male: n=11, CDC stage C3: ns=9, CD4+ T-cells/μL at baseline: 197 [130-220], 10% [7-17]; months on ART: 20, [6-114]. The regimen was well tolerated. 1 patient discontinued because of incompliance. HIV RNA remained below 50 copies in 14 patients and CD4+ T-cell count improved significantly, (week 24: 230/μL (14%), [170-290, 10-17%]; week 48: 260/μL, 17% [195-415, 13.5-18.5%]) p<0.05

Conclusions: This clinical pilot study shows that the boosted double PI combination of ATV/SQV without the addition of NA may be an effective and generally well-tolerated NA-sparing treatment strategy for patients with poor immunologic response despite undetectable viremia.

D.7 (Vortrag)

Long-term response on CD4 T-cell count recovery in HIV-infected patients receiving highly active antiretroviral therapy (HAART)

Kramer K.1, Vogel M.1, Voigt E.1, Wasmuth J.1, Schwarze-Zander C.1, Rockstroh J.1

1Department of Medicine I, University of Bonn, Bonn, Germany

Objective: Several valid options for HAART initiation exist for the treatment naive, HIV-infected individual. Currently however, there is an ongoing controversy over the potency of NNRTI vs. PI based regimens on immune reconstitution. We examined the potential superiority of one of these therapy arms.

Methods: Single cohort study. Retrospective chart review. CD4 T-cell count was analyzed every 3 months in participants who had been HAART-naïve at the time point of HAART initiation and had a plasma HIV RNA load <80 copies/ml for ≥3 years and no change in their original HAART.

Results: 60 patients were identified. 54 male, 6 female patients, median age was 37. Median baseline CD4 count was 166 cells/μL and increased to 301 cells/μL three years after HAART initiation. Median baseline HIV RNA was 99000 copies/ml. In our study age (p=0.682), gender (p=0.978), AIDS (p=0.177), duration of HIV-infection (p=0.501), baseline CD4 cell count (p=0.082), baseline HIV RNA (p=0.541) or hepatitis-coinfection (p=0.733) were not associated with CD4 T-cell count recovery. Furthermore, PI containing regimens were neither superior nor inferior to NNRTI containing regimens (p=0.617). However, there was a significantly (p<0.05) higher rise in CD4 T-cells in patients receiving regimens without zidovudine (AZT), whereas HIV-infected individuals who were treated with AZT-containing regimens experienced a less pronounced immune reconstitution.

Conclusions: In this study, PI or NNRTI based HAART was not superior to one another with regard to immune-reconstitution over a period of 3 years. AZT-containing regimens, however, showed significantly less pronounced rise of CD4 counts compared to AZT-free regimens, which supports an omission of zidovudine in first-line therapy in future.

D.8 (Poster)

Efficacy and safety of Atazanavir (ATV) based HAART in virologically suppressed patients switched from Lopinavir/Ritonavir (LPV/RTV) treatment

Gate1 J.1, Branco T.2, Sasset L.3, Pulido F.4, Macor A.5, Nakonz T.6, Reeb I.7, Gruber C.1, Oedeschoo L.5, Wirtz V.8, Ledesma E.9, BMS 097 study team

1Hospital Clinic, Barcelona, Spain, 2Hospital Do Desterro, Lisbon, Spain, 3Hospital Cittadella, Padova, Italy, 4Hospital Doce de Octubre, Madrid, Spain, 5Hospital Amedeo di Savoia, Torino, Italy, 6Bristol-Myers Squibb GmbH & Co.KGaA, München, Germany, 7Bristol-Myers Squibb, Brain-l’Alleud, Belgium, 8Bristol-Myers Squibb, Wallingford, United States of America

Background: BMS 097 study demonstrated that simplification from stable PI + ritonavir (RTV)-containing to unboosted ATV-containing regimens maintained virologic suppression with lipid improvements through 48 weeks. This analysis reports the safety and efficacy of subjects on LPV/RTV at enrollment.

Methods: Subjects on PI containing regimens with RNA <50c/mL without virologic failure on PIs were randomized 2:1 to ATV 400 mg QD (nucleosides unchanged). 54% percent of subjects were on a PI/rtv regimen at entry; of those, 2:1 to ATV 400 mg QD (nucleosides unchanged). 54% percent of subjects were on a PI/rtv regimen at entry; of those, 68% on LPV/RTV are included in this post-hoc analysis.

Results: 153 patients with a mean prior exposure to LPV/RTV of 79 weeks were included. Baseline characteristics of subjects on LPV/RTV at entry were similar to the overall study population (Table 1).

Viral rebound, discontinuation for any reason before Week 48 or never treated.

**18 subjects received RTV (concomitant use of TDF).

New onset gastrointestinal symptoms of any grade were reported in 2% of subjects on ATV, 13% on LPV/RTV.

Table 1

<table>
<thead>
<tr>
<th>Efficacy Results 48 weeks</th>
<th>Switch to ATV**</th>
<th>Continue LPV/RTV</th>
<th>Viral rebound</th>
<th>1% (11/100)</th>
<th>9% (5/53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure for any reason**</td>
<td>26% (25/100)</td>
<td>28% (15/53)</td>
<td></td>
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</table>
Use of Tenofovir DF in experienced patients – 96 weeks data from a German outpatient cohort

Schewe C.K.1, Fenske S.2, Schnaumann E.3, Trein A.3, Ranneberg B.4, Gallo L.4, Mertenskoetter T.4

1Infektsionsmedizinisches Centrum Hamburg, Praxis St. Georg, Hamburg, Germany, 2Infektsionsmedizinisches Centrum Hamburg, Grindelpraxis, Hamburg, Germany, 3Praxis Schwebstrasse 57, Stuttgart, Germany, 4Gilead Sciences, Martinsried, Germany

Background: Tenofovir DF (TDF) was first approved for the treatment of experienced patients in the European Union in 2002. At that time, data on the safety profile in pre-treated patients were limited to the pivotal studies GS-902 and GS-907, both looking at TDF as an add-on to an existing suboptimal HAART. To further define the safety profile of this new nucleotide analogue as a component of antiretroviral therapy in daily practice, this Gilead-sponsored prospective cohort study was established.

Methods: 231 HIV+ adult patients were enrolled in 32 German centres between March 2001 and January 2003. Patients were followed for up to 96 weeks; efficacy (VL, CD4), tolerability and adherence were documented every three months.

Results: Patients were pre-treated, male (n=194) and had already received NRTIs (n=225), NNRTIs (n=133) and/or PIs (n=132). Median duration of prior HAART was 688 days (19-4495 days). The major reasons for the use of TDF were therapeutic failure of prior HAART (n=140), side effects (n=31), existing lipodystrophy (n=32) and/or adherence problems (n=63).

156/231 patients were documented for 96 weeks, 21 patients discontinued early due to virological failure or suboptimal response, 50 were lost to follow up and 4 patients changed their HAART due to adverse events.

In an AT(as treated)-analysis over 96 weeks, median CD4 count increased from 325 cells/mm3 to 497 cells/mm3; median viral load decreased from 6,100 copies/ml at BL to less than 50 copies/ml in week 96. Tenofovir was primarily combined with ddI (n=59) or 3TC (n=118), third agents used were protease inhibitors (mostly LPV/r) or NRTIs.

No serious adverse events related to TDF use and three mild to moderate adverse events related to TDF were reported. One patient stopped TDF due to an increase in creatinine, values returned to normal after cessation of TDF.

Conclusion: In antiretroviral experienced patients, Tenofovir DF as part of a combination therapy in daily practice proved efficacious and showed good long term tolerability.
D.11 (Poster)

Virological medical quality management - 7 year follow-up of HIV treatment

Knechten H.1, Höhn C.1, Ehret R.1, Wiesmann F.1, Braun P.1
1PZB Aachen, Aachen, Germany

Purpose: The HIV treatment guidelines have been modified recently and recommend that a viral load <50 copies/ml should be a goal of therapy in treatment-experienced patients. We analysed data of different antiretroviral treatments and their virological efficacy over the past seven years in Germany.

Methods: Up to 23 participating medical-centres and between 997 (2000) and 2120 (2006) data sets were available. Antiretroviral regimens (ART) were divided into combinations containing either three nucleos(t)ide analogues (NRTI), two NRTI + one protease-inhibitor (PI), two NRTI + one non-nucleoside-reverse-transcriptase-inhibitor (NNRTI) or "other" regimens. Therapy success was defined by achieving HIV-1 RNA <50 copies/ml. Proportion and efficacy of first-line regimens were evaluated additionally.

Results: The proportion of patients receiving ART remains constant between 77.1% (2000) and 76.6% (2006) accompanied by an increase of therapy success from 71.9% to 83.0%, respectively. The combination of 2 NRTI + 1 PI was the preferred combination in the last 2 years with 38.6% in 2005 and 40.6% in 2006 and replaced combinations including NNRTI which were the favourite (40.9%-41.7%) in the previous years followed by 3 NNRTI and "other" combinations. The therapy success of the different regimens increased from 2000 to 2006 as follows: 3 NRTI: 68.2% to 81.2%; 2 NRTI + 1 PI: 68.7% to 81%; 2 NRTI + 1 NNRTI: 72.8% to 89.1% and other regimens: 44.5% to 77.4%. In 2006 the proportion of first-line regimens was 26.4% and showed a therapy success of 83.2% separated in 3 NRTI with 76.5%; 2 NRTI + 1 PI with 76.2%; 2 NRTI + 1 NNRTI with 91.7% and other regimens with 75%.

Conclusions: Over the past 2 years a change in the prescribing patterns could be seen. The availability of new boosted PIs could be a cause of the increase in the PI use. The increasing proportion of the "other" regimens could result from a high proportion of heavily pre-treated patients and new treatment strategies, e.g. double-PI regimens. All four therapy regimens achieved an increasing therapy success, may be due to a simplified mode of intake (once-daily regimens) and improved drug formulations. The feedback given to the individual centres could lead to an improvement of the quality in HIV-treatment as well.

D.12 (Poster)

Improvements in self-reported gastrointestinal tolerability, Quality of Life (QoL) and therapy preference with lopinavir/ritonavir (LPV/r) after switching from BID soft-gel capsule (SGC) to BID tablets (TAB)

Schranz D.1, Brockmeyer N.H.2, Fischer K.1, Petry R.3, Hover M.4
1Praxis, Berlin, Germany, 2Rahm-Universität, Bochum, Germany, 3Abbott GmbH & CoKG, Wiesbaden, Baden, Germany, 4Klinikum Dortmund GmbH, Dortmund, Germany

Objective: Assessment of tolerability, perceived QoL and therapy preference in German HIV+ patients (pts) switching from LPV/r SGC to LPV/r TAB, dosed at 400/100mg BID.

Methods: 24 physicians from medical practices and hospitals were recruited to administer two anonymous, linked self-report patient surveys. The surveys examine overall quality of life including, special aspects as well as the occurrence of loose stool, diarrhea and use of anti-diarrheal medication. 402 patients on LPV/r SGC completed surveys before switching to TAB and at subsequent visit following the switch to LPV/r TAB.

Results: During a period of 4 weeks prior to switching from LPV/r SGC to LPV/r TAB, 61.7 % of pts reported >1 loose stool per day vs. 55.9 % after the switch. 46.3 % of pts report-ed >1 diarrhea per day prior to switching vs. 32.8 % of pts after switching. 40.3 % of pts used anti-diarrheal medication before switching vs. 30.3 % of those afterwards.

Conclusion: In this unselected group of patients a trend to improved Quality of Life and reduced GI side effects is observed after switch from LPV/r SGC to LPV/r TAB.

D.13 (Vortrag)

Long-term efficacy of Enfurvitide – final results of the RADATA-Fuzeon cohort

Hoffmann C.1, Lorenzen T.1, Bogner J.R.2, van Lanzen J.3, Staszewski S.4, Arbter P.5, Faekhenheuer G.5, Gute P.6, Stoll M.7, Hintsche B.8, Waller J.9, Waeule B.10, Stoer A.1, Plettenberg A.1
1Ifi-Institut für interdisziplinäre Medizin, Hamburg, Germany, 2Medizinische Poliklinik, Klinikum der Universität München Innenstadt, Infektionsambulanz, München, Germany, 3Universitätsklinikum Hamburg-Eppendorf, Ambulanzzentrum Infektiologie, Hamburg, Germany, 4Universität Frankfurt, HIV-Center, Frankfurt, Germany, 5Praxis für Allgemeinmedizin, Krefeld, Germany, 6Klinikum der Universität zu Köln, Klinik I für Innere Medizin, Köln, Germany, 7HIV-Schwerpunktpraxis, Frankfurt, Germany, 8Medizinische Hochschule Hannover, Abteilung Klinische Immunologie, Hannover, Germany, 9Praxis für Innere Medizin, Berlin, Germany, 10Roche-Pharma AG, Grenzach-Wyhlen, Germany

Background: Data on long-term efficacy of enfuvirtide outside clinical trials is limited. In the Radata-Fuzeon cohort, data of HIV-1-infected patients (pts) treated with enfuvirtide in clinical practice were collected from 32 German centers. The setting offered planning of background therapy according to resistance analysis, adherence questionnaire, therapeutic drug monitoring and external expert advice.

Methods: All pts in whom a switch to a new enfuvirtide-based antiretroviral therapy (ART) was intended were included in this prospective cohort study. Clinical, immunological and virological outcomes were measured every three months.

Results: Of 233 pts included, 173 received enfuvirtide and were eligible for analysis. Pts were heavily pretreated at baseline (median time on ART: 80 months, number of prior regimens: 10), showing a median of 7 (range, 1-18) and 2 (range, 1-4) resistance mutations in the reverse transcriptase and in the protease gene locus, respectively. Pts had a median viral
load (VL) of 5.00 log10 and a median CD4-T-cell count of 88/µl (1-797) at baseline. After a median follow up of 27 months, 96 pts (55 %) had discontinued enfuvirtide, and the median time on enfuvirtide was 17 months. Main reasons for discontinuation were virological failure (39 %) and injection site reactions (21 %).

By ITT-analysis, 25 % and 16 % of the pts had reached a VL of < 400 and of < 50 copies/ml at week 48, respectively. Compared to baseline, 47 % of the pts had a VL decline of at least 1 log at week 12. The corresponding CD4-T-cell counts had increased by 101/µl at week 48. By OT-analysis, the percentage of the pts with a VL < 400 and a VL < 50 copies/ml were 46 % and 33 % at week 48. Virological response at month 3 was achieved more frequently in pts with higher CD4 counts (> 100/µl) and lower VL at baseline (< 100.000 copies/ml). Reported adherence did not predict virological outcome.

Conclusions: Enfuvirtide showed a remarkable treatment success in this large cohort of heavily pretreated patients. Response rates may be even higher in patients without severe immunodeficiency or high viremia. Discontinuation rates due to side effects were relatively low. Efficacy results of this cohort study are comparable to the 48 week data of the TORO 1 and 2 studies.

D.14 (Poster)
Lopinavir/Ritonavir containing ART during the pregnancy of HIV-infected women
Savric M.1, Gingelmaier A.1, Kästner R.1, Weissbencher T.1, Mylonas I.1, Friese K.1
1Ludwig-Maximilians-Universität München, I. Universitätsfrauenklinik, München, Germany

Objective: Highly active antiretroviral therapy (HAART) is administered to HIV-infected pregnant women to reduce the vertical transmission of HIV and/or to provide necessary maternal treatment due to an advanced disease. The aim of this study was: a) to evaluate complications during pregnancy and b) to assess the infant outcome of women taking a Lopinavir/Ritonavir (LPV/r) containing regimen.

Methods: Retrospective analysis of 38 pregnant women receiving a LPV/r containing ART at any time of their pregnancy (years 2002 – 2006). Evaluated parameters: ART, CD4-count and viral load at the beginning of pregnancy and perinatal, severe adverse effects of ART, pregnancy complications, mode of delivery, gestational age (GA) at delivery and infant outcome.

Results: The 38 pregnancies resulted in 40 live births (92 % cesarean section, 8 % vaginal delivery) and one stillbirth in GA 33 (complication of the umbilical cord). There were two cases of successful multiple pregnancies among this cohort (1x triplets, 1x twins).13 women (35 %) had a preterm birth <37+0 GA, 5 of them in GA 37, 4 in GA 35 and 4 in GA 26, 29, 33 and 34. In 7 cases (19 %) a premature rupture of the membranes was assessed. The viral load was suppressed below detection rate (<50 copies/ml) in 74% of the cases (28/38) till delivery. The CD4 count at the beginning of pregnancy was between 81-700/µl (mean:381/µl) and between 109–969/µl at delivery (mean:490/µl). In this group no birth defects could be identified and none of the infants acquired a vertical HIV-infection.

Conclusion: In our study the use of LPV/r during pregnancy was shown to be an effective and safe therapy for mother and child, though a high rate of pregnancy complications such as premature rupture of membranes and preterm birth has to be taken into account.

D.15 (Poster)
Once-daily (QD) Regime in einer Schwerpunktklinik
Holm S.1, Kuhlmann B.1
1Infectiologische Schwerpunktklinik, Hannover, Germany

Fragenstellung: Derzeit sind fünf antiretrovirale Substanzen für die einmal tägliche Einnahme zugelassen. Viele Behandler fürchten bei reinen QD-Regimen eine rasche Resistenzentwicklung aufgrund potentiell zu niedriger Serumspiegel, insbesondere bei Complianceproblemen. Ziel war die Analyse der aktuell in unserer Schwerpunktklinik verabreichten QD-Regime auf ihre virologische- und immunologische Wirksamkeit.

Methodik: Retrospektive Datenerhebung der aktuell seit mindestens 3 Monaten mit einem QD-Regime behandelten Patienten und Analyse folgender Parameter:
• First-, second-, third
• Umstellunggründe
• Zusammensetzung der Regime
• Einnahmedauer
• Viruslast bei Start und aktuell
• CD4-Zahl bei Start und aktuell
• Compliance

Ergebnisse: Derzeit erhalten in unserer Praxis 154 Patienten ein QD-Regime, davon 141 länger als drei Monate, 22 Frauen(16%),119 Männer(84%) mit einem mittleren Alter von 43.5 Jahren.

Ein Großteil der Patienten ist mehrfach vorbehandelt; nur bei 19 Patienten handelt es sich um die erste ART, bei 59 um die zweite- und bei 63 um die 3. oder 4. ART.

Gründe für die Umstellung auf ein QD-Regime:
Bei 17 Patienten Firstline, 19 Patienten Therapievereinfachung, 71 Patienten Nebenwirkungen, bei 6 Patienten Complianceproblem.

Die einzelnen Regime setzen sich wie folgt zusammen:
• Truvada-Reyataz/r x 47; Truvada-Sustiva x 32; Truvada-Viread x 37; Truvada-Videx x 1; Kivexa-Reyataz/r x 8; Kivexa-Sustiva x 7; Kivexa-Viread x 6; Kivexa-Viread x 2; Videx-Emtriva-Reyataz/r x 1

Die mittlere Therapiedauer beträgt 20.9 Monate, (Median 19 Monate).

Immunologischer- und virologischer Verlauf:
Bestimmt wurden CD4-Zellen und Viruslast zum Start des jetzigen Regimes und der aktuellste Wert.

Die mittlere Helferzellenzahl stieg von 461 CD4+ Zellen/µl auf 575 CD-Zellen/µl. 84 Patienten starteten ihre jetzige Therapie unter der Nachweisgrenze von 40 kop/ml, aktuell haben 134 der 141 Patienten (95%) keine messbare Viruslast.

Bei 6 der übrigen 7 Patienten ist eine Compliancestörung bekannt Die mittlere Viruslast dieser Patienten sank von 17400 kop/ml auf 400 kop/ml.

Schlussfolgerung: QD-Regime zeigen in unserem Kollektiv eine gute und andauernde Wirksamkeit. Derzeit liegen 95% der Patienten unter der Nachweisgrenze von 40 kop/ml.
**D.16 (Vortrag)**

Changes over time in risk of initial virological failure of antiviral therapy in Austria

Sturm G.1, Sarcletti M.2, Geit M.3, Rieger A.4, Schmied B.3, Zangerle R.2

1Österr. HIV-Kohortenstudie, Innsbruck, Austria,
2Medizinische Universität Innsbruck, Innsbruck, Austria,
3AKH Linz, Linz, Austria,
4Medizinische Universität Wien, Wien, Austria,
5ÖWS Wien, Wien, Austria

**Aim of the study:** Triple-combination antiviral therapy for HIV infection has been in use for a decade, but the extent to which treatment success has changed is uncertain. We examined risk of initial virological failure of antiviral therapy according to the year of starting therapy.

**Method:** We included subjects from 5 HIV treatment centres in Austria who started combination antiviral therapy from 1996 to 2004. Based on the first viral load measurement from 9 to 15 months after combination antiviral therapy initiation, virological failure was defined as a viral load of more than 400 copies/mL. We used the following 2 inclusion strategies: (1) including all subjects, with missing VL measurement counted as virological failure (n = 1959; strategy A); (2) including all subjects with VL measurement (n = 1462; strategy B);

**Results:** From 1996 to 2002, risk of virological failure fell from 69.2% to 31.7% for strategy A, 41.5% to 13.8% for strategy B. Missing viral load measurement one year after initial therapy decreased only to a small amount (27.8% and 17.9% for the years 1996 and 2004, respectively).

**Conclusions:** Over a 9-year period of combination antiviral therapy use in clinical practice, risk of initial virological failure of treatment has decreased. These data suggest the trend is sustained in all years.

**D.17 (Poster)**

Incidence of clinically significant renal events among patients treated with Tenofovir (TDF) in comparison to patients who never received TDF as part of their ART. Results of an observational cohort study

Schewe K.1, Fenske S.2, Weitner L.1, Adam A.1, Buhk T.2, Stellbrink H.J.2

1Infekionsmedizinisches Centrum Hamburg, St. Georg, Hamburg, Germany, 2Infekionsmedizinisches Centrum Hamburg, Grindelpraxis, Hamburg, Germany

**Objective:** TDF is a highly potent NRTI used for the treatment of HIV-infected patients. Renal toxicity may occur with TDF use; however reported toxicity rates and severity vary across studies. We performed a retrospective analysis of our patient cohort to evaluate incidence of clinically significant renal toxicity in clinical practice and underlying risk factors.

**Methods:** Clinical and laboratory data from 1992 until Dec. 1st, 2006 are included in this analysis. Identification of patients (pts) reaching a composite endpoint of either ≥ 0.5mg/dl increase of serum creatinine (Scr) on a single occasion on treatment with TDF or pts who discontinued TDF due to renal events by screening of the data base. Comparison to HIV-treated pts who never received TDF.

**Results:** Data of 1191 HIV-infected pts were analysed. Of 926 pts (69%) receiving antiretroviral therapy (ART), 492 pts (60%) had received TDF for a mean duration of 27.4 months (1125 patient-years (pt-yrs)), while 434 pts (40%) had never received TDF (mean observation: 51.4 months; 1871 pt-yrs). Pts on TDF were older (mean 46.1 vs. 43.8 yrs), had longer duration of ART (mean 8.36 vs. 4.63 yrs), lower CD4 nadir (207/ul vs. 302/ul) and lower current CD4 count (517/ul vs. 559/ul) than non-TDF pts.

18/492 TDF-pts experienced a 0.5 mg increase of Scr above baseline (BL) (incidence 1.8 /100 pt-yrs) compared to 21/434 pts in the non-TDF group (incidence: 1.1/100 pt-yrs). 9 pts discontinued TDF due to renal toxicity after a median of 9 months resulting in a partial (n=5) or complete (n=4) return of Scr to pre-TDF levels. 21 of the TDF treated patients met the prespecified composite endpoint (incidence: 1.9 per 100 pt-yrs). 11 pts continued TDF despite elevated Scr; Scr returned to BL in 3 pts, remained elevated in 6 pts and further increased in 2 pts. In 6/18 pts with rising Scr glucosuria was present, proteinuria in 12/18 pts, low phosphate in 5/16 pts. Additional risk factors were present in 16/21(76%) TDF-patients with renal toxicity.

**Conclusion:** In our cohort, the incidence of clinically significant renal toxicity was 1.9% in TDF-pts versus 1.1% in non-TDF pts. This difference may be mainly explained by additional renal risk factors like difference in age, duration of HAART and lower CD4 count in the TDF group.

**D.18 (Poster)**

HIV-positive Schwangere – muß die Sectio wirklich immer sein?

Kästner R.1, Sovic M.2, Müller M.1, Sonnenberg-Schwan U.3, Gingelmaier A.4

1Universitätsfrauenklinik München, Psychosomatik, München, Germany, 2Universitätsfrauenklinik München, Geburtshilfe, München, Germany, 3All Around Women Special, DAIG e.V., München, Germany, 4Universitätsfrauenklinik München, Infektiologie, München, Germany

**Fragenstellung:** Warum erhalten in Deutschland HIV-positive Schwangere fast ausnahmslos eine Sectio?

**Methodik:** Psychosomatischer Ansatz, um die Leitlinien unterchiedlicher Länder hinsichtlich ihrer Entstehung und Umsetzung zu hinterfragen, Literaturrecherche und persönliche Kommunikation mit Behltern und Betroffenen in verschiedenen Ländern

**Ergebnisse:** Zwischen 1999 und 2003 wurden in Deutschland mehr als 600 HIV-positive Schwangere in spezialisierten Zentren betreut und in 98,4% per Sectio entbunden. Demgegenüber entbinden in benachbarten europäischen Ländern und in den USA ca. 20 – 30 % bei Vorliegen optimaler Voraussetzungen vaginal, ohne eine höhere Rate an vertikalen Trans-
mission. Dieselben optimalen Voraussetzungen liegen im deutschen Kollektiv in mindestens 50 % aller betreuten Fälle vor. Angst, organisatorische Schwierigkeiten und mangelnde Bereitschaft einen informed consent auch unter Einbeziehung der psychosomatischen Faktoren anzustreben erscheinen ursächlich für die anhaltend hohe Sectiorate.

Schlussfolgerung: Ist die Schwangere compliant, nimmt eine HAART ein mit der die Virustat unter der Nachweisgrenze liegt und fehlen geburts- und Risikofaktoren, dann sollte ein hypothetischer Nutzen der primären Schnittenbindung deren Risiken gegenübergestellt werden und der Betroffenen die Möglichkeit zur Mitentscheidung eingeräumt werden.

D.19 (Poster)
Duration of NNRTI treatment after switch to a first Nevirapine- or Efavirenz-containing regimen.
An observational cohort analysis

Schewe K.1, Adam A.1, Goldbach J.2, Weitner L.1
1Infekionsmedizinisches Zentrum Hamburg, St. Georg, Hamburg, Germany, 2Boehringer Ingelheim Pharma GmbH & Co. KG, Medizinische Wissenschaft, Ingelheim, Germany

Purpose: To determine the duration of NNRTI treatment from switch to a first episode of nevirapine (NVP) or efavirenz (EFV) containing therapy in a HIV specialised practice.

Methods: Observational cohort study of patients (pts) treated with NVP or EFV between January 2000 and December 2004. Fishers exact test or Chi2 tests, Kaplan-Meier estimates and log rank tests were used for the analysis.

Results: 125 pts and 117 pts with NVP and EFV treatment were identified: male 93%, mean age 40.6 yrs, mean duration of pre-treatment 3.7yrs, mean duration of treatment 3.1yrs with no sig. difference between the groups. Of pts with values available at baseline and at 1 year (NVP: 62pts, EFV: 42pts): Baseline viral load was higher among pts receiving EFV (51% <50 copies/mL) vs NVP (68% <50 copies/mL). At one year VL was undetectable in 86% in both groups. Baseline mean CD4 count was similar (EFV 474 cells/µl, NVP 495 cells/µl) with a significant increase in CD4-cell percentage at one year (no difference between groups). The mean treatment duration was significantly longer in pts who received NVP than EFV (804.0±568.7 days vs. 550.7±477.1 days, respectively, p<0.001). Treatment discontinuation was comparable in both groups (NVP 50.4%, EFV 43.6%, p=0.305). The time to treatment discontinuation was comparable among both groups (Kaplan Meyer analysis, p=0.46 logrank-test). Main reasons for discontinuation were adverse events (NVP 12.8%, EFV 19.7%, p=0.1643) and treatment failure (NVP 10.4%, EFV 7.7%, p=0.51).

Conclusion: In clinical practise switch to NVP or EFV based regimens result in comparable durability and efficiency.

D.20 (Poster)
Efficacy and tolerability of Fosamprenavir/ritonavir (FPVr) once daily (QD) with 100mg Ritonavir® in clinical practice: a 24 week analysis

Ulmer A.1, Mülller M.1
1Praxis Ulmer Frietsch Müller, Stuttgart, Germany

Background: Fosamprenavir (FPV) is licensed in Europe for BID dosing with low dose Ritonavir® and 2 NRTIs. Efficacy and safety of FPVr 1400/200mg QD and 700/100mg BID in ART-naive patients has previously been shown in 2 major studies, SOLO and KLEAN. Available pharmacokinetic (Ruan 2004) and clinical data from pilot studies (Hicks 2006, Smith 2006) suggest sufficient FPV drug levels with 100mg r QD to treat HIV wild type virus.

Objective: We analyzed this concept retrospectively in an observational cohort from our private clinic.

Methods: Retrospective chart review of HIV-positive patients being followed in a routine clinical care setting with following criteria: Treatment (Tx) with FPVr 1400/100mg QD. Patients had to be either Tx-naive, PI-naive or had to have a viral load (VL) of <50 cps/ml and had to have no previously reported PI-failure (Switch-patients). Available values for VL, CD4 cell count, tolerability and safety were analyzed at baseline (BL) and week 4, 12 and 24.

Results: 16 patients (50% women) on ART with FPVr 1400/100mg QD were analyzed (5 were Tx- or PI-naive and 11 had switched to FPVr QD due to side effects under their prior ART). TDF/FTC (N=14), ABC/3TC (N=1) and TDF/3TC (N=1) were given as backbone Tx. Median VL at BL was 29.382 cps/ml (6 patients >100.000 /ml). Median CD4 at baseline was 310 cells/µl (2 patients <100/µl). After 24 wk 13/16 (81%) patients had a VL of <50 cps/ml at the last timepoint assessed. 3 patients had >50/ml (60, 199 and 118/ml). Mean CD4 increased by 152 cells/µl at week 24 with all patients increasing. A grade 1 Total Chol and grade 3 Trigl (grade 3 at BL) was observed in 1 patient each. Most frequently reported side effects were gastrointestinal in nature (mild to moderate) in 8 patients, which were fully reversible in 5 patients after 4 weeks. No patient so far has stopped treatment due to side effects or lack of virol. response.

Conclusions: In this small retrospective observational cohort a FPVr 1400/100mg QD containing ART has been shown to be efficacious and well tolerated up to 24 weeks, so far confirming the results from recently reported pilot studies. Further controlled trials are needed to finally evaluate this patient-friendly concept.

D.21 (Poster)
Efficacy and safety of fosamprenavir (FPV) 1400 mg boosted with 100 mg ritonavir once daily (QD) versus FPV 700 mg boosted with ritonavir 100 mg twice daily (BID)

Khavkin P.1, Silva E.2, Brenda D.1, Gate P.3, Mösch M.4, Haberl A.1, von Hentig N.5, Staszewski S.1
1Klinikum der J.W.Goethe Universität Frankfurt, HIVCEN- TER, Frankfurt, Germany, 2HIV Treatment & Clinical Research Unit, Federal University of São Paulo, São Paulo, Brazil, 3Private Practice Friedenstrasse, Frankfurt, Germany, 4Private Practice Kaiserstrasse, Frankfurt, Germany, 5Klinikum der J.W.Goethe Universität Frankfurt, Department of clinical Pharmacology, Frankfurt, Germany

The aim of this databank analysis was to compare ART regimens containing 2 NRTIs combined with fosamprenavir (FPV) 700 mg boosted with ritonavir (RTV) 100 mg BID vs. FPV 1400 mg with 100 mg RTV QD in respect to virologic and immunologic response as well as the side effects, especially concerning lipid values.

Data were analyzed from HIV patients in the Frankfurt HIVCENTER Cohort. The first group includes 58 patients who were taking two or three nucleoside reverse transcriptase
Didanosine in a large and unselected German patient population: Efficacy, safety and clinical outcome

Fenske S.1, Postel N.2, Steoehr A.3, Lauenrooth-Mai E.4, Eckert M.5, Reeb L.5, Schewe K.6

1ICH Grindel, Hamburg, Germany, 2Bristol-Myers Squibb GmbH&Co.KGaA, Medizinische Abteilung, München, Germany, 3ifi-Institut für interdisziplinäre Medizin, Hamburg, Germany, 4Privatpraxis, Berlin, Germany, 5SIMW GmbH, Wegberg, Germany, 6Infekionsmedizinisches Zentrum Hamburg, Hamburg, Germany

Background: Didanosine (ddI) is a potent antiretroviral agent which has been investigated in numerous cohort and clinical studies. However to date there are no data on the use of ddI in a large and unselected patient group in Germany.

Objectives: To assess clinical outcome, efficacy and safety of ddI in antiretroviral treatment (ART)-naïve and –experienced HIV+ patients in clinical practice. To assess the prevalence of M184V mutation at study entry.

Methods: Single-arm, non-interventional, multicenter, prospective cohort study in 121 HIV specialised outpatient departments throughout Germany. Patients eligible for analysis were treated with ddI-containing ART in 2003-04. Clinical and laboratory status, CD4 cells and viral load (VL) were assessed at baseline (BL) and months 3 and 6. Intention-to-treat-analysis (missing=ignored). Query management for implausible reports.

Results: 342 patients (79% male, 15% female) with a mean age of 40 yrs [range 21-68] were eligible for analysis. 232 pts (68%) were ART experienced; 69% had current or previous symptoms of HIV infection and/or AIDS. Median duration of treatment was 184 days. M184V mutation was present at baseline in 86% of 74 pts in whom genotypic data were available. DdI was most frequently combined with tenofovir (60%). Median CD4 cell count increased from BL (296/µl, range 4-1302) to 379 (+83) and 424 (+128) at months 3 and 6, respectively. Median VL decreased from BL (7,740 cp/ml, range <50-1,900,000 cp/ml) to ≤50 cp/ml at both months 3 and 6, respectively. During treatment 3 pts (0.9%) had newly diagnosed opportunistic infections. 27 pts had adverse events. Subclinical elevations of pancreatic enzymes were observed in 25 (7.3%) and 14 (4.1%) pts at BL and month 6, respectively; acute pancreatitis was rare (1 case). Neuropathy occurred in 3 cases, lactic acidosis in 1 case; unexpected side effects were epistaxis, taste loss and hypotension. A case of convulsions was the only unexpected severe adverse event.

Discussion: In this non-controlled observational study didanosine-containing ART was associated with substantial clinical, immunologic and virologic improvement in a mainly pre-treated patient population with relatively advanced HIV disease. No unexpectedly high rate of side effects was detected.

D.23 (Poster)

Data from the Connect cohort confirm that Enfuvirtide is effective and well tolerated in treatment experienced patients – 24 week interim results from Germany

Degen O.1, Gläßel F.2, Knechten H.3, Köppe S.4, Gute P.5, Tappe A.7, Wellmann E.7, Stellbrink H.-J.8

1University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 2HIV-treating physician, München, Germany, 3HIV-treating physician, Aachen, Germany, 4HIV-treating physician, Berlin, Germany, 5Praxiskzentrum - Kaiserdamm, Berlin, Germany, 6HIV-treating physician, Frankfurt, Germany, 7Roche Pharma AG, Grenzach, Germany, 8ICH Hamburg, Hamburg, Germany

Objective: The CONNECT cohort is an observational study that assesses the efficacy and tolerability of treatment with enfuvirtide in a non-selected patient population. Within the cohort, a connected nurse program provides support for physicians and counseling of patients for facilitating the self-administration of enfuvirtide and for improving the handling of side effects. An interim analysis of 39 patients who completed 24-weeks of treatment is presented.

Methods: Multicenter, prospective, open label, 24 week observational study. Assessments at week 4, 12 and 24 include change in viral load, CD4 count, antiretroviral therapy (ART) and concomitant medication from baseline. Tolerability assessments include safety laboratory parameters, injection side reactions (ISR) and adverse effects (AEs). Resistance data and Genotypic Susceptibility Scores (GSS) are also obtained (HIV-GRADE), susceptible and limited susceptible drugs were calculated as 1, intermediate as 0.5 and resistant as 0 points.

Results: 24-week interim analysis of 39 patients. Baseline characteristics: 84.62% male, median age 44 years, median time since first diagnosis 13.5 years (IQR 11-17), Proportion of patients with HIV stage A 12.8%, B 25.6% and C 59.0%, respectively. Median baseline VL 4.64 log10 HIV RNA copies/mL (IQR 3.7-5.7), median CD4 count 150 cells/mm³ (IQR 39-279). 43.6% of patients received TPV and 30.8 % DRV as part of their ART regimen. 12.8 % of patients were enfuvirtide-experienced. Week 24 results: 66.7% of patients had a VL < 400 copies/mL and 53.8% < 50 copies/mL (ITT). Median decline in VL was 2.26 log10. There were no clinical grade 3 and 4 adverse events. Enfuvirtide was stopped in 5.1% of the patients. Resistance data were available from 34 of 39 patients, GSS scores ranged from 2 to 18 (median 6.8).

Conclusions: Viral load response in this cohort appears to be better then in the TORO studies, probably due to relative high numbers of susceptible drugs in the background therapy. This results indicate that response to enfuvirtide might be improved by use earlier in resistance development. Professional training and support program might have helped to improve adherence and treatment response.
Effect of switch from lopinavir soft gel capsules to lopinavir mexitrel formulation on gastrointestinal side effects, quality of life, lipid, virologic and immunologic parameters

Schewe K.1, Fenske S.2, Schneisser N.3, Weiner L.1, Adam A.1, Buhk T.2, Stellbrink H.J.2, Hansen S.4, Gellermann H.4

1Infekionsmedizinisches Centrum Hamburg, St. Georg, Hamburg, Germany, 2Infekionsmedizinisches Centrum Hamburg, Grindelpraxis, Hamburg, Germany, 3University of Cologne, 1st, Department of Internal Medicine, Division of Infectious Diseases, Cologne, Germany, 4IPM-Studycenter, Hamburg, Germany

Objective: Lopinavir (LPV) tablets have been available in Germany since July 2006. Compared with soft gel capsules LPV tablets have no need for refrigeration, no food restrictions and a reduced number of pills. Ws prospectively assessed the gastrointestinal side effects, quality of life, lipid, virologic and immunologic parameters before and after switch to LPV tablet formulation.

Methods: Multicentre, prospective, observational cohort study. All patients (pts) on LPV softgel capsules were given the augmented symptom distress module questionnaire (ADSM) within one month before and 1-2 months after switch to LPV tablets. ADSM documents the presence and severity of 22 symptoms during the previous 4 weeks. Lipid, virologic and immunologic parameters were collected as part of clinical routine. Pts were required to have taken LPV soft gel capsules for at least one month prior to enrollment and no changes in concomitant antiretroviral medication was allowed. Paired T test and Signed-rank test were performed.

Results: As of July 2006, 261 pts were on treatment with LPV soft gel capsules in the participating centres. 139 pts participated in this study: m=128, f=11, mean age 44yrs, mean duration of HIV infection 10yrs, mean duration of antiretroviral treatment 6,2 yrs, mean duration of LPV treatment 39 months. 62 pts had advanced disease. HI viral load, CD4 cell count, fasting cholesterol and triglycerides did not change after switch. 127 pts completed both ASDM questionnaires. During the period of one month prior to switch disturbing nausea or vomiting was present in 18% of pts and in 16% thereafter (n.s.). Disturbing swelling, abdominal pain or flatulence was present in 39% of pts before switch and in 36% thereafter (n.s.). Disturbing loose stool or diarrhoea was present in 64% of pts before switch and in 49% thereafter (p<0.001). General tolerability improved in 35% and deteriorated in 7% of pts (n.s.). General well being improved in 30% and deteriorated in 6% (n.s.). Handling of LPV tablets was rated more convenient by 86% (p<0.001).

Conclusions: Switch from LPV soft gel capsules to tablets resulted in a significant reduction in the severity of diarrhea and a significant improvement in convenience. Lipid, virologic and immunologic parameters remained stable.
D.26 (Poster)

Efficacy of efavirenz-based HAART after switching from a protease inhibitor

Khaykin P.1, Brenda D.1, Carlebach A.2, Knecht G.3, Müller A.1, Stürmer M.4, Staszelowski S.1

1Klinikum der J.W.Goethe Universität Frankfurt, HIVCENT-TER, Frankfurt, Germany, 2Private Practice Friedenstrasse, Frankfurt, Germany, 3Private Practice IFS, Frankfurt, Germany, 4Klinikum der J.W.Goethe Universität Frankfurt, Department of Virology, Frankfurt, Germany

Objective: The aim of this database analysis was to investigate the efficacy and safety of efavirenz (EFV)-based HAART after switching from protease inhibitor (PI)-based regimens.

Methods: Data were analyzed from 50 HIV+ patients who were taking two or three NRTIs and one PI or boosted PI (PI/r) and then switched the PI to EFV. The reasons for switching were side effects, virologic failure, and non-compliance.

Summary of results: 22/50 patients were still on the EFV at the time of analysis. Viral load in the OT analysis decreased from 4.9 log10 to 1.6 log10 copies/ml. Of the patients who discontinued EFV, reasons given were virologic failure in 20%, adverse events in 22% and non-compliance in 14% of the patients. Patients who showed virologic failure had prior experience with different therapy regimens or showed 2 or 3-class resistance. Among the patients who stopped EFV therapy due to adverse events, CNS side effects were the most common.

Conclusions: Modification of a HAART regimen may lead to viral suppression if EFV is substituted for a PI or PI/r. However, some patients in our study demonstrated adverse events or virologic failure. Most of the patients who discontinued EFV had 2- or 3-class resistance in their treatment history.

D.27 (Poster)

Darunavir (TMC114) in highly pre-treated HIV-1-infected patients: Clinical experience obtained from routine clinical practice

Schmitz B.1, Cichon P.1, Egle A.2, Geit M.3, Gmeinhart B.4, Haas B.5, Kanatschnigg M.6, Kapper A.5, Rieger A.4, Sarcletti M.7, Schlag M.8, Taylor N.9, Zangerle R.7

1Otto Wagner Hospital, II. Medical Department Pulmological Centre SMZ Baumgartner Höhe, Vienna, Austria, 2II. Medical Department University of Salzburg, Division of Hematology, Oncology and Infectious Diseases, Salzburg, Austria, 3General Hospital of Linz, Department of Dermatology and Venerology, Linz, Austria, 4University of Vienna Medical School, Department of Dermatology, Division of Immunology, Allergy and Infectious Diseases, Vienna, Austria, 5General Hospital – Graz West, I. Medical Department, Graz, Austria, 6General Hospital Klagenfurt, I. Medical Department, Klagenfurt, Austria, 7University of Innsbruck, Department of Dermatology and Venereology, Innsbruck, Austria, 8Janssen-Cilag Pharma GmbH, Vienna, Austria

Background: The activity of boosted Darunavir (DRV/r, 600/100 mg bid), a novel protease inhibitor (PI), against PI-resistant virus has been proven in clinical trials. A Named Patient Program allowed to assess treatment results obtained in routine care settings.

Objective: To evaluate the safety and efficacy of DRV/r containing ART when used in routine clinical practice and factors influencing outcomes.

Methods: 31 HIV-1-infected patients were included. Patients were at least 3-class-experienced. All were naïve to DRV. Median baseline CD4 cell count: 160 (2-914), median HIV-viral load: 3,99Log10 (1,69-6,18), 5 subjects had viral load (VL) < 50 c/ml. Patients were followed up according to local standard of care. Genotypes were used to determine DRV-specific resistance-associated mutations (DRV-RAMs) and genotypic sensitivity scores (GSS) for the optimized background regimen (OBR).

Results: At cut-off (Feb 07), treatment with DRV/r was initiated in 28 patients. The OBR contained 2 or 3 NRTIs. TMC125 was added in 4 patients. Ten subjects (36%) used Enfuvirtide (EFN), thereof 7 (25%) naïve. Median follow-up time: 25 weeks (range 4-84), 16/23 subjects (70%) reached VL<50 c/ml at week 12, 10/15 (67%) at week 24, and 3/4 (75%) at week 48. Mean increase in CD4 cell count was 58, 88, and 142 at week 12, 24, and 48, respectively. There was 1 treatment discontinuation (death, not related to DRV). Two serious adverse events (not related to DRV) and 3 non-serious side effects were reported. The latter were GI-related and mild to moderate in severity. DRV-RAMs at baseline were infrequent: 75%, 7%, and 18% of patients had 0-1, 2, and >2 DRV-RAMs, respectively. Response at week 12 was decreased in patients with a GSS of £ 0.5 (less than 1 fully active drug in OBR) and in the presence of > 2 DRV-RAMs. There was no difference in response of EFN-users (ENF-naïve) as compared to ENF non-users, however, in patients using ENF naïve, ENF represented the only fully active drug in the OBR.

Conclusions: DRV-based CART showed very good safety and efficacy in a group of highly pre-treated patients in routine care settings. Careful consideration of treatment history, DRV-RAMs and GSS can help to design the optimal DRV-based CART. Further follow up of efficacy and safety is needed to prove long-term outcomes.

D.28 (Vortrag)

Transfer of autologous gene-modified T lymphocytes in HIV-infected patients with advanced immunodeficiency and multidrug resistant virus

von Laer D.1, von Lunzen J.2, M870 study group

1Georg-Speyer-Haus, Frankfurt am Main, Germany, 2Universitätskrankenhaus Eppendorf, Infektiologie, Hamburg, Germany

Aims: Drug toxicity and viral resistance limit long-term efficacy of antiviral drug treatment for HIV infection. Thus, alternative therapies need to be explored.

Methods: Here, we tested the infusion of T lymphocytes transduced with a retroviral vector (M870) that expresses an HIV entry inhibitory peptide (maC46). Gene-modified autologous T cells were infused into 10 HIV-infected patients with advanced disease and multidrug resistant virus during antiretroviral combination therapy.

Results: T cell infusions were tolerated well with no severe side effects. A significant increase of CD4 counts was observed post infusion. At the end of the one-year follow-up, the CD4 counts of all patients were still around or above baseline. Gene-modified cells could be detected in peripheral blood, lymph nodes and bone marrow throughout the one-year fol-
Efficacy and tolerability of TDF/FTC-containing first line HAART in clinical practice – 24 week data from a German outpatient cohort

van Lunzen J.1, Fäkenhuener G.2, Lutz T.3, Klauke S.4, Mauss S.5, Knechten H.6, Braun P.6, Gallo L.7, Mertenskoetter T.7, Ranneberg B.7

1Universitätsklinikum Eppendorf, Ambulanzzentrum des UKE GmbH, Bereich Infektiologie, Hamburg, Germany, 2Med. Einrichtungen der Universität Köln, Klinik I für Innere Medizin, Köln, Germany, 3Infektiologikum Frankfurt, Praxis Friedensstraße, Frankfurt, Germany, 4Infektiologikum Frankfurt, Praxis Stresemannallee, Frankfurt, Germany, 5Center for HIV and Hepatogastroenterology, Düsseldorf, Germany, 6Praxiszentrum Blondelstrasse, Aachen, Germany, 7Gilead Sciences, Martinsried, Germany

Background: First line HAART in recent pivotal trials has been associated with high efficacy and good tolerability. However, clinical practice often differs from the trial situation – patients have comorbidities, co-infections and monitoring can be more limited. To evaluate efficacy and safety of first line HAART in a day to day setting, this Gilead-sponsored non-interventional cohort was established.

Methods: 554 HIV-positive antiretroviral naïve adult patients were enrolled in 50 German centres between July 2005 and August 2006. All patients will be followed up for three years; efficacy (VL, CD4), tolerability and regimen changes are documented every three months. In addition, resistance profile and renal safety are monitored. All patients received TDF/FTC in combination with an NNRTI or PI/r as their first regimen.

Results: BL data are available for 524/554 patients. To date, 411/554 (74%) patients have reached week 24. Patients were mostly male (81%) with a median age of 39 years (IQR 33 – 45 years). At BL, median CD4 count was 204 cells/mm3 (IQR 110 – 293 cells/mm3), median VL was 5.0 log10 copies/ml (IQR 4.4–5.3). Last HIV-status (CDC) was C in 22%, 48% started therapy with CD4 < 200 cells/mm3. Primary resistance data have been obtained for 342 patients; overall rate for primary resistance was 10%. At week 24 in an AT(as treated)-analysis 84.9% reached VL < 50 copies/ml (VL < 500 copies/ml: 98%), CD4 increased to 360 cells/mm3 (median, IQR: 249–491).

TDF/FTC was combined with an NNRTI (38%) or PI/r (61%). TDF/FTC was discontinued in 17/411 patients (4.1%), virological failures were rarely reported (n=8, 1.9%). Overall tolerability of 1st line HAART was good; 97 adverse events and 7 SAEs were reported.

Mean creatinine clearance (Cockcroft-Gault) stayed within the normal range (112 ml/min at BL and 106 ml/min at week 24).

Conclusion: In clinical practice, 1st line HAART including TDF/FTC in antiretroviral naïve patients proved efficacious and showed good short term tolerability.

D.30 (Poster)

C2F5 as a secretable fusion inhibitor for gene therapy of HIV infection

Kimpel J.1, Newrzela S.1, Hermann F.1, Egerer L.1, von Laer D.1

1Georg-Speyer-Haus, AG von Laer, Frankfurt/ Main, Germany

Objectives: The HIV entry mechanism is an attractive target for gene therapy approach. Antibodies directed against epitopes of gp41 (eg C2F5) act as fusion inhibitors. Two major aims should be achieved with an effective HIV entry inhibitor: Protection of the transduced (selective advantage) and the untransduced cells (bystander-effect). In an earlier study we have demonstrated that membrane-anchored fusion inhibitor C46 leads to protection from HIV infection of the transduced T cells. The disadvantage of this approach is that only a fraction of T cells can be transduced and no bystander-effect is achieved. A secreted principle for HIV entry inhibition could enable effective protection of the transduced cells and also give a bystander effect.

Methods: The aim of the present study was to generate a secreted entry inhibitor by cloning a retroviral vector for expression of HIV neutralizing antibody C2F5.

Primary T and B cell lines were transduced with the retroviral vector and analyzed for C2F5 secretion via a T20-binding ELISA. Functionality of produced antibodies was examined in a single round infection assay with HIV pseudotyped lentiviral particles.

Primary murine T cells as well as hematopoietic stem cells were transduced with the retroviral vector construct for expression of C2F5 in vivo. For this purpose Rag-1-deficient mice were re-populated with genetically modified cells.

Results: After transduction of human cell lines as well as primary murine cells C2F5 production could be detected in therapeutic concentrations. Secreted antibodies showed effective entry inhibition in a single round infection assay. Transplantation of primary cells into Rag-1 deficient mice lead to significant titers of C2F5 in mice sera. Both, T and B cells expressed functional active C2F5 antibodies.

Conclusion: In summary we could show that after retroviral gene transfer C2F5 antibody was produced in vitro and in vivo. Functionality of secreted antibody was proved in a single round infection assay. This approach is especially interesting as transduced T cells can migrate into tissues like lymph nodes in which HIV infection is elevated. We propose that a bystander-effect renders high transduction efficacy unnecessary, thus lowering the risk of insertional mutagenesis.

D.31 (Poster)

Development of retroviral vectors encoding secretable entry inhibitory peptides for HIV gene therapy

Egerer L.1, Hermann F.1, von Laer D.1

1Georg-Speyer-Haus, Applied Virology and Gene Therapy, Frankfurt am Main, Germany

Objective: We are working on the development of retroviral vectors encoding secretable C-peptides for HIV gene therapy. C-peptides are efficient inhibitors of viral entry into target cells. In a previous clinical trial, our group used a retroviral vector (M87o) encoding a membrane-bound version of the C-peptide C46 to protect T cells from HIV infection. To im-
Methods: As the C46 peptide itself is too short for secretion, we are testing different strategies to achieve secretion:

First, the C46 was elongated by different linker sequences, further on a “multimer” of several C46 units linked by protease cleavage sites was generated. A third approach is the fusion of C46 to a secretable scaffold protein.

Cell lines were transfected or transduced with vectors encoding the different secretable C46-derived peptides (sC46). Cell lysates and cell culture supernatants were analysed in respect of protein expression and secretion rates as well as inhibitory capacities. In addition, the impact of glycosylation of the peptides on the secretion rates and inhibitory potential was analysed.

Results: The transfection and transduction of cell lines with the different sC46-encoding vectors resulted in reasonable expression and secretion of sC46 peptides. Mutation of multiple glycosylation sites lead to a decrease of expression and secretion.

In a single round infection assay the supernatants from transfected cells were able to inhibit the entry of viral particles into two different cell lines, but they were quite ineffective compared to the closely related fusion inhibitor T-20.

Conclusions: Subsequent work will be directed at further improvement of the inhibitory efficacy of the peptides. Afterwards reduction of the immunogenicity of the peptides and further testing of their efficacy in T lymphocytes will be analysed.

D.32 (Poster)
Efficacy data of the German open-label study to assess the safety of tipranavir co-administered with low-dose ritonavir (TPV/r) in patients with advanced HIV-1 infection and limited treatment options

Goldbach J.1, Moll A.2, Esser S.3, Theobald T.4, Maus S.5, van Lunzen J.5, Eskoetter H.1

1Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany, 2HIV specialised practice, Berlin, Germany, 3University Hospital, Essen, Germany, 4HIV specialised practice, Munich, Germany, 5HIV specialised practice, Duesseldorf, Germany, 6University Medical Center, Hamburg-Eppendorf, Germany

Purpose: To assess the safety and efficacy of TPV/r under conditions comparable to those to be expected for TPV/r in a real world clinical setting.

Methods: Adult patients (pts) had to be triple antiretroviral (ARV) class experienced having failed at least two previous PI-based regimens. The study medication was TPV/r 500/200 mg, twice daily added to a optimised background regimen based on genotypic resistance data chosen by the treating physician.

Results: Data of 254 HIV-1 infected pts (median age 44 years, 229 males, 25 females) from 70 centres were available for analysis. Most pts were in stage CDC B3 (28%) and C3 (57.1%). Pts were highly pre-treated with a median prior exposure to 12 ARVs: 5 NRTIs; 1 NNRTI and 4 PIs. 17.7% of pts were pre-treated with the fusion inhibitor enfuvirtide (ENF). Hepatitis B and C co-infection was reported from medical history for 12.6% and 3.9% of the pts respectively. In an on treatment analysis after 12 months of therapy pts achieved a median VL reduction from baseline (median 4.7 log10 copies/mL) of -1.9 log10 copies/mL and the median increase of CD4 cell count from baseline (median 157 cells/mL) was +71.5 cells/mL. 55.9% of pts started ENF with TPV/r at baseline. After 12 months use of ENF in conjunction with TPV/r compared to TPV/r without ENF provided a greater median decrease of VL (-2.28 vs. -1.43 log10 copies/mL respectively) and a greater median increase in CD4 cell count (+87 vs. +59 cells/mL respectively).

Conclusions: Patients participating in the German open label safety study were in an advanced stage of HIV-1 infection and highly pre-treated with low CD4 cell count and high viral load. Treatment with TPV/r, especially in combination with a new class (ENF) was associated with potent and durable VL reduction and increase of CD4 cell count, demonstrating an improvement of immunological status.

D.33 (Poster)
Switch to a completely ONce daily regimen containing Emtricitabine/Tenofovir-fixed dose combination plus Third QD partner: 24 weeks interim analysis of the SONETT trial

Weitner L.1, Kuhlmann B.2, Fenske S.3, Freiwald M.4, Ebrahimi R.5, Mertenskoetter T.6, Ranneberg B.7, Araseth K.7

1Infektionsmedizinisches Centrum Hamburg, Praxis St. Georg, Hamburg, Germany, 2Praxis Georgstrasse, Hannover, Germany, 3Infektionsmedizinisches Centrum Hamburg, Grindelpraxis, Hamburg, Germany, 4Private Practice, Berlin, Germany, 5Gilead Sciences, Foster City, United States of America, 6Gilead Sciences, Martinsried, Germany, 7Epimed, Berlin, Germany

Background: Study GS-934 found superior responses in terms of virologic suppression, CD4 response and discontinuations for adverse events in ART-naive pts randomized to TDF+ FTC+EFV in comparison to AZT+3TC+EFV. We evaluated the impact of switching patients with adherence or tolerability problems from CBV (AZT/3TC) + 3rd partner to a regimen of TDF (TDF/ FTC) + divergent qd partner in a 48 wk prospective open-label single arm multicenter Phase III trial.

Methods: 52 patients on a stable CBV-containing HAART for 12 wks with VL < 50 c/mL and CD4 > 50 cells/mm3 were switched to TDF + 3rd partner. Assessments including VL and CD4 were performed at BL and wks 4, 12, and 24 post-switch. Summary of Results: 7/52 patients discontinued early. At BL, median CD4 was 526 (IQR: 317-774) cells/mm3, median Hb was14.8 (IQR: 14.1-15.3) g/dL. 41/52 patients had taken CBV for >1 yr; 26 switched to TDF for simplification, 20 due to AEs, 6 for both reasons. TDF was mainly combined with EFV (n=30) or NVP (n=13). Viral Suppression was maintained with viral load < 50 copies/mL at week 24 in 43/51 (84%) enrolled patients. In 2 additional patients viral loads of 50 and 59 were observed at Week 24; both dropped to <50 levels later. CD4 increased numerically with a median of 526 cells at BL and 558 cells at week 24. Median Hb increased to 15.6 (IQR: 14.6 – 16.3) g/dL (p < 0.001) at week 24. No study drug-related adverse events grade 3 or 4 were reported, only two cases of Grade 1 creatinine increase were observed.
Conclusions: Results support switching from a stable CBV-containing HAART to a completely qd regimen of TVD plus third divergent partner given that virologic (< 50 c/mL) and immunologic control were maintained with the additional benefit of Hb increasing significantly.

D.34 (Poster)
Successful salvage therapy with Darunavir and TMC-125 in a patient with a four-class drug resistant Tipranavir-experienced HIV-1 strain
Harrer E.1, Müller S.M.1, Korn K.2, Walter H.2, Schmidt B.2, Harrer T.1

1Universitätsklinikum Erlangen, Medizinische Klinik 3, Klinische Infektionsimmunologie, Erlangen, Germany, 2Universitätsklinikum Erlangen, Institut für Klinische und Molekulare Virologie, Erlangen, Germany

Introduction: Multiresistant HIV-1-infected patients failing therapy with tipranavir and T20 have only limited treatment options. TMC-125 and darunavir are newly introduced antiretroviral drugs with potent activity against resistant HIV-1-variants. Here, we report on the successful salvage therapy in a multiresistant patient using TMC-125 and darunavir.

Methods: The then 34-year old patient was diagnosed with HIV-1-infection in 1993 when he presented with herpes zoster and a CD4 count of 120/µl. Since 5/1993 he was treated with all available antiretroviral drugs: AZT, AZT+DDC, AZT+DDI, then 3-5 drug combinations including D4T, 3TC, DDI, ABC, TDF, lopivire, EFV, HU, RTV, SQV, NNY, IDV, APV, LPV, TPV, alpha-IFN, T20. Most newly started therapies could have induced a transient rise of CD4 counts and a reduction of HIV-1 viremia, but viral load could never be suppressed below the limit of detection. In July 2006 he showed a high viral load on treatment with AZT, 3TC, TDF and tipranavir/r. Genotypic resistance analysis showed resistance to all drugs of the current and preceding antiretroviral regimens with following mutations: NRTI: M 41 L, E 44 A, D 67 N, L 74 I, V 75 M, F 77 L, V 118 I, M 184 V, H 208 Y, L 210 W, R 211 K, T 215 Y, K 219 N; NNRTI: K103N, P1: L 10 I, I 13 V, K 20 R, L 33 F, M 36 I, V 54 S, A 71 V, V 82 T, I 84 V, L 90 M. gp41 was not analysed, but T20 resistance had been documented two years ago.

Results: In August 2006, as his viral load increased to 170 000 and his CD4-count fell to 45/µl, tipranavir/r was exchanged by a combination of darunavir/r and TMC-125. AZT,3TC and tenofovir were continued and, in addition, T20 was reinitiated, but was stopped after 4 days due to strong local injection site reactions. For the first time in the patient’s treatment history, this combination could decrease viral load below 50 copies/ml. 6 months after switching therapy his viral load is still suppressed and his CD4 count increased to 226/µl.

Conclusion: This case demonstrates that the combination of darunavir/r and TMC-125 can exert a potent antiretroviral effect even on highly resistant HIV-1 variants. Due to different patterns of resistance mutations darunavir/r may retain activity against tipranavir resistant HIV-1 strains.

D.35 (Poster)
Behandlung von Patienten mit Darunavir im klinischen Alltag – Woche 12 Ergebnisse Therapieverlauf, Vorhersagbarkeit des Therapieansprechens mithilfe verschiedener Resistenzalgorithmen
Baumgarten A.1, Berg T.2, Dupke S.1, Carganico A.1

1Gemeinschaftspraxis Dupke/Carganico/Baumgarten, HIV-Schwerpunktpraxis, Berlin, Germany, 2Labor Berg, Berlin, Germany


Methoden: Die Umstellungen erfolgten resistenzgesteuert auf ein DRV-haltiges Regime mit begleitendem optimalen Backbone. Als OBR wurde bevorzugt T2ZV und TDF (58%) eingesetzt. 32% der Patienten (n=6) erhielten zusätzlich ENV. Ergebnisse nach Woche 12: Eine VL-Reduktion von 1log Stufe gelang bei 95% der Pat. (n=18), eine Reduktion um 2log Stufen bei 84% (n=16). 58% der Pat. (n=11) hatten nach drei Monate eine Viruslast von <50 kopien/ul. Die mediane Helferzellzahl lag bei Baseline bei 224 /µl und stieg bis Woche 12 um 87 CD4-Zellen im Median auf 311/µl. Die Verträglichkeit der neuen Regime war bis Woche 12 gut, so dass keine Umstellungen oder Therapieabbrüche aufgrund von Toxizitäten erfolgen mussten.


Hintergrund:

Darstellung: In einer Umfrage an Patienten, die eine schwere Gastrointestinale Erkrankung hatten und die Tabelle bei Raumtemperatur gelagert werden mussten, erhielten sie einen erweiterten Fragebogen mit 5 Items. Die Medikamenteneinnahme kann nun unabhängig erfolgen und die Tabl.-Einnahme angaben. 70% (19) der Patienten mit SGC hatten 1-3x/d Stuhlgang und nicht Dosis vergessen zu haben, während 63% (17) dies unter Tabl.-Therapie angaben. 48% (13) litten nie unter Durchfall, während unter Tabl.-Therapie 56% (15) unter SGC-Einnahme gaben an, zwar Dosis vergessen zu haben, aber nur 60% (16) mit Tabl. dies angaben. 67% (18) der Patienten mit SGC befanden sich gut, während 60% (16) mit Tabl. dies angaben.

Diskussion: Bezüglich der NW oder der Befindlichkeit wurde untersucht, ob sich Unterschiede hinsichtlich der zwei Fragestellungen: Beschwerden, v.a. Diarrhöen.

Erläuterungen: Die Adhärenz der Patienten war 93% (25) mit der Tabl.-Therapie zufrieden. Keine Dosis vergessen zu haben, während 63% (17) dies unter Tabl.-Therapie angaben. 70% (19) der Patienten mit SGC befanden sich gut, während 60% (16) mit Tabl. dies angaben. 48% (13) litten nie unter Durchfall, während unter Tabl.-Therapie 56% (15) unter SGC-Einnahme gaben an, zwar Dosis vergessen zu haben, aber nur 60% (16) mit Tabl. dies angaben. 67% (18) der Patienten mit SGC befanden sich gut, während 60% (16) mit Tabl. dies angaben.

Zielsetzung: Ob die chronische HIV Infektion zur Atherosklerose beiträgt, wird kontrovers diskutiert. Wir untersuchten die Beziehung zwischen HIV Infektion, antiretroviraler

**Erläuterungen:**

Detection of abacavir hypersensitivity by ELISpot method

**Objective:** Abacavir (ABC) causes a potentially fatal hypersensitivity reaction (HSR) in 5-8% of HIV-infected patients occurring usually within the first 6 weeks after starting treatment. HSR is diagnosed clinically and, actually, the testing for HLA-B*5701 becomes available as a further predictive test. The correlations between the occurrence of HSR, patch test reactions to ABC, and HLA-B*5701 are evaluated in the PREDICT Study. A safe diagnostic tool to confirm ABC-HSR is mandatory. Therefore, we here evaluated an ELISpot method to measure cellular in vitro responses to ABC.

Methods: ABC-ELISpot was performed in HIV-infected patients with clinically determined HSR to ABC who had stopped the ABC treatment for more than 6 weeks (n=11) and HIV-patients taking ABC for more than 12 weeks without suspected HSR (control group, n=13). Twenty of the HIV-patients were male, 4 female, the average CD4 T cell count was 338/ml (range 26-954). Peripheral blood mononuclear cells from all patients were stimulated by 1, 4, and 10 mg/mL of abacavir sulfate in 200 mL of cell culture medium. Following preincubation for 2 days, the cells were incubated in ELISpot plates for 2 further days and the production of interferon-gamma producing cells was measured.

Results: Patients with vs. without HSR displayed a significantly higher number of ABC-specific cells (7.6±4.7 vs. -0.2±1.1 spots increment, P=0.03). Using a threshold of 2 spots increment - which was determined by discrimination and receiver operating curve (ROC) analyses - HSR could be predicted with a sensitivity of 64% and a specificity of 85%. Of note, 2 patients were HLA-B*5701 positive, both suffered from HSR, and both were positive to the ELISpot.

Conclusions: We established the first ABC-specific ELISpot method which appears as an additional tool to detect HSR retrospectively. Its application could avoid the risk of life-threatening reactions during rechallenge with ABC in HIV-patients with vague suspicion of HSR.
Medikation und sonographischen Zeichen der Frühatherosklerose (Messung der Intima-Media-Dicke) im Kontext kardiovaskulärer Risikofaktoren.

**Methodik:** Ein Fall-Kontrollstudien-Design mit 292 HIV-positiven Individuen und im Verhältnis 1:4 nach Alter und Geschlecht-gematchten HIV-negativen Kontrollen (n=1.168).

In beiden Gruppen wurden einzzeitig Risikofaktoren, Blutdruck, Serum-Cholesterin und -Triglyceride sowie die Intima-Media-Dicke (IMT) im Arteria carotis-System erfasst. Mit multivariaten Regressionsmodellen untersuchten wir die Effekte von HIV Status und antiretroviraler Medikation auf die IMT.

**Ergebnis:** Die IMT in der A. carotis communis (CCA) war 5.70% ([3.08-8.38%], p<0.0001) oder 0.044mm [0.021-0.066mm] (p=0.0001) mächtiger bei HIV-Positiven, nach Adjustierung mehrerer Risikofaktoren. Im Bereich der Carotisbifurkation (BIF), war die IMT bei HIV-Positiven um 24.4% [19.5-29.4%] oder 0.250mm [0.198-0.303mm] mächtiger (p<0.0001). In der Analyse der antiretroviralen Medikamente zeigten sich höhere CCA- und BIF-IMT-Werte, bei Individuen, die eine antiretrovirale Kombinationstherapie (HAART) einnahmen.

**Schlussfolgerungen:** HIV-Infektion und HAART sind unabhängige Risikofaktoren für frühe Karotisatherosklerose. In Analogie zu grossen, populations-basierten Kohortenstudien ist ein um 4-14% höheres Risiko für ein kardiovaskuläres Ereignis bei HIV-positiven Individuen anzunehmen. Dies entspricht einem ca. 4-5 Jahre höheren "Gefäßalter". Die zugrundeliegenden Pathomechanismen bedürfen weiterer Klärung.

[Tabelle 1: Deskriptive Statistik]

[Tabelle 2: Effekt von HIV-Infektion auf die IMT]
D.39 (Vortrag)
Mitochondrial membrane potential of peripheral mononuclear cells in therapy naïve HIV infected patients
Sternfeld T.1, Tischleder A.1, Schuster M.1, Bogner J.1, German Competence Network HIV/AIDS
1Medizinische Poliklinik, University of Munich, Department of Infectious Diseases, München, Germany

Background: Mitochondrial toxicity was proposed to be caused by antiretroviral therapy (ART). We analyzed the influence of HIV infection on mitochondrial membrane potential (MMP) as a marker of mitochondrial function of peripheral mononuclear cells (PBMC) in patients without ART. The correlation of clinical and immunological parameters to MMP was investigated.

Methods: We studied 58 HIV infected patients never treated with ART (mean CD4 cell count: 418/µl, mean HI viral load VL 76.000 cp/ml, mean duration of known HIV infection 53 months) and 8 HIV negative controls. MMP of PBMC was measured by flow cytometry using the lipophilic dye JC-1.

Results: The mitochondrial membrane potential of HIV infected patients was significantly lower than for HIV negative controls (p=0.0001). In HIV infected patients, MMP of PBMC was highly correlated to CD4 cell nadir (p=0.0001, r=0.5), CD4 cell count at baseline (p=0.014, r=0.3), percentage of CD4 positive cells (p=0.018, r=0.3), VL (p=0.001, r=-0.4), and time since first positive HIV test (p=0.03, r=0.3). In multivariate analysis, the CD4 cell count (p=0.001) and the time since first positive HIV Test (p=0.04) remained significant in contrast to HI viral load.

Conclusions: HIV-infection itself has a significant influence on mitochondrial membrane potential of PBMC and is correlated to the immune status of the patient.

D.40 (Vortrag)
Lipoatrophy and ubiquitous mtDNA depletion in mice following long-term stavudine treatment
Stankov M.1, Schmidt R.E.1, Behrens G.1, Competence Network HIV/AIDS
1Hannover Medical School, Clinical Immunology, Hannover, Germany

Background: Mitochondrial DNA (mtDNA) depletion has been proposed as an important factor leading to peripheral lipoatrophy in HIV-patients receiving antiretroviral therapy. The extent to which mtDNA depletion occurs in other organs and tissue in humans has not been evaluated and animal models for lipoatrophy have not been established so far.

Methods: Groups of mice were treated with d4T, AZT or vehicle (5-20 mice per group) for up to 15 weeks with daily human doses adjusted for murine body surface area. In order to better parallel the pharmacokinetics in humans drugs were administered via oral gavage. MtDNA content was determined by Real-Time PCR in liver, muscle, heart, brain, and fat tissue. Adiponectin and leptin were measured by ELISA in the serum.

Results: Over a time period of 15 weeks mice receiving d4T or AZT gained less weight (d4T from 25.3±0.17g to 29.1±0.2g; AZT from 25.8±0.2g to 30.2±0.2g) as compared to control animals (from 26.1±0.2g to 34.8±0.2g) while no differences in food and water intake were detected. Post mortem examination revealed that mice on AZT treatment but particularly animals receiving d4T had less of both peripheral as well as central fat. Similarly, d4T treated animals had lower serum adiponectin levels as compared to control mice (2.6±0.1 µg/ml vs. 3.05±0.1 µg/ml; p<0.05) and lower serum leptin concentrations (222.5±72.5 mg/ml vs. 621.8±166 mg/ml). Analysis of mtDNA content revealed depletion of mtDNA in organs including the brain (-20%) and fat tissue (-27%) but the most profound and significant depletions were evident in muscle (-56%), liver (-64%), and heart (-45%).

Conclusion: This is the first study to show fat loss and hypoadipocinemia in mice after treatment with thymidine-analogues. Long-term treatment of mice with d4T led to mtDNA depletion that was not restricted to fat tissue. These data indicate that mtDNA depletion is an unspecific event during treatment with thymidine-analogues. If indeed mtDNA depletion is a major contributor to mitochondrial dysfunction, potential long-term toxicities in various organs need to be considered.

D.41 (Vortrag)
Comparison of Dual-energy X-ray Absorptiometry (DEXA) and morphological mitochondrial alterations in adipocytes in HIV-positive patients
Bellutti M.1, Gisinger M.1, Sarcletti M.1, Zangerle R.1
1Medizinische Universität Innsbruck, Innsbruck, Austria

Background: DEXA is regarded as a useful objective method for diagnosis of HIV-associated lipoatrophy. Mitochondrial alterations are a common feature in HIV-positive patients and can be seen in both treated or untreated individuals.

Methods: Fat biopsies from the gluteal region of 39 HIV-infected patients were taken in the years 2001 and 2002 and analyzed by electron microscopy. Simultaneously DEXA Scan of the whole body was performed.

Results: The median age of patients is 43.0 years, 25.6% were women. Mitochondrial alterations in adipocytes has been observed in 30 of 39 biopsies (76.9 %). Focally (up to 10% involvement) mitochondrial alterations has been found in 15 patients (38.5 %) and in 15 patients more than 10% of the mitochondria revealed damage. In 8 patients alterations affect more than 75% of mitochondria. Comparing the group with mitochondrial damage vs. no mitochondrial alterations the mean proportion of total body fat (18.3 % vs. 23.9 %), arm fat (18.7 % vs. 25.8 %), leg fat (16.3 % vs. 19.1 %) and trunk fat (19.0 % vs. 26.4 %) was lower, but did not reach statistical significance. In the group with no or up to 10 % damage compared with the group of more than 10 % involvement there was a statistic significant difference of the mean proportion of fat in arms (25.2 % vs. 13.0 %; p=0.0001), trunk (24.2 % vs. 15.5 %; p=0.001) and total body fat (22.4 % vs. 15.3 %; p=0.003). Similar results were obtained for men and women (20.8 % vs. 11.3 %; p=0.002 and 36.8 % vs. 20.0 %; p=0.015, respectively). Comparing the fat proportion in legs and mitochondrial damage no significant difference was found (18.4 % vs. 14.7 %; p=0.233). No difference in fat proportion and age was observed. The specific role of antiretroviral therapy in lipoatrophy in this study remained unclear.

Conclusions: Mitochondrial damage is frequently observed in adipocytes of HIV-infected patients and it might be associated with lipoatrophy. Multiple factors might influence the distribution of fat in the body in HIV-positive patients. Therefore more and more controlled studies are needed to evaluate the role of mitochondrial damage in HIV-infected patients.
Mitochondrial toxicity in HIV- and ART-exposed pregnancies

Gingelmaier A.1, Mylonas I.1, Walker U.A.2, Kost B.1, Kästner R.1, Soivic M.1, Grubert T.A.3

1Ludwig-Maximilians-Universität, Universitätsfrauenklinik, Innenstadt, München, Germany, 2Medizinische Universitätsklinik, Rheumatologie und klinische Immunologie, Freiburg, Germany, 3Gynäkologische Praxis, Ravensburg, Germany

Objectives: Nowadays, nucleoside reverse transcriptase inhibitors (NRTI’s) are administered routinely to HIV-infected pregnant women for the reduction of vertical transmission of HIV and for the treatment of the disease. The consequences for the newborn like a potential mitochondrial toxicity are further on unclear. The objectives of this study were:

a) evaluation of a mitochondrial toxicity of the HIV- and NRTI-exposed placenta and
b) clinical manifestations in the newborns.

Methods: The quantity of the mitochondrial DNA (mtDNA) of placental tissue was assessed using Taqman-PCR. Additionally, an analysis of the mitochondrial morphology was performed by electron microscope. The examined placentas derived from HIV-infected pregnant women in comparison to placentas of a control group. The HIV- and NRTI-exposed newborns were examined clinically and the lactate level of the peripheral blood was measured.

Results: The mt-DNA count per cell of 46 HIV- and NRTI-exposed placentas was reduced significant in comparison to 22 placentas of HIV-uninfected women (p=0.047). The morphology of the mitochondria differed not significant between the two groups. The lactate levels of the HIV- and NRTI-exposed newborns were elevated considerable within the first days of live, but no other symptoms occurred.

Conclusion: This study provided evidence that there could be a mitochondrialopathy of the placentas and newborns of HIV-infected mothers with ART treatment in pregnancy. To what extent this will have an impact on the further live of the HIV-uninfected child remains unclear.

Atherogenic risk in HIV-infected children on HAART due to triglycerides and small, dense LDL

Thiemeyer N.1, Neubert J.1, Verweel G.2, Königs C.3, Notheis G.2, Baumann U.1, Feiterna-Sperling C.4, Buchholz B.4, Richter W.O.5, Niehues T.1

1Heinrich Heine University, Centre for Pediatric, Düsseldorf, Germany, 2University of Rotterdam, Centre for Pediatric, Rotterdam, Netherlands, 3Johann Wolfgang Goethe University, Centre for Pediatric, Frankfurt, Germany, 4University Hospital Munich, Children’s Hospital, München, Germany, 5Medical School Hannover, Children’s University Hospital, Hannover, Germany, 6Institute for Lipoprotein Metabolism, Windach, Germany

Background: Hypertriglyceridemia is associated with HIV-infection whether treated or not. In non-HIV-infected subjects atherogenic risk is thought to be due to small, dense low-density lipoprotein (sdLDL) derived from triglycerid (TG) rich lipoproteins.

Objective: To investigate whether different antiretroviral substance classes are associated with elevation of TG and sdLDL.

Methods: We studied 66 children (9.0 ± 4.6 years old, 37 girls) who were treated with two NRTI plus NNRTI (n = 24, group 1), two NRTI plus lopinavir/ritonavir (n = 33, group 2), or lopinavir/ritonavir plus NNRTI (n = 9, group 3). Among 13 different lipid parameters SdLDL-apolipoprotein B-100 was measured after ultracentrifugation of serum in the infranatant with a density > 1.44 g/ml. The data were compared to data from healthy controls (n=28).

Results: The main findings were elevated TG in 7/24 children of group 1, 18/33 of group 2 and 5/9 of group 3 (median TG: 94, 109, 229 mg/dl). Elevated sdLDL-ApoB-100 was found in 7/24 children of group 1 (3 with elevated TG), 7 children of group 2 (3 and 5 children of group 3 (2). The mean concentration of sdLDL-ApoB-100 did not differ significantly between the three groups (11.6 ± 5.8; 11.9 ± 6.7; 14.4 ± 6.2 mg/dl). Eleven children have a high capacity to catabolize TG-rich VLDL producing elevated sdLDL leading to normal fasting TG.

Conclusions: No single antiretroviral substance class is associated with elevation of TG and sdLDL. In our cohort 22/66
children have an increased atherogenic risk profile based on either TG levels and/or sdLDL. A careful clinical follow up of children on HAART is required to monitor atherogenic complications.

D.45 (Poster)
HIV or ART? Gender differences in the causal attribution of symptoms and adverse events

Objective: This multicenter study examines differences between men and women with HIV on physical symptoms, symptom severity, and the causal attribution of those symptoms as related to HIV disease, antiretroviral treatment (ART), or other reasons.

Method: A total of 163 patients (55% male, 45% female) filled in a self-report questionnaire consisting of information on their ART, a comprehensive physical symptom checklist including a rating of symptom severity and the most likely cause: HIV, ART or other/unknown reasons. Self reported laboratory abnormalities were compared to laboratory reports provided by their physicians.

Results: Women and men did not differ on the means of perceived symptom severity, sum of symptoms (28 ±15), and percentage of symptoms attributed to ART (27 ±22%). However, men attributed their symptoms significantly more often to HIV than women (25 ±25% vs. 16 ±20%, p = .01) and less often to other/unknown reasons (47 ±28% vs. 58 ±27%, p = .02). In contrast, women were significantly more likely to attribute laboratory abnormalities to ART (p = 0.04) and to discontinue Kaletra due to side effects (p = .03). Conversely, men were significantly more likely to take Kaletra than women (p < .01) and to have elevated triglycerides (p = .01). Overall, patients reported only between 5 to 30% of the detected laboratory abnormalities. There were no gender differences on awareness of laboratory abnormalities, except for women being significantly more likely than men to be aware of elevated creatinine levels (p = .02) and to change ART due to elevated creatinine levels (p = .02).

Conclusions: Results suggest that people with HIV attribute about half of their symptoms neither to HIV nor to ART. The finding that men are more likely than women to relate their symptoms to HIV may have implications for the motivation to remain on the same ART regimen, even if side effects occur. In contrast, women may be more prudent in avoiding side effects of ART. The striking lack of awareness of laboratory abnormalities in both men and women may indicate a potential gap in physician-patient communication. The causal attributions of physical symptoms and laboratory abnormalities differ between men and women, which has implications for clinical practice and research.

D.46 (Vortrag)
Der Uridin-Spiegel im Plasma korreliert mit klinischen und laborchemischen Markern der mitochondrialen Toxizität

1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany, 2Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany

Hintergrund: Mitochondriale Toxizität wird unter anderem durch Hemmung der DNA-Polymerase g vermittelt. Experimentell konnte gezeigt werden, dass das Nukleosid Uridin diese Toxizitätseffekte verhindern kann.

Fragenstellung: Im zeitlichen Verlauf sollte an einem größeren Kollektiv untersucht werden, ob die Uridinspiegel mit klinischen Befunden unter ART, mit der ART oder Nebenwirkungen korrelieren.


Ergebnisse: Patienten im CDC-Stadium C (n=33) hatten mit 5,28±1,68 µmol/l einen deutlich niedrigeren mittleren Uridinspiegel als Patienten im Stadium A (n=98, 6,19±1,9 µmol/l) und B (n=51, 6,36±2,2 µmol/l).

Bei Patienten, die dideoxy-NRTIs erhielt (n=43), fanden sich die niedrigsten Uridinspiegel der 4 Therapiegruppen (mit dideoxy-NRTI, NRTI, NRTI-frei, ohne Therapie) mit einem MW von 5,7±1,63 µmol/l.

Der Uridinspiegel der Patienten, die mit NRTIs, aber ohne dideoxy-NRTIs behandelt wurden (n=111), betrug 6,15±2,13 µmol/l und war bei den Patienten ohne NRTIs (n=7) im Mittel bei 6,34±2,74 µmol/l. Patienten ohne ART (n=21) wiesen die höchsten Uridinspiegel auf (6,53±1,55 µmol/l). Dabei waren die Werte therapienäher Patienten (n=16) mit 6,39±1,66 µmol/l im Vergleich zu Patienten in Therapiepause (n=5) mit 6,99±1,14 µmol/l erniedrigt (p<0,05).


**D.47 (Vortrag)**

**Effects of HIV protease inhibitor regimen on platelet function and endogenous thrombin potential (ETP)**

**von Hentig N.H.1, Graff J.1, Foerster A.K.1, Staszewski S.2, Klauke S.1, Gute P.1, Harder S.1**

1J.W.Goethe-University Hospital, Clinical Pharmacology, Frankfurt am Main, Germany, 2J.W.Goethe-University Hospital, Medical HIV Treatment and Research Unit, Frankfurt am Main, Germany, 3IFS Stresemannallee, Frankfurt am Main, Germany, 4Infektiologicum Friedensstrasse, Frankfurt am Main, Germany

**Introduction:** More recently, thromboembolic complications in HIV patients have been described. Especially the influence of protease inhibitors on platelet activation and coagulation are currently under discussion.

**Methods:** HIV positive, protease inhibitor naive patients (n=20) were investigated before and 4-8 weeks after the start of a protease inhibitor (PI) including combination therapy. Therapy consisted of boosted PI regimen (n=14) plus reverse transcriptase inhibitors (NRTI) or a double PI regimen (n=6) without NRTI comedication. Protease inhibitors administered were saquinavir (n=15), lopinavir (n=7), fosamprenavir (n=2) and atazanavir (n=2), all co-administered with low-dose ritonavir.

**Results:** CD 62P, PAC1, platelet-monocyte interaction [CD41, CD11b (all mean fluorescence intensity)] and CD40L (%+ platelets) were assessed by flow cytometry. To investigate the influence of platelets on coagulation the endogenous thrombin potential (ETP) was determined.

**Conclusions:** Effects of the evaluated protease inhibitor HIV therapy on platelet function assessed under field conditions seem to be minor and do not affect all investigated parameters. We found no evidence of generally increased platelet activation in HIV patients under the described PI therapy.

**D.48 (Poster)**

**Hepatotoxicity during therapy with Tipranavir, Citalopram and Finasterid – a case report**

**Gühl C.1, Heinz W.1, Winzer R.1, Langmann P.2, Klinker H.1**

1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany, 2Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany

**Background:** Tipranavir (TPV) is a new Protease inhibitor. Side effects like hepatotoxicity have been decreed, but are generally considered to be rare. Interactions of co-medication with TPV are hard to predict and even little investigated. In combination with Ritonavir (r) TPV itself inhibits cytochrome P450-CYP3A, thus combination with drugs metabolized via CYP3A can cause interactions and side effects. We report one case of severe hepatotoxicity during therapy with TPV/r, Citalopram and Finasterid.

**Case:** A 38-years old male HIV-positive patient, was planned to have a new antiretroviral therapy (ART). He had various regimens before and was not taking any mediation due to insufficient medical adherence, various resistances and missing therapeutic options at that time. Lab results showed elevating viral load and a decreasing CD4-cell-count, thus treatment with Tenofovir (TDF), Emtricitabint (FTC) and TPV/r was started, whereas TDF and FTC had already been taken before. In the course, blood results showed elevating liver enzymes with a peak (GOT 168U/l, GPT 654U/l, GGT 454U/l) seven months after starting the ART. As therapeutic drug monitoring (TDM) showed low plasma levels of TPV (8.1 to 18.5µg/ml), and Ritonavir (57 to 303ng/ml) these drugs were not supposed to have caused hepatotoxicity. Other causes of elevated liver enzymes like alcohol, viral hepatitis or opportunistic infections could be excluded. The patient mentioned concomitant use of the antidepressiv Citalopram and the hair restorer Finasterid. Elevation of liver enzymes is considered to be a rare side effect of these drugs and has been little investigated. As both drugs are metabolized via CYP3A4, inhibition of this cytochrome can increase their plasma concentration. Due to this knowledge and the normal TDM, the medication has been stopped. GOT and GPT decreased during time (GOT 31U/l, GPT 54U/l six months-follow up), GGT decreased to 342U/l and therefore has to be followed up.

**Conclusion:** Drug interactions are complex, but should be in mind when confronted with side effects like hepatotoxicity. Especially free available or herbal drugs should asked for when taking patient’s history. TDM helps to find or exclude the causative drug, and cases like the reported one emphasises its importance.

**D.49 (Poster)**

**HDL-cholesterol predicts parameters of insulin resistance in HIV-patients with lipodystrophy.**

**Wiese M.1, Kaspari M.1, Moebius U.1, Schmidt R.E.1, Behrens G.1**

1Hannover Medical School, Clinical Immunology, Hannover, Germany

**Background:** The prevalence of lipodystrophy remains at a high level among HIV-patients receiving antiretroviral therapy. Insulin resistance (IR) as a potential cardiovascular risk factor is frequently associated with lipodystrophy but difficult to assess.

**Methods:** Prospective cross-sectional study of untreated HIV-patients (A) and HIV-patients without (B) and with lipodystrophy (C).

**Results:** In total 53 patients were included, 15 in each group A and B, and 23 patients in group C. Lipodystrophy was determined by physical examination and DEXA scan prior to oral glucose tolerance test and indirect calorometry. Patients with lipodystrophy had significantly less peripheral fat (3.29±0.26 kg, p<0.006) compared to A and B (5.84±0.65kg and 6.22±0.76kg, respectively) and a higher central to peripheral fat ratio (2.64±0.24, p<0.005) compared to untreated patients (1.31±0.06) or patients without lipodystrophy (1.71±0.13). Patients in group A, B, and C had a comparable HOMA index (A:1.07±0.14; B:1.73±0.39; C: 1.61±0.18 mmol/lµU/ml) but patients with lipodystrophy had significant higher values parameters indicating IR including glucose, proinsulin, and C-peptide at 120 min in an oral glucose tolerance test. Fasting HDL cholesterol values were closely correlated to HOMA
Effects on mitochondria. Data are very limited. There is concern that HIV-infection and antiretroviral therapy change the content of mitochondria in PBMCs in adults. Similar results are expected in children, but data are not yet available. Analysis using the Primagen Retina Mitox DNA assay. Sixty healthy children from 6 months to >16 years are being analyzed as controls. The intraindividual changes were also observed without further analysis using the Primagen Retina Mitox DNA assay. 16 patients from 2 to 17 years at study onset have been analyzed so far. 6/16 patients started ART, while 10/16 patients changed their regimen. The results showed great variation ranging from <15 to 529 cps/cell, the average mitochondrial content was 105 cps/cell. Out of the patients having started ART, 3/6 showed an increase of mitochondria/cell whereas 2/6 showed a decrease. 1/6 patient showed an initial increase followed by a decrease. For the patients who changed therapy, 5/10 had d4T replaced by a different NRTI: 1 patient showed a decrease, 2 no change and 2 an increase in mitochondrial content. For the remaining patients changes from ddI/d4T to 3TC/ABC resulted in a slight decrease, AZT replaced by d4T in a decrease, 3TC replaced by FTC in a slight increase, whereas changes from TDF to FTC had no lasting effect. One patient was excluded from analysis. For the healthy controls (10/ age group) the mean 117cps/cells with great interindividual variations. A trend for a decrease in mtDNA/cells for older children is observed (130 cps/cell for 6-12-months old to 95cps/cell for 13-17 yrs old individuals).

Monitoring of mitochondrial DNA in HIV-positive children starting or changing ART showed unexpectedly low copies of mitochondria with large intra- and interindividual variation. The intraindividual changes were also observed without further ART changes. These great variations were also observed in healthy controls. These observations question the use of measuring mtDNA in ART exposed children to monitor side effects of ART.

D.50 (Vortrag)
Evaluation of mitochondrial DNA in HIV-positive children starting or changing ART compared to healthy controls


1JW Goethe University, Department for Pediatrics, Hemostasis and Immunodeficiency Treatment and Research Unit, Frankfurt, Germany, 2Primagen, Amsterdam, Netherlands

HIV-infection and antiretroviral therapy change the content of mitochondria in PBMCs in adults. Similar results are expected in children, but data are very limited. There is concern that early and lifelong exposure to antiretrovirals has severe effects on mitochondria.

Thirty patients from the Frankfurt Pediatric Cohort were followed for one year after starting or changing antiretroviral therapy (2 NRTIs plus PI/r or NNRTI). Sixty healthy children from 6 months to >16 years are being analyzed as controls. After ethics approval and informed consent, PBMCs were isolated, platelets depleted and cells were cryopreserved for analysis using the Primagen Retina Mitox DNA assay.

Sixteen patients from 2 to 17 years at study onset have been analyzed so far. 5/16 patients started ART, while 10/16 patients changed their regimen. The results showed great variation ranging from <15 to 529 cps/cell, the average mitochondrial content was 105 cps/cell. Out of the patients having started ART, 3/6 showed an increase of mitochondria/cell whereas 2/6 showed a decrease. 1/6 patient showed an initial increase followed by a decrease. For the patients who changed therapy, 5/10 had d4T replaced by a different NRTI: 1 patient showed a decrease, 2 no change and 2 an increase in mitochondrial content. For the remaining patients changes from ddI/d4T to 3TC/ABC resulted in a slight decrease, AZT replaced by d4T in a decrease, 3TC replaced by FTC in a slight increase, whereas changes from TDF to FTC had no lasting effect. One patient was excluded from analysis. For the healthy controls (10/ age group) the mean 117cps/cells with great interindividual variations. A trend for a decrease in mtDNA/cells for older children is observed (130 cps/cell for 6-12-months old to 95cps/cell for 13-17 yrs old individuals).

Monitoring of mitochondrial DNA in HIV-positive children starting or changing ART showed unexpectedly low copies of mitochondria with large intra- and interindividual variation. The intraindividual changes were also observed without further ART changes. These great variations were also observed in healthy controls. These observations question the use of measuring mtDNA in ART exposed children to monitor side effects of ART.

D.51 (Poster)
Influence of HIV on lipid changes after initiation of antiretroviral therapy

Mauss S, Berger F, Ahmann C, Schmutz G, Richter W

1Center for HIV and Hepatogastroenterology, Duesseldorf, Germany, 2Institute for Lipid Metabolism, Windach/Munich, Germany

Objective: Both, HIV and antiretrovirals induce lipid changes, which may result in complex interactions. In some published studies a substantial number of non-fasted samples were included. In addition LDL-cholesterol was never directly measured, thus being prone to be biased by high triglyceride levels.

Methods: In this cohort of 112 patients starting antiretroviral therapy, fasting lipids were assessed prospectively. LDL and VLDL-cholesterol were directly measured. No lipid lowering therapy was used. Baseline characteristics: 97/112 male, median CD4+ cells 251/µL, HIV-RNA 112,000 copies/mL, age 39 years. The NRTI backbone consisted of TDF or AZT plus 3TC or FTC in 93/112 patients. The third drug was either EFV (n=43), NVP (n=29), LPV/r (n=19) or other. At week 24 <40 copies/mL was achieved in 82% of patients. For analysis non parametric tests were used (Spearman, Mann-Whitney).

Results: Baseline lipids and lipoproteins were predictive of changes after 24 weeks independent from antiretroviral therapy. Baseline lipids were inversely correlated with change for total cholesterol (TC) (r=-0.43), LDL-cholesterol (r=-0.44), LDL-ApoB (r=-0.56), VLDL-cholesterol (r=-0.33), VLDL-ApoB (r=-0.51) and triglycerides (r=-0.37) (p<0.01 for all variables). Lipoprotein (a) showed a positive correlation with baseline levels (r=0.33; p=0.01). HDL increased in 83% of patients, but did not correlate with baseline levels. Baseline HIV-RNA (log) showed a positive correlation with increase in TC (r=0.38), LDL (r=0.26) and LDL-ApoB (r=0.23) while baseline CD4+ cells showed a negative correlation with these parameters (TC r=-0.23; LDL r=-0.26; LDL ApoB -0.26) (p=0.05).

Conclusions: Lower baseline levels of TC, LDL, and VLDL are associated with more pronounced increases of these lipids after initiation of antiretroviral therapy as does the replicative activity of HIV and the degree of cellular immunodeficiency. So the dynamic in lipid changes may be partially explained by successful suppression of HIV activity in addition to pharmacological effects. Most patients (83%) showed a low HDL (<1 mmol/L). The low HDL at baseline can be explained by a strong effect of HIV on HDL which may explain the increase of HDL in the vast majority of patients after suppressing HIV.
are prone to develop disorders of fat and glucose metabolism.

Methods: With ACT by end-organ HSR can to an acute, life-threatening reaction and is strongly contraindicated. Immunologically, it holds true whether in considering the diagnosis of an IV reaction, non-Coombs and Gel. The method of the trial is the approach of a type IV allergen is the epitope test. Hypotheses, improved diagnosis, confirmed an organ-specific assay that can be used to detect the contribution of various factors. Treatment of a HIV-positive with a unknown HSR is set forth as the result of various interventions.

Method: 39-year-old HIV-positive patient (CDC stage B3, CD4 manufactured 293/3, HIV bDNA 24,668 Eq/ml) reactivated at 4. Reacted for 4 days, a two-phase or type 1 reaction, also in the ablation phase, lasting 48 h and 72 h persisted. In the 24th phase, the patient reacted in a type 2 reaction, and a positive reaction occurred 12 h after the test. The HLA-typing and the determination of other factors that are involved in type 1 reactions, and a high risk of an allergic reaction, in this case, one of the above-mentioned HLA assoziiert HLA B*5701 Typ.

Schlussfolgerung: In the Epikutantestung the patient, the clinical diagnosis of a HSR can be treated. The aim is a reaction with the patient without a type 1 reaction. As required by the PREDICT-study, which also includes the type 2 test patients with the clini schen test bed reaction. The allergic reaction in the HSR after the Einnahme durchgeführt and evaluiert. Ein solcher Test dient der Bestätigung einer klinisch vermuteten ABC and is not as Screening Method geeignet.

D.53 (Poster)
Protease inhibitors, body fat distribution and insulin resistance affect fat metabolism in HIV-patients
Blass S.1, Wingensiefen S.1, Ellinger S.1, Vogel M.2, Spengler U.2, Rockstroh J.K.2, Stehle P.1, von Rucker A.3
1Department of Nutrition and Food Sciences, Nutrition Physiology, University of Bonn, Bonn, Germany, 2Department of General Internal Medicine I, University of Bonn, Bonn, Germany, 3Department of Pathology, University of Bonn, Bonn, Germany

Background: HIV patients with antiretroviral therapy (ART) are prone to develop disorders of fat and glucose metabolism. The aim of our study was to identify patients with disorders of fat metabolism (FM) taking into account the contribution of ART, body fat distribution (BFD) and disorders in glucose metabolism (GM).

Methods: In fasting plasma, triglycerides (TG), total cholesterol (TC), LDL cholesterol, HDL cholesterol, VLDL, VLDL-ApoB as well as parameters of GM (glucose, insulin, c-peptide and insulin resistance) were determined in 44 HIV patients (16 ART-naïve, 19 with protease inhibitors (PI), 9 without PI (non-PI) and 11 healthy subjects. Waist circumference (WC) and waist-to-hip ratio (WHR) were measured by standard procedures as markers for BFD.

Differences between the groups were determined by the two-way ANOVA and Tukey test. Effects of BFD and GM on markers of FM were assessed by univariate analysis. P-values £ 0.05 were considered as significant.

Results: As expected, patients treated with PI had higher concentrations of TG (250±159 vs. 117±50 mg/dl; p=0.038), LDL-cholesterol (49±32 vs. 24±11 mg/dl; p=0.043), VLDL-ApoB (20±8 vs. 12±4 mg/dl; p=0.017) and lower concentrations of HDL-cholesterol (35±7 vs. 50±9 mg/dl; p<0.001) than HIV negative controls. Moreover, HDL-cholesterol was found in PI medicated patients compared to patients with other ART (35±8 vs. 45±9 mg/dl; p=0.016). Use of PI affected FM (TG: p=0.038, LDL-cholesterol: p=0.027, VLDL-ApoB: p=0.006). WC and WHR had an impact on TG (WC: p=0.008; WHR: p=0.005), VLDL-cholesterol (WC: p=0.018; WHR: p=0.014) and VLDL-ApoB (WC: p=0.022; WHR: p=0.016) in patients without ART, but not in patients with PI. HOMA influenced VLDL-TG (p=0.027) and c-peptide on VLDL-ApoB (p=0.009) in patients with PI.

Conclusion: As BFD affects FM in ART-naïve patients, WC and WHR should routinely be controlled to avoid disorders in FM. In the PI group, this effect from BFD seems to be superimposed by PIs medication itself. Disorders in GM also account for changes in FM. Thus, disorders in FM and GM should be avoided, e.g. by a healthy lifestyle.

D.54 (Poster)
Abnormal coagulation parameters in HIV-infected children under ART
Linde R.1, Königs C.1, von Hentig N.2, Graff J.2, Stumpf A.1, Dunsch D.1, Klingebiel T.1, Kreuz W.1
1JW Goethe University, Department for Pediatrics, Hemostasis and Immunodeficiency Treatment and Research Unit, Frankfurt, Germany, 2JW Goethe University, Department for Pharmacology, Frankfurt, Germany

Bleeding disorders have been discussed as possible side effects in HIV-positive patients under antiretroviral therapy (ART) and may become more significant under intensified regimens. After observing occasional epistaxis in HIV-positive children under ART, their coagulation parameters were monitored.

Coagulation parameters including platelet counts, global coagulation parameters, von Willebrand (vWF) parameters, were monitored under ART and when ART was started or changed. Additionally the platelet function was determined on a PFA-100 with epinephrine (epi) or ADP induction. Starting in 2002, coagulation parameters of 48 HIV-positive children were monitored.

Children without therapy did not show any obvious alterations in coagulation parameters except for a slightly prolonged PFA epi in one patient. About a third of the children on ART showed slightly and inconsistently prolonged PFA values (epi and ADP) with normal platelet counts and vWF parameters. There was no difference between PI- or NNRTI-based regimens. Three children receiving TPV/r showed a maximal prolonged PFA epi with normal platelet counts and normal coagulation parameters. In two of these patients PFA epi normalised when TPV/r was stopped for virological rea-
D.55 (Poster)
Determination of HLA-B*5701 status prior to Abacavir exposure results in higher prescription frequencies and lower rates early therapy terminations

Kohgruber N1, Fischer G2, Rieger A1

1Univ. Klinik für Dermatologie, Medizinische Universität Wien, Abteilung für Allergologie, Immunologie und infektiöse Hauterkrankungen, Wien, Austria, 2Univ. Klinik für Blutgruppenserologie und Transfusionsmedizin, Medizinische Universität Wien, Wien, Austria

Background: Treatment with Abacavir (ABC) results in a hypersensitivity reaction (HSR) in about 8% of patients. The risk of HSR may limit ABC prescription or may result in premature treatment cessation, both due to precaution of physicians and patients. Pretesting for HLA-B*5701 prior to ABC initiation results in significant reduction of HSR incidence and thus may lead to a change of prescription frequencies and a more sustained adherence to ABC.

Methods: In this single centre study, we prospectively collected data about ABC prescription frequencies and early therapy cessations after a pre-test for HLA-B*5701 was introduced in August 2005. Those data were compared to retrospectively evaluated data about the period before HLA-B*5701 testing was performed. All patients with > 60 days of follow-up were included.

Results: After HLA-B*5701 testing was introduced, 141 ABC naïve patients started ABC therapy between August 05 and November 06. 5 (3.5%) patients discontinued ABC in < 42 days based on patients (n=3) or physicians decisions (n=2). Reasons for patients driven terminations were anticipation of HSR (n=1) or misinterpretation of unrelated symptoms (n=2), physicians withdrew ABC because of symptoms highly presumptive HSR (n=1) or secondary syphilis misdiagnosed as HSR (n=1). In comparison, 157 patients initiated ABC without HLA-B*5701 prescreening between 1997 and 2005 at a mean per year prescription rate of 19.9 (± 12.3; 1-38). A mean of 15.7 % (± 7.9; 6-30) stopped ABC thereafter during the first 42 treatment days because of HSR related reasons. Retrospectively, 5 ABC treated patients of initially undetermined HLA status were tested B*5701 positive. Three of those 5 subjects stopped ABC during the initial 42 days, 2/5 HLA-B*5701+ patients tolerated ABC for 3 and 4 years, respectively.

Conclusion: HLA-B*5701 predetermination results in more confident and thus more frequent ABC prescriptions and decreased rates of ABC terminations unrelated and related to HSR.

D.56 (Poster)
Gastrointestinal bleeding due to livercirrhosis under HAART- a case report

Degen O1, Hertling S1, Kreuzberg C1, Zoufaly A1, van Lunzen J1

1University medical center Hamburg-Eppendorf, Hamburg, Germany

Objective: Liver-relate death in HIV positive patients was the most frequent cause of non-AIDS-related death in the D:A:D Study. Most of the patients in this trial were HBV or HCV coinfected. However in clinical practice there are increasing numbers of patients with steatosis or fibrosis of the liver without concomitance as viral hepatitis or alcohol abuse. We report a patient with development of esophageal bleeding due to cirrhosis of the liver under long term HAART.

Case report: Case report of a 76 year old Caucasian patient HIV positive since 1987. Risk of infection was MSM. He is after esophageal candidiasis in stage CDC C3. In 1987 a healed hepatitis B was found. ART was started in 1996 and he was treated with more than 18 drugs from all available classes. Until today the liver function was normal without elevation of liver enzymes and normal blood coagulation and other synthesis factors. The patient is rare drinking alcohol. 1999 a abdominal ultrasound was performed with signs of liver steatosis, a gastroscopy in 2002 was without pathological findings. In 2004 the ART was switched to AZT, 3TC, TFV and Tipranavir. In May 2006 we found anemia with Hb of 10.8 g/dl, the haemocult-test was positive.

The ultrasound showed advanced damage of the liver-parenchym without singes of decompensation. No thrombosis of the V. portae in the Duplex. The hepatitis serology was negative for B and A, as 1987 with a healed hepatitis B. No autoimmunehepatitis or lack of alpha-1 antitrypsin. In liver-biopsie the parenchyma was fine dropted fatty degenerated. The gastroscopy showed hypertensive gastropathie and III° esophageal varicosis with red spots. A ligation therapy of the varicosis was done and a beta blocker was added to therapy. The PI in the ART was switched from Tipranavir to Darunavir.

Discussion: In this case we report a HIV positive patient with gastrointestinal bleeding due to hypertensive gastropathie and esophageal varicosis by liver cirrhosis. The only known risk factor is HAART over 10 years. Physicians should be aware of liver damage in patient under HAART also when the routinely performed liver function test and enzymes were normal.

D.57 (Poster)
Attenuation kognitiver Funktionen unter HAART mit ddI, ddC und 4T im Vergleich zu HAART ohne ddI, ddC und 4T

Hudelmaier B1, Reichelt D2, Oelker-Günberg U3, Klönne K3, Gregor N1, Summ O1, Biehl K4, Evers S1, Husstedt I.W4

1UKM Münster, Neurologie, Münster, Germany, 2UKM Münster, Innere Medizin D, Münster, Germany, 3UKM Münster, Medizin D, Münster, Germany, 4UKM Münster, Medizin B, Münster, Germany

Seit der Einführung von HAART hat sich die Überlebenszeit nach Feststellung der Diagnose HIV-assoziierte Enzephalopathie (HIVE) von ca. 12 Monaten auf ca. 43 Monate erhöht.

D.58 (Poster)

Objective determination of the volume with Primos 3D body optical measurement in the use of calcium hydroxylapatite compound in HIV-infected patients with severe facial lipodystrophy

Tomi N.S.1, Bechara F.1, Hoffmann K.1

1St. Josef Hospital Ruhr-Universität Bochum, Klinik für Dermatologie und Allergologie, Bochum, Germany

Objectives: Radiesse, a filler with a calcium hydroxylapatite compound, was used in HIV-infected patients with severe facial lipodystrophy. To evaluate the efficacy of this filler, volume augmentation before and after therapy was measured for the first time with the Primos 3D body optical measurement.

Methods: Pictures in 5 patients with severe lipodystrophy secondary to HIV infection were taken with Primos 3D body optical measurement before and after augmentation. Radiesse was injected with 0.5 to 2.0 ml into the buccal, malar and/or temporal areas. Volume augmentation was calculated by using the 3D pictures before and after with primos software.

Results: All 5 patients received an immediately acceptable therapeutic esthetic effect. No severe side effects instead of redness, mild swelling and bruising was noted. Volume augmentation in all patients was reproducible seen in the pictures and calculations by Primos 3D body optical measurement.

Conclusions: In patients with severe facial lipodystrophy an immediate benefit of calcium hydroxyapatite compound could be demonstrated. Applications were well tolerated and no serious side effects were noted. The efficacy, easiness of injection, and safety profile of Radiesse makes this filler a potentially attractive treatment for severe facial lipodystrophy in HIV patients. In addition the first time augmentation with Radiesse could objectively be demonstrated and measured with Primos 3D body optical measurement. We suggest to use such modern tools because they are more valid and objectively in documentation of the course and treatment results with fillers.

D.59 (Poster)

Massive repeatable hyperlipidemia after switch from lopinavir to boosted fosamprenavir respectively boosted atazanavir

Potthoff A1, Brockmeyer N.H.1, Kompetenznetz HIV/AIDS

1St. Josef Hospital, Dermatologie, Bochum, Germany

Introduction: Hyperlipidemia is one of the known cardiovascular risk factors (CVRF). During therapy with protease inhibitors (PI) dyslipidemia can be seen frequently. Switching to (unboostered) atazanavir was one of the suggested ways of management, because of the favorable lipid profile.

Case report: A 32 year old male was treated with combivir and lopinavir since 2003. The patient complained of persisting diarrhea. His history revealed a cryptococcal meningitis and hepatitis A, B and C (PCR neg.). Cigarette smoking was the only verified CVRF.

In August 2005 lopinavir was changed to fosamprenavir. In December 2005 cholesterol was elevated up to 496mg/dl and triglycerides up to 1932mg/dl. The HAART was switched to tenofovir, emtricitabine and boosted atazanavir, the patient was prescribed bezafibrat 200mg and a low-fat diet was initiated. In spite of this, triglycerides rose to 3173mg/dl and cholesterol stayed at 474 mg/dl. In addition, the patient complained about nausea and stomach ache that was attributed to steatohepatitis with 4-times elevated liver enzymes. HAART was paused which led to a decrease of cholesterol to 246mg/dl and of triglycerides to 359 mg/dl. Liver enzymes went back to normal. The HAART was resumed with combivir and boosted atazanavir and again triglycerides rose to 2529 mg/dl and cholesterol to 352mg/dl. The patient was switched to trizivir and tenofovir. With this combination HIV load was undetectable, cholesterol was 221mg/dl and triglycerides were 446 mg/dl.

Discussion: Hyperlipidemia is common in patients treated with HAART and can be influenced in most cases by statins or fibrates in combination with a low-fat diet. The role of triglycerides as a CVRF is not entirely clear, but it is commonly accepted that values higher than 1000 mg/dl should be treated because of the risk of steatohepatitis and pancreatitis. In our patient this was only possible by switching the PI containing regimen. Reproducible drastic hyperlipidemia has not been described before in atazanavir containing regimen. It has been discussed if the booster abolished the positive effects that have been seen when switching from other PIs to atazanavir. However, our patient had previously been treated with boosted lopinavir without significant hyperlipidemia.
**D.60 (Poster)**

**Lipid profile, cardiovascular risk factors and metabolic syndrome in a group of Brazilian outpatients**

*Silva E.*, **Bassichetto K.C.*2, **Lewi D.S.*

1HIV Treatment & Clinical Research Unit, Federal University of São Paulo, São Paulo, Brazil, 2Department of Municipality Health of the City of São Paulo, São Paulo, Brazil

**Objectives:** Evaluation of the lipid profile, cardiovascular risk factors using the Framingham score and the metabolic syndrome of the people living with HIV/aids that receive or not antiretroviral therapy attended at the clinics of the Federal University of São Paulo and in the Ambulatory of the Secretary of Health of the city of São Paulo.

**Methods:** During 18 months 319 patients were selected.

**Results:** We included 243 patients with antiretroviral therapy and 76 naïve patients. The median age was 39.7 years and 60.9% of the patients were male. The major cardiovascular risk factors in this population were: 26.8% smoking, 19.2% hypertension, 4.0% diabetes, 40.2% of familiar history of atherosclerosis. In the lipid profile the median of the total cholesterol (205 x 108 mg/dL), HDL-c (51 x 43 mg/dL) and triglycerides (219 x 164 mg/dL) were higher in the group with antiretroviral therapy. According to the Framingham equation, 88.6% and 95.9% of the patients in the group 1 and 2 respectively has a low risk of cardiovascular disease. The metabolic syndrome was present in 12.6% of the patients with antiretroviral therapy and in 11.6% (p=0.832) in the naïve group.

**Conclusion:** The median of total cholesterol, HDL-c, triglycerides were higher in the group with antiretroviral therapy. The cardiovascular risk was low in the two groups according to the Framingham score. The presence of metabolic syndrome was analogous in both groups.

**D.61 (Vortrag)**

**Increase of susceptibility to Atazanavir (ATV) and Saquinavir (SQV) in multidrug-resistant HIV-1 infected patients carrying Protease-Inhibitor (PI) mutation L76V**


1PZB Aachen, Aachen, Germany, 2Universität Erlangen, Erlangen, Germany, 3Universität Köln, Köln, Germany, 4Institut für Immunologie, Kaiserslautern, Germany, 5MedLab Berlin, Berlin, Germany, 6Universität Frankfurt, Frankfurt, Germany, 7ID-Ambulanz Dortmund, Dortmund, Germany

**Background:** L76V is a rarely observed mutation in clinical isolates of HIV-1 infected patients (pts) with increasing prevalence from 0.17%–1.5% (1998-2005). It is selected under Lopinavir-(LPV), Amprenavir-(APV) and possibly Darunavir-containing treatment and is associated with strong resistance against these drugs. It is furthermore discussed to confer increased susceptibility to ATV and SQV. Our objective was to elucidate the clinical implication of the L76V mutation in the response to PI-containing regimen in pts with strongly limited therapy options.

**Methods:** Virological, immunological and genotypical data of 30 therapy-experienced, HIV-1 multiclass-resistant, L76V-positive pts were obtained retrospectively. 24 pts were three-class resistant and 6 showed NRTI- and PI-resistance. 11 pts started a new regimen containing boosted ATV and/or SQV (Group A). 10 pts switched to ATV or SQV plus LPV or APV to maintain selection pressure on L76V (Group B); and 9 pts received LPV or APV regimens (Group C). 26 pts received an optimized backbone therapy, mostly NRTI. Viral-load (VL) and CD4 counts were determined at baseline, and week 12-96. Success of therapy was defined as VL-reduction <50 copies/mL.

**Results:** Long term therapy success was observed in 4/11 of group A (three included new drug classes) and 5/10 of group B, where selection pressure on L76V was constantly maintained (1 included new drug classes). Additionally, two pts of group B showed an initial reduction of VL below 50 copies/mL followed by a virological failure after 24 weeks. There was no success of therapy observed in group C. 3 pts of each group without success received a second resistance-testing. While L76V could no longer be detected in group A, it still was detected in all pts of the other groups.

**Conclusions:** L76V was detected under LPV and APV regimens. ATV- and/or SQV-containing regimens were more successful than regimens without these drugs. Thus, ATV and/or SQV are encouraging options in deep salvage-situations with viruses carrying the L76V mutation. Like in group B, it seems to be an advantage for long-term success to maintain selection-pressure on L76V by combining ATV and/or SQV with L76V-selecting drugs like APV or LPV.

**D.62 (Vortrag)**

**Cell associated and extracellular saquinavir, lopinavir and ritonavir concentrations in samples from HIV-infected patients receiving double boosted protease inhibitor therapy**


1Vivantes Auguste-Viktoria Klinikum, Berlin, Germany, 2Deutsches Herzzentrum Berlin, Berlin, Germany, 3Labor Dr. Berg, Berlin, Germany, 4Institut für Virologie, Universität Erlangen, Erlangen, Germany, 5Deutsches Primatenzentrum, Göttingen, Germany

**Introduction:** Treatment failure of ritonavir-boosted protease inhibitors does not regularly result from the selection of virus populations with mutations in the protease gene. It has been suggested that intracellular protease inhibitor concentrations are decreased in these instances. However, it is unclear which parameters impact on intracellular drug levels. This study was designed to investigate the relationship between intra-and extracellular PI concentrations in heavily pre-treated patients receiving double boosted PI.

**Methods:** Paired peripheral blood mononuclear cell samples and serum samples were collected from patients receiving treatment with lopinavir/ritonavir and saquinavir in standard dosages. Drug concentrations were measured using LC/MS/MS. Cell associated concentrations were calculated assuming a median lymphocyte volume of 0.4 μL. Associations between drug concentrations were assessed using the Spearman Rank correlation.

**Results:** 52 paired samples from 10 patients collected 12 h ± 2h after drug intake were analysed. Median (range) serum concentrations of LPV, RTV and SQV were 3825 ng/mL (0 -
9100), 138 ng/mL (14 - 518) and 335 ng/mL (60 - 4890). Median (range) cell / serum ratios for LPV, RTV and SQV were 0,06 (0,00 - 1,64), 0,21 (0,00 - 4,64) and 5,16 (0,92 - 17,95). Intracellular SQV concentrations were highly associated with serum SQV levels (p<0,0001) while no such associations were observed for LPV and RTV. However cell intracellular LPV was highly correlated with intracellular RTV (p<0,0001). 

Conclusions: The intracellular drug accumulation of protease inhibitors is unlikely to be the sole result of passive drug influx. As cellular RTV and LPV levels do not correlate with and are generally lower than the corresponding serum levels and SQV concentrations highly exceed extracellular SQV concentrations other mechanisms like active drug transport seem to be involved. While the intracellular accumulation of LPV may be driven by intracellular RTV, the intracellular accumulation of SQV seems to depend on high extracellular SQV levels.

D.63 (Vortrag)
Rapid selection of drug-resistant HIV-1 during the first months of suppressive ART in treatment-naïve patients

Metzner K.1, Allera K.1, Rauch P.1, Harrer T.2
1University of Erlangen-Nuremberg, Institute of Clinical and Molecular Virology, Erlangen, Germany, 2University of Erlangen-Nuremberg, Department of Internal Medicine III, Immunodeficiency Center, Erlangen, Germany

Objective: Efficient antiretroviral therapy (ART) of HIV-1 infection reduces the viral load to undetectable levels and restores the immune system. However, therapy failure appears in a substantial fraction of patients and is mostly associated with the appearance of drug-resistant viruses. It is still not clear when the drug pressure leads to the earliest selection and appearance of drug-resistant HIV-1 populations. In this study, we wanted to determine whether drug-resistant viruses are already selected during viral decline within the first months of ART.

Methods: 15 mostly chronically HIV-1 infected patients were included. None had received ART prior to this study. The selection of three key resistance mutations, L90M (protease), K103N and M184V (reverse transcriptase), were measured by allele-specific real-time PCR allowing to track minority quasispecies with a discriminative power between 0.01-0.2%. The major variant can be replaced by a minority when drug pressure is changing. For NNRTIs a single resistance mutation, such as K103N, is sufficient for therapy failure. In this analysis the genotype of 163 therapy naive patients and the minor populations at reverse transcriptase position 103 were under examination.

163 therapy naive HIV-1 patients of a multicenter study RESINA underwent genotypic resistance test. Using realtime-PCR on a Light Cycler 2.0 with one labelled probe and two different primerpairs the amount of mutant variant at aminoacid position 103 of the RT of each patient sample were detected. With population based sequencing in 11 of 163 patients (6,7%) NRTI associated mutations could be detected. Of this patients haboured 3 NRTI mutations each of the other 10 patients 1 mutation. In 8 patients a revertant could been seen at position 215. In two patients (1,2%) 1 NNRTI mutation was detected, but in non patients K103N was found by this method. Using the realtime PCR assay minority variants of at least 0,2% of the total viral population could be savely proven. In the population of 163 patients 34 samples (20,85%) showed a resistant minority K103N. The number of NNRTI and NNRTI mutations in these 163 patients detected by population based sequencing was representative for the RESINA cohort of 831 patients (NRTI 5,4%, NNRTI 3%). The resistant minority at position 103, which was detected in 20,85%, may lead to an early virologic failure because the resistant minority can replace the majority under the selective pressure of a NNRTI. The transmission of resistance at position 103 is higher than estimated by the results of sequencing. For drugs with a low genetic barrier, it could be important to detect minorities.

D.64 (Vortrag)
Detection of minor variants at reverse transcriptase K103N of HIV strains in therapy naïve patients

Baldwin M.1, Oette M.2, Rockstroh J.3, Fätkenheuer G.4, Hoffmann D.5, Pfister H.1, Kaiser R.1
1University of Cologne, Institute of Virology, Cologne, Germany, 2University of Düsseldorf, for Gastroenterology, Hepatology and infectious Diseases, Düsseldorf, Germany, 3University of Bonn, Department of Internal Medicine 1, Bonn, Germany, 4University of Cologne, Department of Internal Medicine, Cologne, Germany, 5University of Duisburg and Essen, Duisburg and Essen, Germany

In therapy naïve patients resistance is associated with a poor treatment outcome of the first-line regimen. The rate of transmitted resistance mutations in therapy naïve HIV-1 patients varies between 10-20% in different studies. The high replication and mutation rate of HIV leads to the coexistence of different strains in one patient. The selective pressure of drugs results in predominance of one strain while other variants form minorities. With this method of population sequencing only quasispecies of more than 20% could be measured. The major variant can be replaced by a minority when drug pressure is changing. For NNRTIs a single resistance mutation, such as K103N, is sufficient for therapy failure. In this analysis the genotype of 163 therapy naïve patients and the minor populations at reverse transcriptase position 103 were under examination.

In therapy naïve HIV-1 patients of a multicenter study RESINA underwent genotypic resistance test. Using realtime-PCR on a Light Cycler 2.0 with one labelled probe and two different primerpairs the amount of mutant variant at aminoacid position 103 of the RT of each patient sample were detected. With population based sequencing in 11 of 163 patients (6,7%) NRTI associated mutations could be detected. One of this patients haboured 3 NRTI mutations each of the other 10 patients 1 mutation. In 8 patients a revertant could been seen at position 215. In two patients (1,2%) 1 NNRTI mutation was detected, but in non patients K103N was found by this method.
Antiretroviral drugs offer a range of therapies for HIV-1-infected individuals. Treating HIV-positive children remains challenging. Only a few drugs are available in adequate formulations. Pediatric guidelines and dosage recommendations are partly based on data from adult trials. Very limited data is available on children younger than 2 yrs, who need to start antiretroviral therapy (ART).

Eight children <24 months (mean: 8.5 months) who started ART according to current guidelines (PAAD) were followed for 18 months. All children were infected by MTCT and received AZT, 3TC and LPV/r as first line therapy in liquid formulations according to dosage recommendations. LPV/r was given at 230mg/m² twice daily. At baseline and monthly visits, virological and immunological parameters were assessed. At steady state, plasma concentrations of LPV/r were determined over a dosing interval of twelve hours.

Viral load (VL) of 6/8 children was >1,000,000 cpS/ml at baseline. 5/8 children reached VL of <400cps after a mean of 26 weeks. Only 4/8 children reached VL<100cps after 10.5 months. CD4 counts remained stable for children who started therapy before a loss of peripheral CD4 cells, whereas other children showed an increase in CD4 cells from 19.8 to 31.3%. LPV/r plasma concentrations were lower than described for older age groups: the mean of the minimal concentration was 1355ng/ml (1h, range: 1160-7400ng/ml). The plasma AUC correlated better with the children’s BMI rather than body surface (r²= 0.2 vs r²=0.58). All patients had difficulties taking the liquid LPV/r formulation due to its taste. 3/8 children had to change their ART as they did not adjust to the taste. One child with insufficient viral suppression acquired a M184V mutation. ART in children <24 months relies on very few drugs. Plasma concentrations of LPV/r in these children are very low despite normal dosing. All children benefited immunologically, those who adjusted to the taste of LPV/r also virologically. Dosing according to BMI rather than body surface might result in better predictable plasma concentrations. This and the clinical relevance of low LPV/r plasma concentrations in young children need to be evaluated in further studies.
D.68 (Vortrag)

Antiretroviral therapy of patients infected with drug-resistant HIV-strains: Analysis of the composition of the first-line regimen in patients with a documented date of HIV-infection in Germany

Poggensee G.1, Kücherer C.2, Werning J.1, Bartmeyer B.1, Fleischhauer C.1, Braun P.3, Cordes C.1, Jessen H.2, Klausen G.2, Schewe K.3, Stoll M.9, vanLanzen J.7, Hamouda O.8

1Robert Koch-Institute, Department of Infectious Disease and Epidemiology, Berlin, Germany, 2Robert Koch-Institute, HIV-Variability and Molecular Epidemiology, Berlin, Germany, 3private practitioner, Aachen, Germany, 4private practitioner, Hamburg, Germany, 5private practitioner, Hamburg, Germany, 6Hannover Medical School, Internal Medicine, Hannover, Germany, 7University Clinic Hamburg Eppendorf, Hamburg, Germany, 8Robert Koch-Institute, Department of Infectious Disease and Epidemiology and the German Seroconverter Study Group, Berlin, Germany

Objectives: Studies of the first-line regimen in patients with transmitted drug resistance are limited. Aim of this study was to investigate the influence of genotypic resistance test results on the choice of first-line treatment in patients with a documented date of HIV-infection with transmitted drug-resistance.

Methods: Genotypic resistance testing was performed in all drug-naïve patients of the HIV-seroconverter cohort. Data acquisition took place between 1998 and 2005.

Start of antiretroviral therapy and drug composition of first-line treatment were assessed. Proportions were given with interquartile ranges. Mantel-Haenzels X2 test and Fisher’s exact test were used. Viral loads and CD4 counts were compared by the Kruskall-Wallis test, p-values were two sided and p-values of < 0.05 were considered significant.

Results: Of 922 tested patients drug resistant HIV was identified in 130 patients. Susceptible strains were found in 792 individuals. Any NRTI resistant HIV was found in 25 individuals (25/35). NRTI resistance alone was detected in 21 patients (21/35). Combinations of NRTI with PI and/or NNRTI resistance were found in 4 patients (4/25). PI or NNRTI resistance alone was assessed in 5 (5/35) and 4 (4/35) patients, respectively. The remaining 5 patients showed different combinations of multi-drug resistance. Antiretroviral therapy was prescribed for 35 patients (35/130) with predicted drug resistant HIV. Treatment regimen of 25 patients (25/35) included at least one inactive drug. One inactive drug was included in the regimen of 17 individuals. The regimen of 5 patients comprised 2 inactive drugs. In 3 patients no active drug was included in the first-line regimen. The majority of mutations conferred AZT-resistance (11/35). Since 2002 72% of first-line treatments included AZT (p=0.011). Since 2003 no PI or NNRTI were included in first-line treatments of patients with predicted PI/NNRTI resistance. AZT was not included in the regimen of three patients who were infected with highly AZT-resistant HIV. CD4-cell counts and viral load did not differ between individuals treated with or without compromised drugs.

Conclusions: More recently a trend to omit compromised PI and NNRTI drugs appeared.

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D.69 (Poster)

Ritonavir-boosted fosamprenavir dramatically increased tacrolimus drug concentrations in an HIV/HCV-infected patient with liver transplantation

Schulbin H.1, Masuhr A.1, Stocker H.2, Müller M.1, Broelsch C.2, Beckebaum S.2, Cincinnati V.2, Arasteh K.1

1Vivantes Auguste-Viktoria Klinikum, Berlin, Germany, 2Universitätsklinikum Essen, Essen, Germany

Introduction: Drug drug interactions with ritonavir-boosted protease inhibitors (PI) are increasingly troublesome, as HIV-infected patients require treatment for other conditions than HIV.

Methods: We describe the case of an HIV/HCV co-infected patient who initiated the immunosuppressant tacrolimus following liver transplantation.

Results: The 36 year old male with HIV/HCV-coinfection underwent liver transplantation in December 2005 for chronic liver failure. Along with his stable antiretroviral therapy consisting of fosamprenavir/ritonavir 700/100 mg, twice daily and coformulated tenofovir/emtricitabine he was started on tacrolimus 5 mg, twice daily. 5 Days after the start of this treatment the serum tacrolimus concentration was 65,4 ng/mL, which is more than six times the desired value of 10 ng/ml. Only after the dosage was reduced to 0,25 mg q 3 days stable drug trough concentrations within the required concentration range could be achieved. Serum amprenavir concentrations were also monitored but were within the normal range as compared to historical controls.

Conclusions: Enhanced tacrolimus exposure in patients receiving coformulated lopinavir ritonavir has been described before. However, no prospective controlled pharmacokinetic studies have been performed. This is the first report on an interaction between ritonavir-boosted fosamprenavir and tacrolimus. As the numbers of HIV-infected patients with solid organ transplantation will rise clinicians must be increasingly aware of potential drug interactions with PI and immunosuppressants such as tacrolimus.

D.70 (Poster)

Low dose Prednisolone helps to delay HAART initiation

Ulmer A.1, Müller M.1, Stützer H.2, Frietsch B.1

1Praxis Ulmer Frietsch Müller, Stuttgart, Germany, 2University of Cologne, IMSIE - Institute of Medical Statistics, Köln, Germany

Objective: HAART is the best and almost the only established treatment option for HIV infected individuals. But it is expensive and complicated, leading to limited access in developing countries with dramatic consequences, connected with side effects and potential resistances. An important issue is to find additional or alternative therapeutic options and to increase the independence of HAART. The study groups of Andrieu and ourselves have already published a CD4-stabilizing effect of Prednisolone. The number of patients and the time of...
observation are meanwhile sufficient for an evaluation on the potential delay of the first HAART start.

**Methods:** All therapy naïve HIV-patients who came to us in the 4 years from 1999-2002 and remained HAART-naïve at least 6 months, either with or without 5mg Prednisolone daily, were included. 46 took Prednisolone, 45 did not. 20 of the latter started to take Prednisolone later. Thus 25 remained as the evaluable control group. Times to start of HAART or death were analyzed using Kaplan-Meier estimates and compared by the logrank test.

**Results:** Mean CD4-baseline-counts were similar in the Prednisolone and the control group (554/μl resp. 564/μl, p=0.83). 5 patients were lost in the Prednisolone group, 6 in the control group, during follow-up. One patient of the control group died of a heroin overdose. The cumulated rate of patients surviving 3 years without HAART was 62% in the Prednisolone group compared to 29% in the control group (logrank, p=0.032). >50% of the Prednisolone group were on HAART after 3.5 years, of the control group after 1.5 years. Estimated overall median observation time was about 4.9 years (reverse Kaplan-Meier).

**Conclusion:** The results are very preliminary, based on a monocentric observation of cohorts from clinical routine practice. There were no standardized HAART-initiation criteria and no ordinary methodical minimization of possible bias. The number of evaluated patients is small, especially in the control group. Otherwise, there is a sound difference. Time to HAART initiation is more than doubled, a result corresponding to the better time dependent CD4-profile of the Prednisolone-treated patients. It seems probable that Prednisolone is appropriate to extend the time prior to the start of HAART.

**D.71 (Poster)**

**Pharmacokinetic of the Lopinavir/r-Meltrexformulierung im Vergleich zur Lopinavir/r-Weichkapsel**

Levy M.1, Winzer R.1, Heinz W.1, Gaul C.1, Klinker H.1, Langmann P.2

1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany
2Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany

**Hintergrund:** Der Protease-Inhibitor Lopinavir (LPV) erreicht in der Kombination mit Ritonavir (r) sichere therapeutische Plasmaspiegel (PS). Die ursprüngliche Formulierung von LPV/r war eine Weich-Gelatine-Kapsel (SGC) in einer Dosierung von 2x3 a 133/33mg zu den Mahlzeiten. Seit Juni 2006 ist die LPV/r Fixkombination als Tablet zugelassen und ersetzt die SGC. Die Dosierung der mittels Melt-Extrusion Technik hergestellten Tablet beträgt 2x2 a 200/50mg.

**Fragstellung:** Da sich LPV/r-SGC und –Tablet. sowohl in Darreichungsform als auch im Einnahmemodus und der empfohlenen Lagerung unterscheiden, wurde prospektiv untersucht, ob sich Unterschiede in der Pharmakokinetic bezüglich der beiden Formulierungen zeigen.

**Methodik:** Bei 14 konsekutiven Patienten unter LPV/r –Therapie wurden vor und nach der Therapieeinstellung von SGC auf die Tablet. insgesamt 123 LPV-PS zu den Zeitpunkten 0h, 3h, 6h und 9h (±15min) nach Einnahme mittels HPLC bestimmt. Zusätzlich dazu wurde eine retrospektive Untersuchung der 3h- und 0h- LPV-PS von insgesamt 366 Plasmasproben (174 Patienten) vorgenommen. Hiervon waren unter SGC 115 Talspiegel von 87 Patienten (Zeitpunkt 0h) und 190 PS von 87 Patienten zum Zeitpunkt 3h nach Einnahme. Unter LPV/r-Tabletten-Therapie waren 33 PS von 25 Patienten zum Zeitpunkt 0h, und 28 PS von 27 Patienten zum Zeitpunkt 3h. Die Datenanalyse erfolgte mittels Mann-Whitney Test.

**Ergebnisse:** Die prospektiven Untersuchung (SGC./.Tablet.) von 14 Patienten ergab zu allen 4 Zeitpunkten keinen signifikanten Unterschied der LPV-PS-Mediane (0h: 4754 ng/ml./4878ng/ml, p=0.99; 3h: 9180ng/ml./8429ng/ml, p = 0.89; 6h: 7556 ng/ml./6425ng/ml, p = 0.91; 9h: 5624 ng/ml./5603ng/ml, p = 0.82). In der retrospektiven Untersuchung (SGC./.Tablet.) von 174 Patienten ergaben sich keine Unterschiede bezüglich der LPV-PS-Mediane zum Zeitpunkt 0h (5087ng/ml./4998ng/ml, p = 0.73), jedoch fanden sich signifikant höhere LPV-PS zum Zeitpunkt 3h (7842 ng/ml./10264 ng/ml, p=0.0002).

**Diskussion:** Trotz Reduktion der „Pillenlast“ sowie verändertem Einnahmemodus und Lagerungsbedingungen können mit der neuen LPV/r-Formulierung gleichwertige, während der 3h-Spitzenpiegel sogar höhere Plasmaspiegel erreicht werden im Vergleich zur etablierten LPV/r-SGC.

**D.72 (Poster)**

**Amprenavir (APV) and Atazanavir (ATV) pharmacokinetics: Therapeutic drug monitoring (TDM) of double-PI therapy (APV/ATV/r) in clinical practice**

Winzer R.1, Heinz W.1, Gaul C.1, Schirmer D.1, Leyh M.1, Klinker H.1, Langmann P.2

1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany
2Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany

**Objective:** The pharmacological interaction of the combination of amprenavir (APV) with Atazanavir (ATV) may be helpful to achieve positive effects on drug levels because of the inhibitory effect of APV on the CYP-System. The aim of the present study was to analyse the drug levels of a APV/ATV/r double-PI regimen during clinical practice.

**Methods:** APV and ATV drug levels of 39 patients (m/f: 30/9) on FAPV fosamprenavir/ATV/r ± optimised backbone were determined with a HPLC-based method at their regular outpatient visits over a total period of 40 months.

**Results:** Under a recommended dosis (FAPV: 1400 mg/d, ATV: 300 mg/d, RTV: 200 mg/d), 364 samples of 39 patients could be determined. 32 samples were excluded because of incomplete data. APV trough levels were 4.211±3.510 ng/ml. APV peak levels (5.840±2.410 ng/ml) were reached between 3-6 h. 6 drug levels were under the lower recommended level for Cthrough (400 ng/ml). ATV trough levels were 1.423±0.494 ng/ml. ATV peak levels (2.068±1.271 ng/ml) were also reached between 3-6 h. 16 ATV drug levels were below the lower recommended level for Cthroug (150 ng/ml). Mean treatment-time was 8.2 ± 8.6 months.

**Conclusion:** During the combination of ATV and APV, the drug levels of ATV and APV reached are stable over a long-term treatment period. Despite of the variance of APV/ATV trough levels, the attended high levels in the salvage situation will be reached in most patients. This treatment should be controlled by therapeutic drug monitoring.
Are there differences in first line treatment between acute and documented seroconverters? Analysis of the composition of first line regimens in patients of the German HIV Seroconverter Study between starting 1987 and 2006

Bartmeyer B.1, Kücherer C.², Fleischhauer C.¹, Poggensee G.¹, Kollan C.¹, Hamouda O.¹, For the German HIV-1 Seroconverter Study Group

¹Robert Koch-Institute, Department of Infectious Disease Epidemiology, Berlin, Germany, ²Robert Koch-Institute, HIV-Variability and Molecular Epidemiology, Berlin, Germany

Objective: The aim of this observational study is to describe differences in onset and composition of first line treatments in HIV infected patients with a documented date of infection. Recommendations when to start therapy are often derived from cohort studies and not from randomized clinical trials.

Methods: Individuals with a first positive and last negative and first positive HIV antibody test within a maximum three year interval were defined as documented seroconverters. Individuals with an acute seroconversion confirmed by laboratory criteria were defined as acute HIV seroconverters. Patients included had a calculated date of infection between and including 1985-2006. Differences in the time of first line therapy onset were assessed using the Kruskal-Wallis test. Logistic regression was used to analyze differences in components of first line regimens between documented and acute seroconverters.

Results: Of 1555 patients in the German seroconverter cohort, recruited until December 2006, 544 have started antiretroviral therapy (ART). For 364 the first line regimen was clearly indicated. Of those 228 were documented and 136 were acute seroconverters. Our sample was composed of 335 males (92%) and 29 females. The majority were men who have sex with men (MSM; 300/364). Whereas the most prevalent female risk group were heterosexuals (21/29). The year of therapy onset ranged between 1987 and 2006. The overall median time between calculated date of infection and onset of first line regimen were 147.5 days. First line therapy in the acute group started significantly (p<0.01) prior to the documented group (13.0 vs. 300.5 days post infection). Regarding the composition of drugs in first line regimens acute and documented seroconverters did not differ. Over time the combination of one any NRTI and one PI was most frequently applied in both groups (150/364). A regimen consisting of one NNRTI and one NRTI was significantly more frequent in the acute group (p<0.01).

Conclusions: In contrast to many prevalent HIV cohort studies the German HIV seroconverter provides an insight into common prescription ART practice in patients with defined duration of HIV infection over 10 yearover 10 years.

For the German HIV-1 Seroconverter Study Group, which is supported by the German Ministry of Health.

Therapeutic drug monitoring (TDM) of fosamprenavir (FPV), prodrug of amprenavir (APV), in clinical practice is helpful to prevent virologic failure and toxicities

Winzer R.¹, Heinz W.¹, Guhl C.², Schirmer D.¹, Leyh M.¹, Klinker H.¹, Langmann P.²

¹Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany, ²Praxis für gastroenterologische und Infektiologie, Karlstadt, Germany

Objective: APV is a widely used PI and metabolized by CYP3A4. FPV is commonly boosted with RTV, a very potent CYP3A4 inhibitor. Therefore any co-administration requires caution. The aim of this retrospective study was to analyze APV drug levels during clinical practice (non-adherence/adherence, therapeutic failure/successful therapy, co-medication/no co-medication, liver disease/no liver disease).

Methods: APV drug levels (n = 99) of 96 patients at their regular outpatient visits were determined with a HPLC-based method. Data were analysed with students T-test.

Results: Under the recommended FPV-dose (1400mg/d + 200mg RTV/d), APV trough levels were 2575±1725ng/ml. APV peak levels (6453±1445ng/ml) were reached between 2-5 h. Drug-levels in patients with clinical suspected non-adherence (11±8h-level:1728±1798ng/ml; n = 9) were lower compared to patients with good adherence (10±6h-level:2407±1647ng/ml; n = 19) but not statistical different from samples without information (8 ± 6h-level: 2632 ± 2079ng/ml; n = 71). There was a trend (p = 0.06) towards lower levels in patients with therapeutic failure (10±4h-level: 2301 ± 1455ng/ml; n = 15). Drug levels were higher and the range wider in patients with co-medication (one drug (n = 6): 2247 ± 2504ng/ml (9±5h-level); two drugs (n = 6): 3560 ± 3044ng/ml (8 ± 5h-level)) but not statistically significant compared to not mentioned co-administration (8 ± 6h-level: 2475 ± 1823ng/ml; n = 88). There was a trend (p = 0.08) towards higher drug levels in patients with chronic liver disease (8 ± 6h-level: 3414 ± 2530ng/ml; n = 16) compared to samples without information (8 ± 6h-level:2424 ± 1852ng/ml; n = 70) or to patients without chronic liver disease (11 ± 6h-level: 2301 ± 1455ng/ml; n = 15). Drug levels were higher and the range wider in patients with therapeutic failure (11 ± 6h-level: 2301 ± 1455ng/ml; n = 15).

Conclusion: There is a trend towards lower APV-levels in therapeutic failure and a trend towards higher APV-levels in chronic liver disease. Especially under co-medication or in experimental ART, TDM should be done even during clinical routine.
Therapeutic drug monitoring (TDM) is getting more and more common in modern antiretroviral therapy (ART). In pediatric patients, ART is often started in the first twelve months of life and probably a life-long therapy is needed. Very limited information on plasma concentration of antiretroviral substances in children is available. Early pharmacokinetic (PK) data from pediatrics have been performed over a full dosing interval with side effects. Some extremely high plasma concentrations were seen for some substances including EFV and LPV/r and correlated to the findings with clinical outcome. Studies are needed to monitor plasma levels of antiretroviral drugs in children and to correlate the findings with clinical outcome.

D.75 (Poster)

12h pharmacokinetic assessments of ART plasma concentrations in a cohort of HIV-positive pediatric patients

König C.1, von Hentig N.2, Scheuplein M.1,  
Beuckmann K.1, Kurowski M.3, Funk M.4, Linde R.1, Krewz W.1  
1JW Goethe University, Department for Pediatrics, Hemostasis and Immunodeficiency Treatment and Research Unit, Frankfurt, Germany,  
2JW Goethe University, Department for Pharmacy, Frankfurt, Germany,  
3HIV Lab, Berlin, Germany,  
4Paul-Ehrlich-Institut, Langen, Germany

Therapeutic drug monitoring (TDM) is an important tool in patient care but the knowledge used over long time periods. Therapeutic Drug Monitoring (TDM) is getting more and more common in modern antiretroviral therapy (ART). In pediatric patients, ART is often started in the first twelve months of life and probably a life-long therapy is needed. Very limited information on plasma concentration of antiretroviral substances in children is available. Early pharmacokinetic (PK) data from pediatric cohorts suggests the need for TDM in this population.

In the Frankfurt pediatric cohort more than 60 pharmacokinetic analyses have been performed over a full dosing interval (i.e. 12 or 24 hrs). Patients were monitored following a standard protocol. PKs were performed after initiation of ART or change of regiment. Parents or patients documented ART intake at the out-patient unit. All protease inhibitors and non-nucleoside reverse transcriptase inhibitors were examined. Results showed a great inter patient variability in plasma Cmin, Cmax and AUC for all antiretroviral substances tested. Most pediatric patients – especially very young children – had plasma levels below the range observed in an adult population. Only some of the patients, who were ten years and older, reached levels close to those seen in the adult populations. Some extremely high plasma concentrations were seen for some substances including EFV and LPV/r and correlated with side effects.

In conclusion, TDM in a pediatric cohort under ART shows very different results to those seen in adults. Most observed plasma concentrations are much lower than in the adult population. Studies are needed to monitor plasma levels of antiretroviral drugs in children and to correlate the findings with clinical outcome.

D.76 (Poster)

Ritonavir (RTV) als häufigster Kombinationspartner der ART – Bedeutung der Therapeutischen Drug Monitors (TDM) für eine individualisierte Therapie

Benneman R.1, Threin A.2, Schirmer D.1, Leyh M.1,  
Winzer R.1, Heinz W.2, Guhl C.3, Schnaitmann E.2, Klinker H.1, Langmann P.3  
1Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany,  
2Schwerpunktpraxis, Schwabstr. 57-59, Stuttgart, Germany,  
3Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany


Ergebnisse: Die RTV Plasmamispiegel nach einer Dosis von 0,1-0,6g/d lagen in Abhängigkeit vom Zeitintervall der Spiegelmessung nach der Medikamenten-einnahme bei 11ng/ml bis 6880ng/ml. Bei 3% der Patienten wurden 1 bis 4 Begleitmedikamente verabreicht. Bei Patienten mit einem Therapieversagens (n=40) waren die RTV-Plasmamispiegel mit 865±1156ng/ml nicht niedriger als bei den Patienten mit einem Therapieansprechen. Bei n=39 Patienten mit einer chronischen Lebererkrankung zeigten die RTV-Spiegel mit 946±1268ng/ml eine etwas größere Schwankungsbreite als bei Patienten ohne eine begleitende Lebererkrankung. Bei Vorliegen von Nebenwirkungen waren die RTV-Spiegel (489±415ng/ml) nicht erhöht. In der Kombination mit anderen PI waren RTV-Plasmamispiegel in der Kombination mit IDV (n=66) von 1209±1224ng/ml, mit APV (n=37) von 527±934ng/ml, mit ATV (n=72) von 383±395ng/ml und mit SQV (n=47) von 1551±2013ng/ml nachweisbar. Es zeigte sich eine deutliche Dosisabhängigkeit. Bei einer RTV Dosis von 0,1g/d lagen die RTV-Spiegel bei 111–688ng/ml, während die RTV-Talspiegel bei 0,2g/d im Bereich von 98–1209ng/ml schwankten.


D.77 (Poster)

Safety of long-term Lopinavir plasma-levels in patients with liver dise

Langmann P.1, Hubert C.2, Winzer R.2, Heinz W.2,  
Guhl C.2, Threin A.3, Schnaitmann E.2, Klinker H.2  
1Praxis für Gastroenterologie und Infektiologie, Karlstadt, Germany,  
2Medizinische Klinik und Poliklinik II der Universität Würzburg, Schwerpunkt Infektiologie, Würzburg, Germany,  
3Schwerpunktpraxis, Schwabstr. 57-59, Stuttgart, Germany

Objective: Chronic liver disease is often found in HIV infected patients. LPV as first choice protease inhibitor is often used over long time periods. Therapeutic Drug Monitoring (TDM) is an important tool in patient care but the knowledge of LPV-plasma-levels in patients with chronic liver disease remain uncertain. With this retrospective analysis we investigated whether there are differences in LPV-plasma-levels between patients with and without chronic liver diseases over a long-time period.
Methods: Over the time course, LPV-plasma-levels in consecutive patients with chronic liver disease (n=30) and consecutive patients without liver disease (n=38) were evaluated. LPV-plasma-levels were determined with a HPLC-based method. CD4-cell count and HIV-viral load were also correlated with liver disease. Statistical analysis was done by multivariate analysis using the SPSS Software.

Results: The LPV plasma-levels of n=450 samples from 30 patients with liver disease (Hepatitis B: n=17, Hepatitis C: n=16, Alcoholic liver disease: n=7) were determined over 18.7±16.3 months (1 - 48.5 months). A median of 10 samples per patient was eligible (2 - 50 samples). All patients received 400 mg LPV bid with various nuke-back-bones. There were no significant differences according to liver disease in LPV-plasma levels (mean Ctrough without: 5.917±4.811 ng/ml, mean Ctrough with liver-disease: 6.564±4.517 ng/ml, p > 0.05). The intraindividual and interindividual variation of LPV-plasma levels, CD4 increase, and HI-virus suppression were determined with liver disease. Statistical analysis was done by multivariate analysis using the SPSS Software.

Conclusion: In this clinical setting no differences in LPV-plasma levels between patients with and without chronic liver disease could be demonstrated. LPV-therapy in patients with chronic liver disease is safe. TDM is a helpful tool in patients with impaired liver function for dose adjustment.

**D.78 (Poster)**

**A weight adapted nelfinavir (NFV) containing ART may decrease pill-burden**

Winzer R.1, Hillenbrand H.2, Galle P.R.1, Löhr H.3, Böcher W.1

1 Medizinische Klinik der Universität Mainz, Mainz, Germany, 2Schwerpunktpraxis, Berlin, Germany, 3Praxis für Gastroenterologie, Wiesbaden, Germany

Background: ART consisting of 2 NRTI + PI or NNRTI is standard today. Most antiretroviral drugs are dosed without consideration of individual patients weight. However, weight based dosing might reduce pill burden and increase treatment adherence, an important factor of treatment response. Thus, we compared a weight adapted NFV containing therapy (25mg/kg/d) with one with standard dosage (2500mg/d) in respect to pharmacokinetic, virological and immunological parameters.

Method: In this prospective, open-label monocenter trial over 48 weeks, patients on stable NFV containing ART (>=3months) were sex and weight-related randomised either to a weight adapted (group A: 25mg/kg/d, n=14) or standard dosage (group B: 2500mg/d, n=14) NFV containing ART in combination with 2 NRTIs. Pharmacokinetic examinations were carried out at baseline, week 4 and week 12, virological and immunological parameters were done every 3 months. Data were analysed by Kruskal-Wallis test.

Results: In total, 28 patients (m/f: 17/11; average age: 43±9years) were randomised; 23 patients reached week 48 (one screening-failure, one lost-to-follow up at week 24, one virological therapy failure at week 36, two study unrelated deaths after week 36). Even though both groups were well matched regarding their body-mass-index (A: 22.83 ± 4.09kg/m², B: 23.95 ± 3.49kg/m²) there were no significant differences concerning most pharmacokinetic parameters (Ctroughbaseline: 1540./820ng/ml, p<0.05 Cpeakbaseline: 1228./2030ng/ml, p = 0.33; Ctroughweek12: 1765./1735 ng/ml, p = 0.66; Cpeakweek12: 1960./2260ng/ml, p = 0.96. Importantly, the virological (A: one virological failure (>1-log-raise) week 48, B: one virological failure week 36) and immunological treatment responses (CD4-increaseweek48: 30./56cells/μl; p = 1.0) did not differ between both groups, although the administered NFV dosages and pill burden were significantly reduced in treatment group A (A: 24.05 ± 2.12mg/kg/d; B: 36.16 ± 8.58mg/kg/d, p = 0.001).

Summary: In this study, there were no significant differences in the treatment response to weight adapted (25mg/kg/d) or standard dosage (2500mg/d) NFV containing antiretroviral therapy. Thus, a reduction of pill burden and treatment adherence seems reasonable under the conditions of therapeutic drug monitoring.

**D.79 (Poster)**

Anticonvulsants in patients on antiretroviral therapy: Case report and literature review

Thaler J.1, Emmelkamp J.1, Bode J.1, Oette M.1, Strzelczyk A.2

1Universitätsklinikum Düsseldorf, Hepatologie, Gastroenterologie und Infektologie, Düsseldorf, Germany, 2Universität Marburg, Neurologie, Marburg, Germany

Objective: To give an overview on published literature on the use of anticonvulsants in patients on antiretroviral therapy and to provide recommendations on their concurrent use.

Background: In patients with HIV infection seizures are a relatively common occurrence. Seizures may be a result of HIV infection of the CNS, a manifestation of an opportunistic infection or a result of mass lesions. As they are likely to recur in HIV-seropositive patients anticonvulsive treatment is generally advisable for a first seizure without a recognisable and reversible cause.

For the clinicians caring for HIV-seropositive patients anticonvulsants and antiretrovirals impose therapeutic dilemmas as they may interact through multiple mechanisms including enhanced or inhibited liver metabolism, competition for protein binding and increased viral replication.

Case report: A 40 year-old patient with HIV Infection presented with a first seizure due to a primary CNS lymphoma. As the patient was under HAART, carbamazepine could not be administered because of significant pharmacological interactions. As with use of valproic acid a seizure control could not be obtained, levetiracetam was introduced because of little or no known interaction with HAART but had to be removed because of a disabling tremor. Finally the introduction of lamotrigine was well tolerated and lead to seizure control.

Methods: A systematic literature review was performed to identify literature on the concurrent use of anticonvulsants and antiretrovirals. Using a standardized assessment form, information was extracted from each publication and systematically reported.

Results and conclusions: There is only limited data available regarding interactions for the use of anticonvulsants in patients on antiretroviral therapy resulting in an urgent need for controlled trials examining pharmacokinetic and pharmacodynamic interactions between anticonvulsants and antiretrovirals. Valproic acid and newer anticonvulsants including gabapentin, lamotrigin and levetiracetam may be considered of reasonable choice compared to first-generation agents. However, close monitoring for anticonvulsant-antiretroviral interactions is advisable because of the potential for toxicity, poor seizure control and incomplete viral suppression.
D.80 (Poster)

Risk factors for treatment denial and loss to follow up in an antiretroviral treatment cohort in Kenya
Karcher H.1, Omondi A.2, Odera J.2, Kanz A.1, Harms G.1
1Institute of Tropical Medicine and International Health, Charité-University Medicine, Berlin, Germany, 2MoH/GTZ PMTCT Project Migori and Kuria Districts, Migori, Kenya

Objective: The aim of the study was to evaluate risk factors for treatment denial and loss to follow up in an antiretroviral treatment (ART) cohort in a rural African setting in western Kenya.

Methods: Sociodemographic and clinical data of patients enrolled in an ART cohort were collected within 18 months of an observational longitudinal study and analysed by logistic and Cox regression models.

Results: Of 159 patients with treatment indication 35 (22%) never started ART. Pregnancy (AOR 3.60, 95%CI 1.10-11.8; p = 0.035) and lower level of education (AOR 3.80, 95%CI 1.14-12.7; p = 0.03) were independently associated with treatment denial. The incidence of total loss of patients under therapy was 43.2 per 100 person years (mortality rate 19.2 per 100 person years plus drop out rate 24 per 100 person years). Higher age (AHR 1.06, 95%CI 1.01-1.12; p = 0.04), AIDS before starting treatment (AHR 5.83, 95%CI 1.15-29.5; p = 0.03) and incomplete adherence to treatment (AHR 1.05, 95%CI 1.03-1.07; p < 0.001) were independent risk factors for death. Incomplete adherence also independently predicted drop out due to other reasons (AHR 1.06, 95%CI 1.04-1.09; p < 0.001).

Conclusion: Pregnancy and lower level of education, higher age, advanced AIDS stage and impaired compliance to ART were identified as risk factors for treatment denial and death, respectively. Targeting adequate counselling activities to patients with these characteristics could help to improve adherence and outcome of treatment programmes in resource-limited settings.

D.81 (Vortrag)

Coinciding with medical recommendations as a reward system?
Engelbach U.1, Dannecker M.2, Haberl A.3, Lenz C.1, Grabhorn R.1
1Klinik für Psychiatrie, Psychosomatik und Psychotherapie/Klinikum der J.W. Goethe-Universität, Frankfurt, Germany, 2hem. Institut für Sexualwissenschaft/Klinikum der J.W. Goethe Universität, Frankfurt, Germany, 3HIV-CENTER - Klinikum der J.W. Goethe-Universität, Frankfurt, Germany

This qualitative study examines the relationship between doctors and HIV-infected patients with regard to perceived problems of adherence to antiretroviral medication. The sample contains 20 HIV-infected patients, who were recruited in the HIVCenter of University/Frankfurt. The attending physicians divided the adherent and the non-adherent patients into two comparable groups. Doctors and patients were asked to complete questionnaires estimating the adherence.

Psychodrama has been the method used to explore the doctor-patient relationship (DPR) from the patient’s point of view. The scene of a doctor-patient conversation was produced through role reversal, videotaped, and transcribed. Objective hermeneutics was used to analyze the collected material: four patients were chosen from the sample, being in maximum contrast to each other with respect to ‘adherence/non-adherence’ and ‘role reversal possible/not possible’. The four transcripts have been analyzed by an interpreting group at the University/Frankfurt. Within the transcripts a structural finding continues throughout as the single reading that cannot be falsified: the participants are tending to involve their doctors into their community implying the dissolution of the asymmetrical structure of the DPR. It is strongly connected to the confused regulation of closeness and distance, to facing the physicians on a level of diffuse social relations, and to the need or desire for being accepted by the doctor as somebody particular. According to the contrast of adherent/non-adherent patients there were differences only concerning the intensity. Hence, for adherent behavior can be hypothesized: an individual level of the need or desire for being accepted by the doctor as somebody special exists within every patient. If this level is reached, i.e. individual claims are met and personal desires are satisfied, the patient will experience satisfaction within the relationship and follow the physician’s advice. Several dimensions of personality could shift this level of need or in extreme cases be dominant enough to apparently override this model. Thus the patient’s satisfaction with the physician could be understood as the fulfillment of his need or desire, the adherence as a reward for satisfied desires.

D.82 (Poster)

Effects of a nurse connection program on patients’ well-being and acceptance of Enfuvirtide-therapy
Banczyk L.1, Stellbrink H.-J.2, Wäsle B.3, Wagner W.3
1Vivantes-Auguste-Viktoria Klinik, Berlin, Germany, 2ICH, Hamburg, Germany, 3Roche Pharma AG, Grenzach-Wyhlen, Germany

Objectives: Enfuvirtide is administered subcutaneously twice daily. The most frequent side effects are injection site reactions.1 Administration mode and ISR are main causes for interruption and cease of therapy. Substantiated knowledge of patient care could play an important role for successful enfuvirtide therapy.2 The effect of nurse training on patients’ well-being and therapy acceptance are to be assessed.

Methods: A Nurse Connection Program for training and experience-exchange has been running since February 2006, with 5 national and 18 regional nurse trainings, so far. In parallel, a non-interventional trial with 2 systematic questionnaires at baseline, week 4, 12 and 24 has been conducted: 1. Nurse experience with first therapy instruction, guidance and estimation of patients’ satisfaction; 2. Patients quality of life.

Results: This interim analysis includes all nurse questionnaires of patients with data at least up to week 12 (n = 45). Baseline: nurses know their patients for 5 years on average, 51% (23) of patients feel insecure at first instruction, 56% (25) administer the first injection on their own, first instruction takes 40 min on average. Recommendations to reduce ISR at baseline: 91% (41) cooling/warming of injection site, 73% (33) massage, 67% (30) antihistamine gel, 20% (9) others (eg injection into the back, injection time up to 10 min). In weeks 4 and 12 additional methods were recommended to reduce ISR: shower/bath before injection, massage device, reconstitution of enfuvirtide powder 12 hrs before application. During treatment, the rate of patients who were at least satisfied with their therapy was 36% (15/42) at week 4 and 51%
(23/45) at week 12, the rate of those being dissatisfied or very dissatisfied was 26% (11/42) and 20% (9/45), respectively. 

Conclusions: Experience within the program suggests that improvement in satisfaction of enfuvirtide patients with therapy may be achieved by a structured training and experience exchange program. Detailed repeated instruction and support may lead to increased treatment acceptance and improved adherence.

2 Foy K et al. J of the Assoc. of Nurses in Aids Care, Vol 16, 2 2005

D.83 (Vortrag)

Gesundheitstrainings HIV/AIDS - a nationwide structured patient education program for people living with HIV/AIDS in Germany

Klumb S.1, Dannecker M.1, Gronski H.1, Schafberger A.1
1Verein Gesundheitstraining HIV/AIDS e.V., Berlin, Germany

Background: In 1998 a working group of HIV+ patients and treatment advocates started to develop a structured patient education program for people living with HIV/AIDS in Germany. From our perspective adherence is a consequence of psychosocial factors and processes.

From July 2005 on eight patient trainings have been conducted, 61 patients were included. Trainings have been conducted in groups. Group size varied (mean 10.1, range 5 - 12). Mean age was 41.2 years. 15.1% of participants were female 84.9 % male.

Two types of research have been conducted resp. are ongoing: an evaluation of the curricula and the qualification of trainers (completed), and an evaluation of health economic consequences and long lasting effectiveness (still ongoing).

Methods: The research utilized questionnaires several times during the program and 6 month after the last training session. In addition two group discussions leaded by the researchers were conducted as qualitative part.

The second part of the research used two questionnaires (MOS-HIV and HADS) and collected “hard data” via self report and patients’ health insurance companies. Questionnaires and data collection was carried out after inclusion but before the first training session and 12 month after the last training session.

Results: 41 patients were included in this OT-style analysis (LOF = 2, 18 did not fill out the last or any other questionnaire). Six month after the last training session 53.7 % (n = 22) stated, that the patient education program has been very helpful and 41.5 % (n = 17) that it has been helpful in terms of living with HIV. Only 2.4 % respectively stated the intervention has been somewhat (n = 1) or not helpful (n = 1).

The 95.2 % (n = 39) patients gave the following key topics as most valuable:
1. exchange of experience (n= 21)
2. develop a new (different) view of living with HIV (more self confidence/ less anxiety / improved QoL) (n= 16)
3. information / diet / sport / coping with stress (n = 12)
4. HAART / management of side effects / therapeutic options and strategies (n = 11)
5. due to knowledge and training a more specific / focussed decision-making (n = 7)

More detailed data and the results of ongoing evaluation of “hard data” will be provided.

D.84 (Poster)

Health related quality of life changes in antiretroviral naïve HIV-infected patients on Atazanavir based regimens: Week 48 results from AI424-089

Iloeje U.1, Kastango K.1, Malan N.2, David N.3, Krantz E.4, Reeb I.5, Nakonz T.5, Matthew M.1, Frederick D.6, Hammond J.6
1Bristol-Myers Squibb, Pharmaceutical Research Institute, Wallingford, United States of America, 2Triple M Research, Port Elizabeth, South Africa, 3Brooklyn Medical Research Center, Cape Town, South Africa, 4Quinta-Research, Bloemfontein, South Africa, 5Bristol-Myers Squibb GmbH&Co.KGaA, Munich, Germany, 6Bristol-Myers Squibb, Wallingford, United States of America

Background: HRQoL declines in HIV-infected patients in the absence of effective therapy or with older more symptomatic ARV regimens. Atazanavir is potent and well tolerated as a once daily protease inhibitor within a HAART regimen. Data on HRQoL in treatment naïve patients on ATV/r or ATV regimens are limited.

Methods: In AI424-089 (a randomized open label study comparing ATV/r 300mg/100mg with ATV 400mg, both in combination with 3TC and extended-release d4T) HRQoL was assessed using the EQ-5D questionnaire, and the MOS-HIV, a disease specific questionnaire. HRQoL was assessed at baseline, Week 24 and 48. Primary endpoints were the physical (PHS) and mental (MHS) summary scores (mean score ±0±10) for the MOS-HIV; and the health index score (HIS), 0.03 change (EQ-5D range 0-1), and visual analogue scale (VAS, range 0 -100) for the EQ-5D. Clinically important changes include a 2 point change (MOS-HIV summary scores) and 0.03 change (EQ-5D HIS). Primary outcomes were changes in scores from baseline.

Results: Of 199 treated subjects, ~88% of the subjects completed the EQ-5D and ~75% of the subjects completed the MOS-HIV at Weeks 24 and 48 (Table 1).

<table>
<thead>
<tr>
<th></th>
<th><strong>Baseline</strong></th>
<th><strong>Week 24</strong></th>
<th><strong>Week 48</strong></th>
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<tr>
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<td>mean(SE)</td>
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<td>mean(SE)</td>
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<tr>
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<tr>
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<td>ATV</td>
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<td>5.1 (1.91)</td>
<td>5.1 (1.91)</td>
</tr>
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</table>

Table 1
D.85 (Vortrag)

Adherence unter HAART - Wo sind die Probleme zwischen Arzt und Patient?

*Pfister H* 1

1www.hiv-facts.net, Frankfurt, Germany

**Arzt:** Erklärt dem Patienten bei Therapiebeginn die Wichtigkeit der Adherence.

Später meist nur Thema bei Therapie-Versagen oder wenn Patient Probleme selbst äußert.

**Patient:** Oft nicht genügend über die Wichtigkeit aufgeklärt.

Großes Unwissen über Resistenz-Problematik.

Fühlt sich oft mit Adherence-Problemen alleingelassen

*Richtig erklären:* Im Gespräch vor Therapiebeginn sollte der Arzt möglichst ausführlich auf die Wichtigkeit der Adherence hinweisen.

Auch in späteren Gesprächen immer wieder nach evtl. Problemen bei der Tabletteneinnahme fragen

Wie einhalten?

Als Arzt den Patienten zur Adherence ermutigen Falls Patienten sich nicht selbst zu Problemen äußern, lieber nachfragen Eine frühzeitige Intervention des Arztes ist leichter und einfacher als eine evtl. schwierige Therapie-Umstellung auf Grund von Resistenzen durch mangelnde Adherence.

Adherence Probleme im persönlichen Umfeld des Patienten sind oft durch eine Intervention des Arztes zu lösen oder zu managen

Diese Umstände erfährt der Arzt NUR im vertrauensvollen Gespräch mit dem Patienten

*Neben- & Wechselwirkungen*

Gegen viele Nebenwirkungen einer HAART gibt es oft einfache Mittel, die diese für den Patienten zumindest mindern könnten.

Auch auf die Problematik von evtl. Wechsel-wirkungen der eingenommenen HAART mit anderen Medikamenten hinweisen (und Drogen!)

*Internet nutzen*

Mittlerweile gibt es Websites, die sich ausführlich mit den Neben- und Wechselwirkungen einer HAART befassen www.wechselwirkungen.de

www.mangelernaehrung-online.de

www.therapie-treu.net

Geben Sie als Arzt dem Patienten das Gefühl, das er mit seinen Problemen nicht alleine gelassen wird

*Medikamentenspiegel*

Nebenwirkungen werden oft durch hohe Medikamentenspiegel zumindest begünstigt.

Nehmen Sie die Möglichkeit der PK der einzelnen Medikamente um evtl. eine Dosisanpassung vornehmen zu können.

**Schlussfolgerung:**

Meist sind einfach Unwissen und/oder Nebenwirkungen der HAART Ursache für mangelnde Adherence der Patienten.

Besprechen Sie z. B. auch die Einnahme auf Reisen, bzw. im Urlaub (Zeitverschiebung).

Zwar macht die genaue Aufklärung des Patienten am Anfang sicherlich mehr Arbeit, aber auf Dauer wird die Therapie mit guter Adherence sicherlich besser laufen!

---

**Conclusions:** Treatment with Atazanavir with or without Ritonavir resulted in clinically important improvements in the HRQoL of these treatment naïve HIV-infected patients.

**D.86 (Vortrag)**


*Boslet H*, *Grabbe S*, *Eser S*.

1Universtitätsklinikum Essen, Klinik und Poliklinik für Dermatologie, Venerologie und Allergologie; HIV-Schwerpunktsambulanz; Psychotherapeutische Beratungsstelle, Essen, Germany


**Methodik:**

1) Definition wirksamer Therapieprinzipien und psychologischer MBSR-Wirkungsebenen;

2) Metaanalysen zur Wirksamkeit von MBSR-HIV Interventionen;

3) Reflektion adäquater psychologischer Interventionsebenen bei strukturellen psychologischen Wirkfaktoren Zielie bei HIV/AIDS;

4) Metareflexion und Anpassung adäquater Messinstrumente zur Wirkung von MBSR-Programmen bezüglich Befindlichkeit, QoL und Adhärenzbefähigung usw.

**Schlussfolgerungen:** Es soll ein integratives MBSR-HIV-Programm aufgebaut und dokumentiert werden. In der Gestaltung wird

1) das MBSR-Programm i.e. eines Achtsamkeits-Fertigkeits-Trainings kombiniert mit

E. Virologie

E.1 (Vortrag)

More than one interaction: GBV-C clinical isolates differ in the ability to interfere with entry and post entry replication steps of HIV

Jung S.1, Tenckhoff S.2, Tillmann H.2, Müller R.1, Hess G.3, Fleckenstein B.1, Reil H.1

1Universitätsklinikum Erlangen, Virologisches Institut, Erlangen, Germany, 2Universität Leipzig, Innere Medizin, Gastroenterologie, Leipzig, Germany, 3Roche, Diagnostics, Mannheim, Germany

Objective: The majority of clinical studies suggest a beneficial effect of GBV-C long-term viremia for HIV patients. In vitro studies reveal a direct influence of GBV-C on HIV replication. Recently we demonstrated that the GBV-C mediated HIV-inhibitory effect is not restricted to X4- or R5-tropic HIV isolates nor to different HIV clades. Now, we studied the HIV inhibitory capacity of different GBV-C isolates and the mechanism in more detail.

Methods: GBV-C viremia and replication capacity of respective isolates were monitored by real-time RT-PCR. GBV-C phenotypes were determined in co-infection experiments. E2 protein was expressed, purified and used to stimulate cells before HIV infection. A single-round-of-replication HIV assay was performed to differentiate between GBV-C mediated inhibition of early and later HIV-replication steps.

Results: GBV-C isolates differ in the ability to suppress HIV replication and thus can be classified as HIV inhibitors and non-inhibitors. The different GBV-C phenotypes could be confirmed independently in a second laboratory, but do not correlate with their replication ability in vitro. The majority of GBV-C isolates leads to suppression of HIV replication independent of entry. But in contrast, some GBV-C isolates interfere only with HIV entry and not with later steps. We could identify the GBV-C E2 protein to be responsible for HIV entry inhibition, but definitely not for post entry events. Therefore other probably nonstructural GBV-C proteins interfere with later HIV replication steps.

Conclusions: Our results reveal that GBV-C mediated HIV impairment depends on different GBV-C proteins which interfere with several HIV replication steps. The GBV-C E2 protein interferes exclusively with X4- and R5-HIV entry, whereas additionally other GBV-C components suppress post entry events. These findings could be supported by the fact that several GBV-C isolates differ in the degree of occurrences of these HIV-inhibitory attributes. The existence of different HIV inhibitory phenotypes may explain the controversial epidemiological data on the influence of GBV-C for HIV progression in vivo. In addition, the identification of the E2 protein as a HIV entry-inhibitor may lead to new HIV therapeutics.

E.2 (Vortrag)

HIV cleavage site mutations in patients with failing protease-inhibitor therapies

Verheyen J.1, Litau E.1, Schuldenzucker U.2, Oette M.3, Fätkenheuer G.4, Rockstroh J.3, Stellbrink H.-J.6, Däumer M.1, Hoffmann D.7, Pfister H.1, Kaiser R.1

1University of Cologne, Institute of Virology, Köln, Germany, 2caesar, Bonn, Germany, 3University Clinic Düsseldorf, Clinic for Gastroenterology, Hepatology and infectious Diseases, Düsseldorf, Germany, 4University of Cologne, Department of Internal Medicine 1, Köln, Germany, 5University of Bonn, Department of Internal Medicine 1, Bonn, Germany, 6Grindelpraxis, Hamburg, Germany, 7University of Duisburg-Essen, Center for Medical Biotechnology, Essen, Germany

HIV cleavage site (CS) mutations increasingly attract attention in the analysis Protease-Inhibitor (PI) resistance. More efficient cleavage of gag precursor proteins enhance replication under selective pressure of PIs and confer PI resistance. Although CS mutations could be correlated with different protease resistance profiles, knowledge about the occurrence of CS mutations under selective pressure of certain PIs remained rudimentary.

We analysed HIV of patients (n=195) under failing PI therapies (APV n=34, IDV n=17, LPV n=71, SQV n=28 or double PIs n = 22) with detectable viral loads in the pol gene as well as in the C-terminal gag region. PR/RT genotypes were interpreted with geno2pheno (www.genafor.org) and CS mutations were scored in comparison to HxB2. Statistical significance was determined using Fisher’s exact test (p<0,05).

109 of 195 viruses harboured at least one CS mutation, which was correlated with the accumulation of major PR mutations (2,46±1,4 vs. 0,74±1,3). The frequency of CS mutations was 15%, 58%, 77% to 87% in HIV with no, one, two or more than two major PR mutations. CS mutations in HIV with predicted resistance to the administered PI were accordingly found in 89% (64/72). However, CS mutations were present in 74% (25/31) of viruses with one or more major PR mutations and at most predicted intermediate resistance to administered PIs. No CS mutation was exclusively found in any PI receiving group apart of 431I in patients with a double PI (SQV/LPV) therapy (2/10 p<0,01). Notably 437V was not detectable in 431I in patients receiving SQV (p<0,05), whereas CS mutations 431V, 436R, 437V, 449F and 453T/L differed not significantly in all salvage patients.

CS mutations were frequently found in HIV of patients with detectable viral loads under PI containing therapies. Whether double PI therapies selected new and specific CS mutations has to be determined in further studies. Especially, viruses with multiple major PR mutations and PI therapy-failure exhibited CS mutations, representing highly PI resistant viruses. Nevertheless, CS mutations were also found in viruses with only predicted intermediate resistance to PIs and detectable viral loads. This could point to CS mutations as being an underestimated mechanism of PI resistance.


**E.3 (Poster)**

**Mechanisms of HIV-1 resistance to a membrane-bound entry inhibitor**


1Georg-Speyer-Haus, Angewandte Virologie und Gentherapie, Frankfurt, Germany, 2Universitätsklinikum Heidelberg, Hygiene-Institut, Heidelberg, Germany

**Objective:** HIV entry into CD4 positive T cells is mediated by its trimeric envelope (env) surface protein. Env consists of the receptor binding subunit gp120 and the transmembrane subunit gp41 which facilitates the fusion of viral and cellular membrane. The process of virus binding and fusion is accompanied by extensive conformational rearrangements within the env protein. The conformational changes in gp41 lead to the formation of the 6-helix bundle, which is crucial for the fusion process. So called C-peptides (e.g. T-20), which are derived from gp41 are efficient inhibitors of viral fusion as they prevent 6-helix bundle formation. In our group a retroviral vector (M87o) has been developed encoding a membrane-anchored C-peptide (maC46). maC46 is highly active even against T-20 resistant virus strains. It was the aim of this project to raise a maC46 resistant virus strain. The resistant virus was genetically as well as phenotypically analyzed.

**Methods:** The CCR5-tropic virus strain BaL sel. MD (resistant to a membrane-bound version of T-20) was passaged on different retrovirally transduced PM-1 T cell lines for more than 150 days, which expressed maC46 at increasing levels. The env gene sequence of the passaged virus was determined. The mutant env was used to pseudotype lentiviral vectors. The particles were used for various single round infection assays to analyse the mechanism of resistance.

**Results:** The maC46 resistance of the selected virus was only weak (app. 5-7 times compared to the parental strain). 5 mutations leading to aa changes could be identified within the env gene of the passaged virus. 3 alteration within gp120 (I187, N305, E353) and 2 mutations in gp41 (V556, A579) could be found. The mutations within gp41 were not sufficient to produce the resistant phenotype. The selected virus shows an increased fusion kinetic, although coreceptor affinity is reduced.

**Conclusion:** It has been previously reported that the fusion kinetic influences the sensitivity of HIV to C-peptide fusion inhibitors, but this is the first time that it could be shown that HIV actually employs this mechanism to gain resistance. We could show that the some resistance mutation have a global effect and lie far away from the region which is targeted by maC46 within gp41.

**E.4 (Vortrag)**

**Selection of peptides inhibiting different steps in the HIV-1 replication cycle from phage displayed peptide libraries**

*Dietrich U.*, Dietz J., Häuter A., Dervillez X.

*Kräusslich H.-G.*, Königs C., Humbert M.

1Georg-Speyer-Haus, Frankfurt, Germany, 2Hôpital Pitié Salpêtrière, Paris, France, 3University Clinics, Virology, Heidelberg, Germany, 4JW Goethe University, Pediatrics III, Frankfurt, Germany, 5Dana Farber Cancer Institute, Boston, United States of America

**Objectives:** The aim of this study was the selection of peptide ligands for different viral and cellular targets in order to interfere with HIV-1 replication at various steps of the replication cycle.

**Methods:** Recombinant target proteins for the selection of peptide ligands were expressed in E. coli or eukaryotic cells. Peptide ligands for various immobilized targets were selected from phage displayed peptide libraries (NEN Biolabs) that express peptides of 7 or 12 amino acids in length in a linear or cyclic form fused to the phage pIII protein. Specificity of binding of the selected phages was confirmed by ELISA and the peptide sequences were deduced from the corresponding nucleotide sequences of the phage genomes. The selected peptides were tested for antiviral activity against HIV-1 in functional cell culture assays (single round infection assays, marker gene transduction assays).

**Results:** We could select peptide ligands for various target structures including HIV-neutralizing antibodies, the viral envelope protein gp120, the highly structured psi-RNA containing the packaging signal for viral genome encapsidation as well as for the multimerizing domain of Gag. Some of the peptide ligands were optimized by mutagenesis or their functionality was improved by multimerization. Functional analyses of the selected peptides revealed interference with HIV-1 replication at different steps of the viral replication cycle (entry, packaging, multimerization) depending on the target structures used for selection.

**Conclusion:** The selected peptides represent good candidates for the derivation of peptidic or non-peptidic antiviral molecules.

**E.5 (Vortrag)**

**Novel role for HIV-1 transframe protein p6* in viral replication**

*Leitherer A.*, Ludwig C., Wagner R.

1Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Molekulare Mikrobiologie und Gentherapie, Regensburg, Germany

**Objective:** The HIV-1 transframe protein p6* is encoded by the very 5´end of the pol gene and so its reading frame overlaps with p1 and p6 in the gag readingframe and the highly conserved ribosomal frameshift site. The p6* protein is located between nucleocapsid (NC) and protease (PR) in the Gag-polyprotein precursor. Besides its aminotermus, also the carboxyterminal portion of p6* is highly conserved and has been reported to play a role in regulation of HIV-1 protease activation. Previously it has been suggested that the Nef protein, a key player of HIV-1 infectivity and progression to AIDS, binds to p6* to facilitate viral replication. This prompted us to analyze the role of p6* for HIV-1 replication.

**Methods:** A panel of recombinant NL4-3-derived proviruses either containing or lacking nef was generated comprising clustered mutations throughout the p6* coding region without manipulating the gag open reading frame or affecting proper frameshifting or release of the viral protease. Besides, the role of a central p6* domain duplicated in the nef-negative virus HX10 was addressed by inserting this region into wild-type NL4-3. The effect of these mutations on viral infectivity and replication has been examined in cell culture.

**Results:** Partially mutated p6* variants did not significantly influence viral infectivity or replication of the corresponding viruses. However, mutation of the entire p6* region decreased significantly viral infectivity irrespective of nef expression. Whereas this fully mutated p6* delayed the replication of nef-
containing viruses, replication was completely abolished in established cell lines in the absence of nef. Furthermore, viral infectivity of nef-positive and -negative NL4-3 viruses was enhanced by the HX10-derived duplication of the central p6* domain which appeared to partly rescue compromised infectivity of nef-lacking viruses. Of note, incorporation of Nef in viral particles was unaffected by any mutation in p6*.

**Conclusion:** Our results suggest a new role for p6* in viral replication associated with Nef function and further experiments are underway to clarify the importance of distinct p6* regions for potential Nef interaction.

### E.6 (Poster)

**Generation of soluble multimeric peptides for inhibition of HIV-1 entry**

**Hitte A.**¹, Krüger T.¹, Daelken B.¹, Wels W.¹, Königs C.², Dervillez X.³, Dietrich U.¹

¹Georg-Speyer-Haus, Institute of Biomedical Research, Virology, Frankfurt am Main, Germany, ²3W Goethe University, Department of Pediatrics III, Frankfurt am Main, Germany, ³Hôpital Pitié Salpêtrière, Paris, France

**Background:** To improve the antiviral activity and the stability of antiviral peptides, we expressed them as soluble multimers in a eukaryotic or prokaryotic expression system. These systems also allow to potentially combine different antiviral functions and, in the case of expression in eukaryotic cells, to introduce posttranslational modifications. We used this system to express a variety of peptides inhibiting HIV-1 entry.

**Methods:** The eukaryotic expression system was established by expressing the fusion inhibitory T20-related peptide C46 (Dervillez et al. 2006). We then expressed peptides corresponding to each of the extracellular loops of CCR5, peptides mimicking HIV-1 entry domains selected by phage display and the CDR3 region of pE51 mAB binding to the co-receptor binding site of gp120 like CCR5. Constructs were cloned into the pEF-IRE5 expression vector between a signal peptide and the human C4bp multimerising domain together with His and Myc-tags for purification and detection. For bacterial expression, constructs were cloned into the pFLAG vector and expressed in E.coli Trx BL21. After affinity purification, the antiviral activity of the multimers was assessed in single round HIV-1 entry assays.

**Results:** The different multimeric extracellular CCR5-constructs were expressed, purified and characterized biochemically. All constructs are heptameric like the natural human C4bp protein. Entry-inhibition assays with JR-FL and D117III HIV-1 pseudoviruses and U87-C4D4-CCR5 cells showed inhibition of HIV-1 entry for most of the multimeric constructs as compared to their monomeric form. This increased potency was very prominent for the multimeric N-terminal CCR5 and the E51 peptides which have an IC50 of 90-120 nM in contrast to the monomers (high micromolar range).

**Conclusion:** The antiviral activity of short peptides can be improved by multimerization. Further improvement of entry inhibition may be possible by combining peptides interfering with different steps of HIV-1 entry. Furthermore, preliminary data also point at improved half-life in vivo and a more favourable tissue distribution and may therefore allow to reduce the number of applications.

This work was supported by the EU-6th FWP TRIoH LSHG-CT-2003-503480.

### E.7 (Poster)

**Rev proteins of human and simian immunodeficiency virus enhance RNA encapsidation**

**Brandt S.¹, Bliesenbach M.¹, Grewe B.¹, Grunwald T.¹, Überla K.¹**

¹Ruhr-Universität Bochum, Molekulare und Medizinische Virologie, Bochum, Germany

**Objective:** The main function attributed to the Rev proteins of immunodeficiency viruses is the shuttling of viral RNAs containing the Rev responsive element (RRE) via the CRM-1 export pathway from the nucleus to the cytoplasm. This restricts expression of structural proteins to the late phase of the lentiviral replication cycle.

**Methods / results:** Using Rev-independent gag-pol expression plasmids of HIV-1 and SIV and lentiviral vector constructs, we have now observed that HIV-1 and SIV Rev enhanced RNA encapsidation 20 to 70-fold correlating well with the effect of Rev on vector titers. In contrast, cytoplasmic vector RNA levels were only marginally affected by Rev. Binding of Rev to the RRE or to a heterologous RNA element was required for Rev-mediated enhancement of RNA encapsidation.

**Conclusions:** In addition to specific interactions of nucleocapsid with the packaging signal at the 5’ end of the genome, the Rev/RRE system provides a second mechanism contributing to preferential encapsidation of genomic lentiviral RNA.

### E.8 (Poster)

**Identification of SH3 domain-containing proteins involved in HIV-related signal transduction pathways**

**Asbach B.¹, Ludwig C.¹, Wagner R.¹**

¹Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Molekulare Mikrobiologie und Gentherapie, Regensburg, Germany

**Background:** The long-term efficacy of vaccine-candidates as well as therapeutics targeted against HIV-viral proteins suffers from the virus’ high variability. During its life-cycle HIV hijacks various cellular systems and interferes with the equilibrium of the cell’s signalling status in favour of viral fitness, e.g. by downregulation of CD4 expression. Consequently, there are many interactions between viral and cellular proteins against which therapeutic vaccines can be directed, that are focused on cellular side.

**Objectives:** Our goal is to identify new interactions in the cell’s complex signalling network, which are crucial for successful HIV replication, focussing especially on SH3 domain-containing proteins. The src-associated protein in mitosis of 68 kDa (Sam68), which contains numerous potential target sites for binding of SH3-domains, has been shown to be a necessary host-factor for HIV-replication, playing an important role in the nuclear export of late viral transcripts. Our aim is to identify new SH3 interactors of Sam68 and to determine their importance in modulating the functions of Sam68 in HIV-replication.

**Methods:** We applied a phage display technique to identify SH3-binders of Sam68. As bait we used recombinant Sam68 purified from E.coli. The phage library consisted of all 296 human SH3-domains as fusions with M13-surface-protein pVIII.
E.9 (Poster)

Is the transmembrane envelope protein gp41 involved in HIV induced immunopathogenesis?

Results of cytokine arrays and microarrays

Denner J, Behrendt R, Lau M, Schmidt C-M, Kurth R.

Robert Koch Institut, Berlin, Germany

Objective: Although the human immunodeficiency viruses (HIV) have long been known to be the cause of AIDS, the precise mechanism of disease induction by these viruses is still unclear. Other retroviruses such as the feline leukemia virus (FeLV) and the Koala retrovirus (KoRV) also induce immunodeficiencies in infected animals, which are clinically similar to AIDS. Reports showing inhibition of mitogen-induced lymphocyte proliferation by inactivated retroviral particles including HIV suggest that a viral protein may be involved in the retroviral pathogenesis.

Methods: To study the influence of the viral transmembrane envelope (TM) protein on cytokine production by normal human lymphocytes, PBMCs from healthy blood donors were incubated with recombinant TM proteins of different retroviruses including HIV. In addition, synthetic peptides corresponding to a highly conserved domain in the TM proteins and designated immunosuppressive (isu-) peptides were also used. Cytokine release was measured using different methods, in addition a microarray analysis (Human Genome Survey Microarray V2.0, 29098 genes) was performed.

Results: The expression of cytokines such as IL-10, IL-6, IL-8, RANTES, MCP-1, MCP-2, TNF-alpha, MIP-1alpha, MIP-1beta, MIP-3 increased upon exposure to the TM proteins and the corresponding isu-peptides. In contrast, the expression of IL-2 decreased and the expression of about 90 other cytokines measured remained unchanged. The extent of changes in the cytokine expression varied from donor to donor. The cytokine data were confirmed by a microarray analysis.

Conclusion: These data indicate that retroviral TM proteins modulate the cytokine production of normal PBMCs and therefore may play an significant role in retrovirus-induced immunopathogenesis. It is important to note that elevated IL-6, IL-10, IL-8, gro-alpha and TNF-alpha and decreased IL-2 values have been regularly observed in HIV-1 infected individuals.

E.10 (Poster)

Isolation of RNA aptamers directed against HIV-1 envelope-derived surface epitopes


1 Georg-Speyer-Haus, Frankfurt am Main, Germany, 2 Astbury Centre for Structural Molecular Biology, Leeds, United Kingdom, 3 Darmstadt University of Technology, Darmstadt, Germany, 4 Institute for Applied Microbiology, Vienna, Austria

Aim: As the limitations of anti-HIV drug therapy become evident, alternative therapeutic strategies are gaining interest. Peptides derived from the heptad repeats of the HIV-1 gp41 envelope glycoprotein have shown a strong potential to inhibit HIV-1 entry. To overcome the several disadvantages excluding a broad application, we have isolated RNA molecules, which were found to interact with the HIV-1 gp4, thus blocking membrane fusion. As another possibility RNA aptamers were selected against HIV-1 gp120.

Method: The isolation of RNA aptamers was performed using the SELEX technology. Several different HIV-1 envelope peptides served as targets in manual or robot-driven selections. The starting DNA libraries contained a 30(50)-nucleotide random region flanked by defined primer binding sites. To ensure the selection of nuclease-resistant RNA aptamers, 2'–NH2 or -F-modified pyrimidines were included during all in vitro transcription reactions.

Results: 10 rounds of selection were performed, followed by an affinity maturation step using neutralizing antibodies for binding competition. The most potent anti-gp41 RNA pool, 435UU, was able to bind to its target with a Kd » 750 nM. Moreover, the 435UU RNA pool demonstrated specific HIV neutralization with IC50 values approx. 250 nM. The selection of anti-gp120 aptamers using HIV pseudoviruses coupled to paramagnetic beads revealed an individual aptamer with an IC50 of about 500 nM. Analysis of individual sequences revealed for all selections still heterogeneous pools. Furthermore, secondary structure prediction using the MFold algorithm displayed only a few defined structural motifs.

Conclusion: In order to increase the selection stringency, new selection and maturation strategies are currently being established.
mß-Gal. Following this functionality assay, the cytotoxicity was addressed by MTT proliferation assays. Modified proteins did not show any cytotoxic activity up to 200 μg/ml. To determine whether the modified serum albumins attach to gp120 we used surface plasmon resonance (SPR) technology. Biotinylated mHSA binds to X4 monomeric glycoprotein 120 with a high binding affinity (Kd = 2.74 x 10^-10 M). Furthermore, a biochemical characterization of hypochlorite-modified proteins has been started to define the binding features. The content of sulfhydryl groups was examined by colorimetric assays. The results show that the sulfhydryl content is decreased by 100% at a HOCl/Protein-Ratio molar ratio of 1:0.5. Together our findings make modified proteins interesting candidates for a novel antiviral therapy against HIV.

E.12 (Poster)
Differentiation of recent and chronic HIV-infections from filter dried-plasma-spots
Loschen S.1, Büting-Feigenbaum J.1, Gohlke-Micknis S.1, Poggensee G.1, Jansen A.1, Hamouda O.1, Kuecherer C.1
1Robert Koch-Institute, Berlin, Germany

Objective: HIV-1 incidence data in Germany are limited because only newly diagnosed infections of unknown duration are registered. The increase of HIV-1 specific antibody levels in the first year after infection is used by the commercial BED-CEIA to differentiate recent and chronic infections. The aim of this study was to compare the sensitivity and specificity of the BED-CEIA for the analysis of plasma samples and filter dried samples. Handling and transport of filter-dried samples is easier as compared to fresh blood and could facilitate HIV-incidence studies.

Methods: The BED-CEIA was validated using a reference panel of 148 baseline and follow-up plasma samples from 81 HIV seroconverters with a documented date of seroconversion. The panel covers a time window from 0 to 222 weeks after seroconversion. Plasma (30 μl) was dropped on filter disks (Whatman #903), dried for >12 h at room temperature (DPS) and eluted with PBS; 2% FCS; 0.05% Tween 20 (450 μl). The optimal sensitivity and specificity of the BED-CEIA to differentiate truly incident and prevalent samples was calculated by varying the window period for recent infections.

Results: Sensitivity and specificity (80% and 86%) of the BED-CEIA were optimal if samples were considered as incident until 20 weeks after seroconversion. 13 of 65 true-incident samples were classified as false-prevalent and 12 of 83 true-prevalent samples as false-incident. Applying the same cut-off, testing of DPS reached a sensitivity of 88% and specificity of 74% (n=8 false-prevalent, n=22 false-incident). By increasing the time window of incidence samples from 20 to 27 weeks after seroconversion the specificity was improved to 78% as the expense of the sensitivity (84%). Under these conditions 12 of 75 true incident samples tested false-prevalent and 16 of 73 true-prevalent samples false-incident. The difference between fresh and dried samples was not significant (pSE=0.346; pSP=0.158).

Conclusion: Filter dried plasma samples can be used for the detection of incident infections in epidemiological studies. The results are comparable to testing plasma directly. An increase of the time span for incident infections to 27 weeks for DPS seems preferable because a lower proportion of samples was classified false-incident.

E.13 (Poster)
“Under-quantification” of HIV-1 RNA by the Cobas TaqMan HIV-1 assay may lead to delayed recognition of resistance development
Weissbrich B.1, Winzer R.2, Guhl C.2, Schubert J.1, Langmann P.2, Heinz W.2, Klinker H.2
1Universität Würzburg, Institut für Virologie und Immunobiologie, Würzburg, Germany, 2Universitätsklinik Würzburg, Medizinische Klinik II, Würzburg, Germany

Objectives: The Cobas TaqMan HIV-1 Test (CTM HIV-1; Roche Diagnostics, Mannheim, Germany) is an assay for the quantification of HIV-1 RNA. It is intended for the use in the clinical management of HIV-1 infected patients. We report on a patient in whom a significant subquantification of HIV-1 RNA was observed when using the CTM HIV-1 assay.

Methods: The CTM HIV-1 assay and the ultrasensitive version of the Cobas Amplicor HIV-1 Monitor v1.5 assay (CA HIV-1; Roche Diagnostics) were used for viral load testing. Resistance testing was performed with the ViroSeq HIV-1 genotyping system (Abbott, Wiesbaden, Germany).

Results: A 54-year-old male patient with HIV-1 infection diagnosed in 1987 was successfully treated with an antiretroviral combination therapy (ART) consisting of protease inhibitors and two nucleoside reverse transcriptase inhibitors (NRTI) since 1997. HIV-1 RNA was below the detection limit (<50 copies/ml) of the CA HIV-1 assay since 1998. In 4/03, ART was switched to a combination of stavudine, lamivudine and tenofovir. In 1/05, a viral load of 1900 copies/ml was observed with the CA HIV-1 assay. Further analysis including retrospective testing revealed the following viral loads for samples from 9/04, 1/05, and 4/05: <40, <40, and 110 copies/ml with CTM HIV-1: 330, 1900, and 1900 copies/ml with CA HIV-1. Because of the viral load increase observed with the CA HIV-1 assay, resistance testing was performed. Seven NRTI mutations were detected (M41L, D67N, T69D, K70R, M184V, T215F, K219Q). The HIV-1 subtype based on the HIV-1 polymerase sequence was B.

Conclusion: In the case of our patient, a significant viral load increase caused by resistance development of HIV-1 was barely detected by the CTM HIV-1 assay. Further studies on the clinical performance of the CTM HIV-1 assay appear warranted.

E.14 (Poster)
Evaluation of viral load (VL) assay performances for the monitoring of HIV-1
Ehret R.1, Braun P.1, Wiesmann F.1, Zabbar F.1, Knickmann M.2, Kühn R.3, Thamm S.4, Warnat G.3, Knechtel H.1
1PZB Aachen, Aachen, Germany, 2INSTO GmbH Aachen, Aachen, Germany, 3Roche Diagnostics, Mannheim, Germany, 4Abbott GmbH&Co. KG, Wiesbaden, Germany, 5Bayer Diagnostics, Fernwald, Germany

Background: Quantification of VL is standard of care in monitoring HIV therapy. We compared the performance of 4 commercial VL-assays: COBAS Amplicor Monitor v1.5 (Roche), Versant bDNA 3.0 (Bayer), both with manual RNA isolation, m1000/m2000rt (Abbott) and COBAS AmpliPrep/TaqMan HIV-1 (CAP/CTM, Roche) both with automated RNA extraction.
Methods: Intra-assay variability for both real time assays (m1000/m2000rt and CAP/CTM) was measured with 10 or 20 replicates of a WHO (NIBSC, UK) and a PEI (Paul-Ehrlich Inst., Germany) standard in different dilutions. Inter-assay variability was measured with dilutions ranging from 50-5x10^5 cps/mL of one clinical sample (3x5 repeats).

20 seronegative samples and a subtype panel (A-H; NRZ, Germany) were analyzed with each assay (2 group O isolates only with m1000/m2000rt). 97 clinical plasma samples were tested in duplicates by all assays performed according to manufacturer’s instruction. Hands-on-time was documented. Deming regression and Bland Altman analysis were used for comparison.

Results: All HIV-seronegative samples were analysed as negative by each system. All subtypes were detected, group O only by m1000/m2000rt. The coefficients of variation (CV) for the different clinical specimen dilutions were between 2.2% and 13.5% for m1000/m2000rt and 6.9% and 32% for CAP/CTM. Linear dilution magnitude for m1000/m2000rt resulted in values below and for CAP/CTM slightly above the nominal concentration, but both systems ensured linearity and correlation for both standards (m1000/m2000rt: CV absolute 11.7-23.9%; R2 0.93-0.97; CAP/CTM: CV 20-50.3%; R2 0.71-0.89). Correlations (R2) and mean differences (Bland/Altman) for all clinical samples were between 0.94 and 0.98 or 0.10-0.40 Dx log, respectively. A reduced hands-on-time was calculated for the fully automated CAP/CTM followed by m1000/m2000rt.

Conclusions: The assays evaluated were comparable in sensitivity and specificity and can be used to monitor the VL of patients infected with HIV-1 group M isolates. m1000/m2000rt can be used for group O. Nevertheless, the VL values obtained were variable, with a mean difference in VL between 0.1 and 0.4 log depending on the system used. This should be taken into account when monitoring VL of the same person with different systems.

F. Immunologie

F.1 (Vortrag)

Analysis of the sequence of HIV-1-protease and the development of drug resistance in the context of HIV-1 protease-specific T-cells

Müller S.M.1, Schütz B.1, Eismann K.1, Bergmann S.1, Walter H.2, Schmidt B.2, Korn K.2, Spretewald B.3, Schmucker M.4, Harrer E.G.1, Harrer T.1, German Competence Network on HIV/AIDS

1Dept. of Medicine III, Immunodeficiency Unit, University Hospital, Erlangen, Germany, 2Inst. of Clin. and Mol. Virology, University of Erlangen, Erlangen, Germany, 3Dept. of Medicine III, HLA Diagnostics, University Hospital, Erlangen, Germany, 4Dept. of Psychology, University of Erlangen, Erlangen, Germany

Objective: Considering the various pathways of the development of drug resistance against protease inhibitors (PI), it is likely that immunological host factors interact with the emergence of resistance mutations in the HIV-1 protease (PR). To determine the influence of HIV-1-specific cytotoxic T-cells (CTL) on the development of drug resistance mutations in HIV-1 PR, we analyzed PR sequences and PR-specific CTL in a HLA class-I-typed cohort of 94 HIV-1-infected patients.

Methods: Correlations between HLA alleles and amino acid substitutions were detected by univariate statistical analyses. T-cell activity was measured by ELISPOT and Cr51-release assays from peptide stimulated T-cell lines.

Results: Drug mutations and drug-associated polymorphisms showed associations to HLA class-I alleles. Based on these associations we defined several new CTL epitopes, which we verified by biological assays. The important drug resistance mutations M46I, which is conferring resistance to most commonly used PIs was found to be associated with HLA A2 and HLA B62. M46I is located in an already described A2 epitope. Additionally, we defined a B62 epitope which comprises the mutation. In both epitopes the M46I-mutation could act as CTL escape mutation. However, many A2-positive patients were able to recognize peptides containing the mutation and were able to mounted oligoclonal CTL responses, whereas the M46I acted as escape mutation in most B62-positive patients.

Conclusions: Our study demonstrates that the HIV-1-specific CTL response shapes the sequence of the PR. Our analyses suggest that the immunoselection exerted by some HLA alleles is facilitates the development of drug resistance mutations in the HIV-1 PR. This interaction between CTL response and drug resistance mutations may have important clinical implications for to the understanding of drug resistance pathways, the sequencing of PIs in antiretroviral therapy and the design of therapeutic vaccines.

F.2 (Vortrag)

Impact of impaired processivity of HIV-1 reverse transcriptase on the rate of G to A mutations induced by APOBEC-3F/-3G

Knoepfel S.A.1, Rauch P.1, Salisch N.1, Allers K.1, Huelsmann P.M.1, Metzner K.J.1

1Institut für Klinische und Molekulare Virologie, Erlangen, Germany

Objective: The cytidine deaminases APOBEC-3F and -3G (apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F/3G) can inhibit human immunodeficiency virus type-1 (HIV-1) replication by inducing G to A mutations in newly synthesized viral DNA. However, HIV-1 is able to overcome the antiretroviral activity of those enzymes by the viral protein Vif. It is presumable that the amount of G to A mutations in newly synthesized viral DNA depends on the time in which the HIV-1 DNA remains single-stranded during reverse transcription. We hypothesize that RTs differing in their processivities and subsequently in their rates of DNA synthesis will have an impact on the rate of G to A mutations introduced by APOBEC-3F/-3G. To prove this, we performed experiments with HIV-1 wild-type (wt) and the M184V- and M184I-variants which confer high resistance against lamivudine and are increasingly impaired in their processivities, respectively, in peripheral blood mononuclear cells (PBMC) but not in T cell lines.

Methods: The different RT-variants were cloned both into pNL4-3(-)vif and pNL4-3(+)-vif. 293T-cells were transfected, 48h later supernatants were DNase treated and used to infect the H9 T-cell line and PBMCs. After 36h, supernatants were transferred to uninfected cells. Additional 6h later, those cells were harvested, DNA was isolated, and part of env-gene was amplified, cloned, and sequenced. The Mann-Whitney test was used for statistical analysis.

Results: Sequences derived form env-clones of HIV-1 NL4-3(+)-vif-wt/M184V/M184I exhibited no G to A hypermutation
independent of the cells used. In H9 T-cells, increased levels of G to A mutations were detected using HIV-1 NL4-3(-)vif, but no significant differences in the amount of G to A mutations was observed in regard to the different RTs. However, increased amount of G to A mutations were seen in viral DNA of PBMCs infected with HIV-1 NL4-3(-)vif-M184I compared with wt- or M184V-RT variants.

**Conclusion:** High reduction of the rate of DNA synthesis (M184I-RT) leads to an increase of the amount of G to A mutations induced by APOBEC-3F/-3G whereas moderate reduction of processivity (M184V) has no effect on the amount of G to A mutations suggesting that APOBEC-3F/G induces G to A mutations in a time-dependent manner.

### F.3 (Poster)

**Peptide HIV p24 aa14-22-mediated HLA-E stabilization alters cross-talk between natural killer cells and dendritic cells**

Schulte D.1, Körner C.1, Krämer B.1, Vogel M.1, Langhans B.1, Nischalke H.D.1, Sauerbruch T.1, Spengler U.1, Rockscheck J.K.1, Nattermann J.1

1Uni-Klinikum Bonn, Medizinische Klinik I, Bonn, Germany

**Introduction:** Recently, we demonstrated the HIV peptide p24 aa14-22 (PEP-I) to bind to HLA-E, the natural ligand of the inhibiting natural killer (NK) cell receptor NKp46. Of note, PEP-I-mediated up-regulation of HLA-E resulted in impaired cytotoxic activity of natural killer cells. Here, we analysed whether this interaction alters cytokine secretion of NK cells and affect the maturation and differentiation of dendritic cells.

**Methods:** NK cells from HIV-infected patients and healthy donors were co-cultured with HLA-E-transfected K562 cells (HLA-E-K562 cells) loaded with and without 10μM PEP-I. Monocyte-derived dendritic cells (MO-DC) were incubated with supernatants from these co-cultures and flowcytometry was performed.

**Results:** Both in HIV-infected patients and healthy controls the interaction of PEP-I with HLA-E selectively reduced secretion of TNFα and IFNγ but enhanced secretion of IL-6 in those NK cells which had been exposed to HLA-E-K562 cells together with PEP-I. Exposure of MO-DC to supernatants from NK cells stimulated by HLA-E-K562 cells plus PEP-I resulted in a reduced expression of the maturation markers CD40, MHC class I and HLA-DR as compared to MO-DC exposed to NK cell supernatants cultured without PEP-I.

**Conclusion:** Here, we show peptide HIV p24 aa14-22-induced HLA-E stabilization alters cytokine secretion of natural killer cells thereby affecting the cross-talk between NK cells and dendritic cells via soluble mediators. Thus, the interaction between peptide and HLA-E affects further immunoregulatory functions beyond its direct inhibition of NK cell cytolytic activity.

### F.4 (Vortrag)

**Characterisation of effector memory phenotypes and CD57-expression on HIV-specific CD8+ T cells**


1Medizinische Hochschule Hannover, Klinische Immunologie, Hannover, Germany, 2Vanderbilt University Medical Center, Department of Microbiology and Immunology, Nashville, United States of America, 3Vanderbilt University Medical Center, Infectious Diseases Unit, Nashville, United States of America

Alterations of effector memory phenotype markers such as CD45RA+/CCR7- and markers associated with terminal CD8+ T cell differentiation such as CD57 are a hallmark of chronic HIV-infection, but the structural and functional basis of these changes remain elusive. Differentiation into effector memory phenotype CD8+ T cells with expression of CD45RA (TemRA) is known to be impaired on HIV-specific CD8+ T cells and CD45RO-positive (TemRO) HIV-specific CD8+ T cells are overrepresented in the majority of HIV-seropositive subjects. Here, we demonstrate that expansions of terminally differentiated HIV-specific TemRA-phenotype cells can be infrequently detected in HIV-controllers as well as in subjects with higher viral loads. Differentiation into TemRA-phenotype on HIV-specific CD8+ T cells was frequently restricted to distinct clonotypes within an epitope-specific T cell receptor (TCR) repertoire. Expression of CD57 on TemRA HIV-specific CD8+ T cells was not significantly increased as compared to HIV-specific TemRO-phenotype cells but we observed a significant reduction of CD57 expression on HIV-specific TemRA phenotype cells as compared to unselected CD8+ T cells with a TemRA phenotype. Our data provide evidence for structural constraints in HIV-specific CD8+ T cell effector-memory maturation in chronic HIV-infection with distinct expressions of markers associated with terminal differentiation.

### F.5 (Vortrag)

**Optimized class C oligodeoxynucleotides (ODN) support the impaired innate immune response of plasmacytoid dendritic cells (PDC) in HIV-infected patients**

Donhauser N.1, Helm M.2, Schuster P.1, Haupt S.1, Vollmer J.3, Schmidt B.1

1Virological Institute, Clinical and Molecular Virology, Universitätsklinikum Erlangen, German National Reference Centre for Retroviruses, Erlangen, Germany, 2Praxis Abelein / Helm, Nürnberg, Germany, 3Coley Pharmaceutical GmbH, Langenfeld, Germany

**Objective:** Human plasmacytoid dendritic cells (PDC) are the major type I-interferon producing cells upon stimulation with CpG oligodeoxynucleotides (ODNs). Patients with human immunodeficiency virus (HIV) infection show a decrease in PDC numbers and a functional impairment. CpG ODNs appear to be attractive therapeutics in HIV, because they may enhance the impaired innate immune response, which may subsequently contribute to the control of virus replication.

**Methods:** The following study was performed using peripheral blood mononuclear cells (PBMC) obtained from 15 untreated HIV-infected patients with CD4+ cell counts between 152
production may be enhanced in particular by optimized C-phatic tissue and decreased production of type I IFNs. IFN of PDC, which may result in their depletion to secondary lymphatic tissue.

Conclusions: HIV-infection leads to a higher activation level of PDC, which may result in their depletion to secondary lymphatic tissue and decreased production of type I IFNs. IFN production may be enhanced in particular by optimized C-class ODNs.

Results: The PDC counts in HIV-infected patients were significantly reduced compared to the control group (p=0.02). The expression of the marker for endocytosis (BDCA-2) was significantly downregulated in unstimulated PDC of HIV-infected patients (p=0.001). After stimulation, the other surface markers were upregulated to a similar extent in patients and controls. The three ODN classes were significantly different in their induction of IFN-alpha production (CpG-A > CpG-C > CpG-B), as were the different C-class ODNs (p<0.05). Lower PDC counts in patients resulted in a significantly lower IFN-alpha production after CpG-A stimulation (p=0.02). This was however not observed using optimized C-class ODNs, which induced remarkable IFN-alpha production in patient PBMC.

The expression of the marker for endocytosis (BDCA-2) was determined by ELISA.

Results: The induction of interferon (IFN)-alpha production was determined by the expression of CCR7, FACS analysis. Migration, activation, maturation, and endocytosis of PDC were determined by the expression of BDCA-2, CD3+CD8+ cells as well as PDC were quantified using FACS analysis. Migration, activation, maturation, and endocytosis of PDC were determined by the expression of BDCA-2.

Cytotoxic T lymphocytes (CTL) were detected by gamma-IFN ELISPOT assay.

Conclusions: The objective of the study was to evaluate the role of CTL escape for disease progression in HIV-1 infection. We analyzed the CTL response to the dominant HLA B8-restricted CTL epitope FLKKEGGL (FL8) in HIV-1 infected patients.

Methods: Fifty seven HLA-I-typed patients at different stages of HIV-1 infection were included in this study. One subject was followed up before and after start of antiretroviral treatment. The main interest was, if there is an improvement of cellular immune response against CMV under antiretroviral therapy.

Results and conclusions: All fusion proteins were efficiently produced and secreted from mammalian cells. The yields of gp120 were not influenced by variations in signal peptide, whereas C3d3 fusion slightly impaired expression rates most probably due to cytotoxic effects on cells. The most efficient gp120 secreting DNA vaccine constructs were tested in BALB/c-mice and in rabbits for the induction of reactive antibodies and T-cell responses. Short and long term immunization protocols revealed no benefit of the C-terminal C3d fusions regarding antibody titers and induction of Env-specific T-cell responses. The functional integrity of C3d following binding of C3d to the receptor CD21 on B cells. The following groups were evaluated: HIV positive patients during antiretroviral therapy in comparison with HIV negative persons with chronic or acute CMV-infection.
negative persons with an acute CMV infection (N=12). To evaluate CMV-specific immune response lymphocytes were isolated by standard procedures. Interferon-g, Interleukin-2, and Tumor-Necrosis-Factor-a production in lymphocytes following short time stimulation with specific antigens (CMV, PMA-Ionomycin as positive control, and negative control) were measured by intracellular cytokine staining and analysis by FACS. The analysis was done as percentage of CD4+ lymphocytes with specific cytokine-detection vs. those without. In HLA-A2 positive individuals a CMV-specific tetramer staining was performed additionally. **Results:** Absolute and relative CD4 count was not significant different between the untreated and treated groups. Significant Differences were seen for HIV positive individuals under antiretroviral treatment vs. no treatment for CMV-specific IFN-γ production in CD4+ lymphocytes (p < 0.05) but not for Interleukin-2 or Tumor-Necrosis-Factor-a. Also the ratio of Interleukin-2/ Interferon-g were significant different. In the longitudinal study all HIV positive individuals generated after initiation of antiretroviral treatment a significant higher percentage of Interferon-g producing cells than before treatment. In acute CMV infection in HIV negative persons the IL-2/Interferon-g ratio was significant lower compared with the other groups. **Conclusions:** Not only the absolute CD4 cell count is rising during antiretroviral treatment, but also the specific qualitative immune response against recall antigens like CMV is improving as showed here by cytokine production and tetramer staining.

**F.9 (Poster)**

**Sequence dependent activation of innate immune system by plasmid DNA in a TLR9 dependent and independent manner**

Kosovar D.1, Lütschg V.1, Wild J.1, Wagner R.1

1Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Molekulare Mikrobiologie und Gentherapie, Regensburg, Germany

**Introduction:** The main limitation of plasmid-based (pDNA) genetic vaccines is low efficiency in non-human and human primates requiring high amounts of pDNA to properly prime cellular and humoral immune responses. Herein, we tested the influence of vector backbone sequence modifications, mainly CpG-content, on the activation of innate immune system ex vivo in a murine splenocyte model and on human dendritic cells (DCs).

**Methods and results:** Various pcDNA5/FRT (Ref; 100% CpG) derived vector backgrounds (pDS [50.6% CpG], pDS110- [47.5% CpG]) were synthesised and analysed phenotypically and functionally on murine splenocytes and human plasmacytoid and myeloid DCs. In contrast to Ref and pDS110-, pDS-DNA induces the secretion of high amounts of IFNγ and IL-6 after in vitro stimulation of naive mouse splenocytes as demonstrated by cytokine ELISA and ELISPOT analysis. Quantification of secreted cytokines indicated a strong Th1- but not Th2-polarisation by pDS-DNA. Elimination of five CpGs within the 110-region overlapping the prokaryotic origin of replication within pDS or translocation of the 110 bp fragment within the plasmid resulted in a significantly reduced stimulation of proinflammatory cytokines suggesting a strong influence of individual CpGs on induced immune responses in a position dependent manner. Whereas pDS-DNA stimulates splenocytes from wildtype mice to produce high amounts of IFNγ and TNFα this effect was totally aborted in TLR9-/- mice. Additionally, ex vivo stimulations of human plasmacytoid dendritic cells with pDS-DNA resulted in secretion of high amounts of type I interferon (IFNa). Confirming the mouse data, deletion of the 110 bp fragment comprising 5 CpG residues (pDS110- ) rendered this plasmid immunosilent with respect to the induction of IFNa. **Summary:** Concerted modification of CpG-amount of the commercial pcDNA5/FRT vector resulted in synthesis of the potent immunogenic DNA expression vector (pDS). Immunogenic properties of pDS, based on CpG content, will make a significant impact for a further rational development of DNA vaccines including HIV vaccine.

**F.10 (Poster)**

**HIV-1 Vpr induces dysregulation of pDC-mediated IFN-γ release by NK cells**

Hong H.1, Bhatnagar N.1, Mönkeneyer M.1, Schmidt R.E.2, Heiken H.1

1Medizinische Hochschule Hannover, Klinische Immunologie K14, Hannover, Germany

**Objective:** Natural killer (NK) cells can lyse virus-infected cells or tumour cells without prior sensitization. In addition, they regulate T cell responses by early production of interferon-γ (IFN-γ). Impairment of NK cell function in HIV-1 infected patients has been extensively studied. However, the exact mechanism of HIV-induced NK cell dysfunction is not yet clear. There has been an increasing interest in the interaction of NK cells with dendritic cells (DCs). Here we addressed the question whether HIV-1 Vpr is able to disturb the interplay between NK cells and plasmacytoid DCs (pDCs).

**Methods:** We sorted NK cells and pDCs from peripheral blood of healthy donors. Highly purified NK cells and pDCs were co-cultured and pre-treated with HIV-1 synthetic Vpr before activation with CpG. NK phenotype was assessed by FACS analysis and function by standard 51Cr release assay and IFN-γ ELISA.

**Results:** In accordance with previously published data, CpG stimulated pDCs were able to activate NK cells as determined by higher CD69 expression, increased cytolytic activity and robust IFN-γ release. HIV-1 Vpr did not impair pDC mediated upregulation of CD69 in NK cells and did not interfere with increased NK killing. However, Vpr substantially decreased pDC induced IFN-γ secretion.

**Conclusion:** Vpr-mediated dysregulation of early IFN-γ production by NK cells could be of considerable importance in the pathogenesis of HIV infection and warrants further studies.

**F.11 (Poster)**

**Comparison of effector functions, immune activation, proliferation and apoptosis of HIV-specific CD8 T cells in the chronic phase of infection**

Vollbrecht T.1, Brackmann H.1, Henrich N.1, Roling J.1, Bogner J.2, Goebel F.D.1, Walker B.D.1, Draenert R.1

1Med. Poliklinik / LMU, München, Germany, 2Partners AIDS Research Center / Massachusetts General Hospital, Charlestown, United States of America

**Background:** CD8 T cell responses are thought to play a pivotal role in the control of acute HIV infection. In the chronic
phase of infection, their importance has remained unclear so far. Studies of CD8 T cell responses based on interferon-g production have shown persistence of these in progressive infection, their importance has remained unclear so far.

Methods: 28 subjects with chronic, untreated HIV infection stratified into 5 groups according to viral load were studied. Intracellular cytokine staining using synthetic peptides as antigenic stimulus was used to study production of interferon-g, TNF-a and IL-2. Tetramer staining was used for content of perforin and granzyme B as well as CD38, HLA-DR, CD57, Ki67, cell cycle analysis. Bcl-2 and CD95. Results: We did not find a significant difference between the five groups for antigen specific production of interferon-g, TNF-a and IL-2. Neither was there a difference in granzyme B and perforin content as outread for the effector function cytolyis. We found highly significant differences between controllers and the four progressor groups for immune activation by CD38 staining (p < 0.05 for all groups) with a VL >200,000 cp/ml having the most CD38 positive cells. The difference was even more pronounced for HIV specific CD8 T cells than for bulk CD8 T cells (p < 0.05). Immune activation of HIV specific cells according to CD38 was correlated with viral load (r2 = 0.51, p < 0.0001) and inversely correlated with CD4 counts (r2 = 0.52, p < 0.0001). We then failed to find differences between markers for cell proliferation as well as for protection of apoptosis (Bcl-2) or death receptors (CD95) of HIV specific cells.

Conclusion: Our study showed a highly significant difference in immune activation as outlined by CD38 staining. But neither enhanced proliferation nor the aptitude for apoptosis can explain the consequences of immune activation and therefore the reason for the difference in immune activation between controllers and progressors.

F.12 (Vortrag)

Interleukin-2 augments dendritic cells numbers in lymphoid tissue

Stellbrink H.-J.1, Tenner-Racz K.2, van Lunzen J.3, Schneider C.4, Racz P.2

1ICH Hamburg, Hamburg, Germany, 2Bernhard-Nocht-Institut, Abt. für Pathologie, Hamburg, Germany, 3Ambulanzcentrum des Universitätsklinikums Hamburg-Eppendorf, Bereich Infektiologie, Hamburg, Germany, 4Universitätsklinikum Hamburg-Eppendorf, Klinik und Poliklinik für Allgemein-, Viszeral- und Thoraxchirurgie, Hamburg, Germany

Background: Autologous dendritic cells have been used for therapeutic vaccination in HIV infected individuals. IL-2 represents a potential adjuvant for therapeutic vaccination in this setting. We therefore investigated if HAART +/- IL-2 impacts on immature (CD1a+ or CD207 [Langerin]+) as well as mature (CD208 [DC-LAMP]+ or CD83+) dendritic cell numbers in the lymphoid tissue.

Methods: 15 chronically HIV-1 infected, antiretroviral naive subjects (group 1: HAART, n=8; group 2: HAART + interleukin-2, n=7; all male) were enrolled in a prospective, randomised, controlled clinical trial on HAART +/- IL-2 (COSMIC). Serial axillary lymph node biopsies were performed at baseline and after at least six months of undetectable plasma viremia. Subjects were selected according to the availability of suitable frozen tissue for the analysis. CD1a+ or Langerin+ immature as well as CD83+ or DC-LAMP+ mature DCs were detected on frozen sections by immunohistochemistry. They were enumerated by FC-based image analysis and expressed as cells per unit area, based on the analysis of 10 non-overlapping fields. Results were analysed by t-test, Mann-Whitney U test, and MANOVA, where appropriate.

Results: Peripheral blood CD4+ T cells were 603 ±165 and 477 ± 176 in groups 1 and 2, resp. (p<0.05). Plasma viremia was 4.3 ±0.61 and 4.53 ± 0.55 log10, resp. (p<0.05). CD4+ cells increased in both groups (p<0.0004) and were higher in the IL-2 group 2 at the 2nd biopsy (p=0.04, MANOVA). Time on treatment until 2nd biopsy (370 vs. 365 days) did not differ between the groups (p=0.86, t-test). Baseline CD1a+ and DC-LAMP+ cell numbers were higher in group 2 (p=0.031 and 0.04, resp., t-test). CD1a+, Langerin+, DC-LAMP+, and CD83+ cells increased in both groups (all p<0.05, MANOVA). The IL-2 group 2 showed a greater increase of Langerin+ (p=0.017), DC-LAMP+ (p=0.021), and CD83+ cells (p=0.027) from baseline as compared with group 1. A trend to increase of CD1a+ cells did not reach statistical significance (p=0.058, all MANOVA).

Conclusions: Interleukin-2 leads to an augmentation of both immature and mature DC subsets in lymphoid tissue. This finding indicates a potential role of IL-2 in dendritic cell-based vaccination strategies.

F.13 (Poster)

HIV-1 Nef induces expression of CCL2/MCP-1 in astrocytes

Lehmann M.H.1, Massanetz S.2, Kramer S.1, Erfle V.1

1GSF-National Research Center for Environment and Health, Institute of Molecular Virology, Munich, Germany, 2Technical University of München, Institute of Virology, Munich, Germany

Objective: Human immunodeficiency virus type-1 associated dementia (HAD) is a severe complication of viral infection clinically characterized by motor and behavioral dysfunctions leading to seizures, coma and finally death. Infiltration of monocytes into the brain play an important role in the pathogenesis of HAD. HIV-1-infected astrocytes express marginal viral structural proteins and high amounts of the HIV-1 Nef protein suggesting a prominent role for Nef. Due to the signalling capacity of Nef we hypothesized that this protein may be capable of inducing a chemotactic factor for monocytes.

Methods: A chemotaxis assay was used to test whether cellular supernatants from human astrocytic U251MG-Nef cells were capable to direct chemotaxis of human monocytic THP-1 cells. Potential factors were identified with a protein array and confirmed by ribonuclease protection assay, RT-PCR and ELISA.

Results: CC chemokine ligand 2/monocyte chemotactic protein-1 (CCL2/MCP-1) was identified as the chemotactic factor mediating chemotaxis of monocytes. Myristoylation-deficient Nef does not upregulate CCL2/MCP-1 expression in astrocytes, and calmodulin is involved in the intracellular signalling pathway triggered by Nef (1).

Conclusions: Recently, it was shown that CCL2/MCP-1 plays a key role in infiltration of HIV-infected leukocytes into the central nervous system (2). Here we find that HIV-1 Nef
probably plays an important role in the pathological expression of this chemokine.


**F.14 (Vortrag)**

**Suppressive HAART abrogates HIV-induced intestinal barrier impairment and mucosal immune activation**


1 Charité, Campus Benjamin Franklin, Med. Klin. I, Gastroenterologie, Infektiologie, Rheumatologie, Berlin, Germany, 2 Charité, Campus Benjamin Franklin, Institut für Klinische Physiologie, Berlin, Germany

**Objective:** A barrier defect of the intestinal mucosa has been suggested as central mechanism of the hyper immune activation characteristic for chronic HIV infection. However, although highly effective antiretroviral therapy (HAART) reduces the general immune activation in HIV-infected patients, the effect of HAART on the HIV-induced epithelial barrier defect is unknown as are its underlying mechanisms. In this study we investigated the effect of suppressive HAART on the HIV-induced intestinal barrier defect and mucosal cytokine secretion.

**Methods:** Epithelial barrier function was characterized in duodenal biopsies obtained from 11 untreated, 8 suppressively treated HIV-infected patients, and 9 HIV-seronegative controls by impedance spectroscopy and 3H-mannitol fluxes. Villus/crypt ratio was determined microscopically. Epithelial apoptotic rate was analyzed by TUNEL staining. Expression of tight junction proteins was quantified by densitometric analysis of immunoblots. Mucosal cytokine production was determined by cytometric bead array.

**Results:** Untreated but not treated HIV infection was associated with a marked reduction of the epithelial resistance, an increase of mannitol permeability and pronounced villus atrophy. Accordingly, mucosal production of interleukin (IL)-2, interferon-γ, IL-4, IL-5, and tumor necrosis factor-α was increased in untreated but not in treated HIV patients. Furthermore, in treated patients epithelial apoptosis was increased, the expression of the sealing tight junction protein claudin-1 was reduced and that of the pore-forming claudin-2 was increased.

**Conclusions:** The HIV-induced intestinal barrier defect and villus atrophy are reversed by suppressive HAART. Accordingly, suppressive HAART strongly reduces the mucosal production of inflammatory cytokines which is highly increased in untreated HIV-infected patients. Finally, we identified increased epithelial apoptosis and an altered tight junction composition as mechanisms of the HIV-induced barrier defect. Our data indicate that interruption of the self-perpetuating cycle of mucosal immune activation by suppressive HAART leads to reconstitution of the epithelial barrier function and may thus contribute to the reduction of systemic immune activation.

**F.15 (Poster)**

Pronounced increase of mucosal FoxP3+ regulatory CD4+ T cells early after the start of ART in chronically SIV infected macaques


1 Medical Clinic I, Charité - Campus Benjamin Franklin, Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany, 2 Medical Clinic I, Charité - Campus Benjamin Franklin, Institute of Pathology, Berlin, Germany, 3 German Primate Centre, Department of Virology and Immunology, Goettingen, Germany

HIV infection is associated with chronic immune activation and progressive loss in the number and function of CD4+ T cells. Antiretroviral therapy (ART) generally results in a reconstitution of T cells. However, in a small fraction of patients receiving ART a hyperinflammatory disorder occurs despite decreased viral load and reconstitution of T cells. The mechanisms responsible for this immune inflammatory reconstitution syndrome (IRIS) are unknown.

Naturally occurring regulatory CD4+ T cells (Treg) constitutively express CD25 and FoxP3 and have recently been described as a subset of T cells with immunosuppressive properties. Previously we found evidences for an important role of mucosal Treg in untreated HIV infection and observed a return of Treg numbers to normal levels after ART. However, the dynamics of Treg normalization following ART are unknown. In this study, we analyzed the peripheral and mucosal lymphocyte subset distribution in the course of untreated and treated SIVmac251 infection in six rhesus macaques by flow cytometry. Quantifications were performed by immunohistochemistry and BD TruCountTM. In addition, functional tests were performed.

Peripheral Treg decreased during untreated SIV infection and normalized after start of ART. In contrast, mucosal Treg increased and reached highest levels early after initiation of ART. We did not find significant correlations between Th1 or Th2 cytokines in the gut mucosa and increasing Treg. Thus, one regulatory function of Treg could consist in sustaining levels of Th1 and Th2 cytokines that hold immune activation and inflammation in a non-detrimental state. CD4+ T cell response against SIV peptides was restricted to the acute phase of infection and not restored after start of ART. Interestingly, there was a highly significant inverse correlation between the SIV specific response in the peripheral blood and the frequency of mucosal Treg. Therefore, we suggest that Treg located at lymphatic sites play an important role in suppressing immune responses. Taken together, our results indicate that Treg accumulate at sites of high immune activation to suppress detrimental hyperactivation. We hypothesize that a loss of Treg induces hyperinflammatory disorder resulting in IRIS in patients receiving ART.
Addressing the human HIV-1 reservoir: I. successful C-type lectin-specific liposomal targeting of immature and mature myeloid dendritic cells, macrophages, and blood monocytes

Gieseler R.K.¹, Marquitan G.², Schwarz A.², Streicher H.³, Fritze A.⁴, Wader T.², Hahn M.², Schubert R.⁴, Scolaro M.J.¹

¹Rodos BioTarget GmbH, Div. of Research & Development, Hannover, Germany, ²LTBH Medical Research Institute, Div. of Research & Development, Alta Loma, California, United States of America, ³University of Sussex, Dept. of Chemistry, Falmer, Brighton, United Kingdom, ⁴Albert-Ludwigs University, Dept. of Pharmaceutical Technology and Biopharmaceutics, Freiburg, Germany

Objective: Antigen-presenting cells (APCs) express C-type lectins (CTLs) that bind infectious agents, such as HIV, by distinctive sugars. Once internalized, HIV evades the required process of degradation, hence establishing highly infectious long-term viral reservoirs. HAART cannot address non-replicative virions. We thus aimed at designing a CTL-specific targeting system that may deliver agents for eradicating APC-resident HIV reservoirs.

Methods: Calcein-loaded (50 mM) DOPC/Chol/DOPE-MBP (36.5:33:0.2:5 mol:mol:mol) 150–200 nm liposomes were tagged with a cholesterol-linked fucose derivative (Fuc-C4-Chol), or the respective mannosse (Man-C4-Chol; pos. ctl.) or galactose (Gal-C4-Chol; neg. ctl.) derivatives. Blood monocytes, MO-derived 5-day immature or 7-day mature myeloid dendritic cells, or 7-day macrophages generated under standard conditions were incubated at 5x10⁴–2x10⁵ cells with 0.1, 1.0, or 10.0 microliters of either of the targeting systems, for 2 or 3 h at 37°C.

Results: Fuc-C4-Chol liposomes highly specifically and efficaciously targeted all APCs. Excellent targeting specificity, time-dependent binding, and highly efficacious uptake of tracer dye by all APC types was verified by fluorescence microscopy and flow-cytometry. Besides faint cytoplasmic distribution, calcein most strongly accumulated in the cells’ endosomal/lysosomal system that typically harbors HIV in reservoir cells. Intriguingly, Fuc-C4-Chol liposomes turned out even more efficacious than Man-C4-Chol-labeled pos. ctl., suggesting increased CTL affinity by favorable steric alteration of the fucosyl residue. Cellular binding of Fuc-C4-Chol- or Man-C4-Chol-targeted liposomes was completely inhibited by 100 mM of soluble L-fucose or D-mannose (pos. ctl.) [D-galactose (neg. ctl.) was ineffective], thus clearly demonstrating high CTL specificity. Moreover, these results were achieved in the presence of mannosse-binding lectin that, despite being known to prevent CD209 binding of HIV, did not hamper the targeting system’s interaction with membrane-expressed CTLs.

Conclusions: Fuc-C4-Chol liposomes may be utilized for directional intracellular delivery of active compounds to CTL-expressing APCs, so as to therapeutically address chronically infected HIV reservoir cell populations.
The observation of CD4+ T cell stabilization by long term application of low dose prednisolone needs verification in a prospective and controlled clinical trial


1Medizinische Hochschule Hannover, Zentrum Innere Medizin, Abt. Klinische Immunologie, Hannover, Germany, 2Klinik der Ludwig Maximilians Universität, Med. Poliklinik, Infektionsabteilung, München, Germany, 3Universitätsklinikum, Klinik I für Innere Medizin, Regensburg, Germany, 4ICH Hamburg, IPM Study Center, Hamburg, Germany, 5Missionsärztesches Institut, Würzburg, Germany, 6Dermatologische Klinik der Ruhr Universität, St. Josef Hospital, Bochum, Germany, 7Universität Köln, Koordinierungszenrum für klinische Studien (KKS), Köln, Germany, 8Praxiszentrum, Stuttgart, Germany

Objective: The benefit of HAART is well established. But until now a gold standard for asymptomatic HIV+ individuals without considerable immuno-deficiency is not yet defined. More recently some ongoing studies address the application of HAART in early stages of asymptomatic HIV-infection and immune modulatory proposals with Interleukin-2. In an alternative approach observational studies during the last decade described a slower decay of CD4+ T cells in asymptomatic HIV infected individuals after treatment with corticosteroids. This observation needs verification in a controlled clinical study. The PreTreat study - an investigator-initiated trial had been submitted recently for a public funding by German authorities.

Methods: PreTreat is intended as a randomized, double-blinded, prospective multicenter phase III trial, which will be performed under the auspices of the German Competence Network HIV/AIDS. Antiretroviral naive patients in early stages of HIV disease will receive prednisolone (5 mg/d) or placebo for 96 weeks. Thus the placebo arm is up to the recent standard of treatment from guidelines, which unisonously recommend a “wait and see” strategy in such patients. Inclusion criteria: HIV+, HAART naive, CD4+ T cells ≥400/µl (±18%), CDC-stage A1, A2 or B1.

Exclusion criteria: Need for HAART, CDC-stage B with pVL > 50,000 cp/ml, HbsAg+, relevant comorbidities. Primary endpoint will be the time to any of the following events:
• Decay of CD4+ T cells below the threshold of 300/µl or <15% (or <400/µl or 18% for three times consecutively);
• Initiation of HAART.
• Disease progression or death.

Secondary endpoints: Decay of CD4+ T cells, CD4/CD8-ratio, pVL, tolerability/adverse events. In addition more detailed functional immunological tests will be performed in subgroups.

Conclusions: As future prospects the PreTreat study will investigate in summary:
(a) whether HAART can be deferred by low dose prednisolone,
(b) the effects on surrogate markers of immune response or viral replication, and
(c) the toxicity of low dose prednisolone in this setting.

The treatment strategy would substitute a period of presently therapeutic nihilism, might reduce long term toxicity of HAART and would be linked with low direct costs.

F.19 (Poster)

Development and immunogenicity of RNA- and Codon-optimized HIV candidate vaccines in phase I clinical trials


1Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Molekularle Mikrobiologie und Gentherapie, Regensburg, Germany, 2Geneart AG, Regensburg, Germany, 3Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Regensburg, Germany, 4BPRC, Rijswijk, Netherlands, 5Imperial College, London, United Kingdom, 6CHUV, Lausanne, Switzerland

The objective of this study was to design HIV-specific T-cell vaccines comprising DNA- and poxviral vectors and to determine the safety, immunogenicity and efficacy of these candidate vaccines in preclinical and phase 1 clinical trials.

Safety and immunogenicity issues were addressed by rational design of RNA and codon-optimized genes encoding a polypeptide comprising Gag, Pol, Nef (GPN) and Env (E) of a clade C HIV isolate that represents the major epidemic in Asia. These expression constructs enabled abundant in vivo expression of HIV proteins in absence of an otherwise non-dispensable viral RNA shuttle protein (Rev) and eliminated the risk for recombination between the vaccine and HIV. Established candidate vaccines comprised
(i) a DNA vaccine lacking antibiotic resistance genes (DNA-C) and
(ii) a replication-deficient vaccinia virus (NYVAC-C), both expressing G and E.

Following immunological and toxicological analysis in mice, preclinical studies were performed in groups of each 10 rhesus macaques using cGMP materials and matching current clinical protocols. DNA-C/NYVAC-C prime/boost regimens induced substantial antiviral cellular immune responses (ELISPOT, gamma-IFN, IL4, IL6) in rhesus macaques, preserved CD4 cell counts at pre-study levels for more than a year. Following heterologous challenge with pathogenic SHIV89.6P, animals efficiently controlled virus replication and protected animals from disease.

Two phase I clinical trials involving 40 HIV-negative volunteers demonstrated the vaccine to be safe, well tolerated and immunogenic in humans. About 50% of the vaccinees that received 2 injections of NYVAC-C responded with detectable levels of HIV specific gamma-IFN+ T-cells. Noteworthy, 2 DNA-C priming immunizations (w0, w4) per se induced statistically significant T cell responses in 30% of the vaccines and properly primed T cells, 2 NYVAC booster immunizations (W20, w24) increased the response rate to >90% and significantly enhanced levels of both HIV-specific CD4+ and partially CD8+ T-cells. T cell responses were stable over time, directed against a broad variety of epitopes with some dominance of Env over Gag.
**F.20 (Vortrag)**

First results of a randomized, controlled phase-II-study with a MVA-Nef vaccine in HIV-1 infected patients with CD4 counts > 250/µl followed by Structured Treatment Interruption (STI)

**Methods:**

In this single blind, randomized controlled phase II study 77 patients received 3 s.c. vaccinations of either 1E8 TCID50 IMVAMUNE®, 1E8 TCID50 or 5E8 TCID50 MVA-nef (n=26,25,26) at weeks 0, 8, 16. At w20 patients were offered a STI with monitoring at weeks 24/26/28/32/40/52 regarding safety, plasma viral load (VL), CD4 counts and immune response to HIV.

**Results:**

Safety: No vaccine related serious adverse reactions were reported. All subjects developed local injection site reactions, mostly mild to moderate. Solicited systemic adverse effects were transient and also mostly mild to moderate, events ≥ grade 3 (fever, myalgia, headache, fatigue) occurred only in single cases. MVA-specific antibodies: Both the vaccinia pre-immune and the vaccinia naïve patients developed a good antibody response to MVA. STI phase: In total 37 of 77 patients stopped HAART after w20. VL increased in all patients with w0 to w8 after STI followed by a subsequent decrease. There is an indication for a trend that the decrease in VL in patients receiving the MVA-nef vaccine is more pronounced than in the control group with IMVAMUNE®. In total 25 patients remained off HAART for at least 32 weeks.

**Conclusions:** MVA-nef proved to be safe and immunogenic in HIV-1-infected patients confirming previous results from clinical studies. Data from the Structured Treatment Interruption indicate a vaccine and dose relationship regarding viral load. Furthermore, the strong induction of an immune response against IMVAMUNE® confirms the potential as a safe and potent smallpox vaccine in HIV-infected subjects. Based on these positive results in HIV infected patients further studies are granted to evaluate the capability of the MVA-vector technology for development of therapeutic HIV vaccines.

Acknowledgement: Partially funded by NIAID (N01-AI-40072).

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**F.21 (Poster)**

Selection of HIV-1 specific scFv antibodies from LTNP derived phage libraries

**Antoni S.**, **Hust M.**, **Dübel S.**, **Dietrich U.**

1Universitätsklinikum Erlangen, Medizinische Klinik 3, Klinische Infektionsimmunologie, Erlangen, Germany, 2Bavarian-Nordic GmbH, Martinsried, Germany, 3Practice Dr. Helm, Nuremberg, Germany, 4Practice Dr. Goeriahn, Munich, Germany, 5Practice Dr. Schneider, Fürth, Germany, 6Practice Dr. Jäger, Munich, Germany

**Introduction:** MVA-BN® is a safe viral vector incapable of replicating in human cells. A derived recombinant vaccine, MVA-nef expressing the nef gene from HIV-1-LAI, has previously shown a good safety profile and the capability to induce Nef-specific CD4+ T-cells and CD8+ CTL. To assess the immunogenicity and safety of MVA nef in dependence of dose and in comparison to MVA (IMVAMUNE®) we performed a study in HIV-1 infected patients on HAART.

**Methods:**

In total 77 patients received 3 s.c. vaccinations of either 1E8 TCID50 IMVAMUNE®, 1E8 TCID50 or 5E8 TCID50 MVA-nef (n=26,25,26) at weeks 0, 8, 16. At w20 patients were offered a STI with monitoring at weeks 24/26/28/32/40/52 regarding safety, plasma viral load (VL), CD4 counts and immune response to HIV.

**Results:**

Safety: No vaccine related serious adverse reactions were reported. All subjects developed local injection site reactions, mostly mild to moderate. Solicited systemic adverse effects were transient and also mostly mild to moderate, events ≥ grade 3 (fever, myalgia, headache, fatigue) occurred only in single cases. MVA-specific antibodies: Both the vaccinia pre-immune and the vaccinia naïve patients developed a good antibody response to MVA. STI phase: In total 37 of 77 patients stopped HAART after w20. VL increased in all patients with w0 to w8 after STI followed by a subsequent decrease. There is an indication for a trend that the decrease in VL in patients receiving the MVA-nef vaccine is more pronounced than in the control group with IMVAMUNE®. In total 25 patients remained off HAART for at least 32 weeks.

**Conclusions:** MVA-nef proved to be safe and immunogenic in HIV-1-infected patients confirming previous results from clinical studies. Data from the Structured Treatment Interruption indicate a vaccine and dose relationship regarding viral load. Furthermore, the strong induction of an immune response against IMVAMUNE® confirms the potential as a safe and potent smallpox vaccine in HIV-infected subjects. Based on these positive results in HIV infected patients further studies are granted to evaluate the capability of the MVA-vector technology for development of therapeutic HIV vaccines.

Acknowledgement: Partially funded by NIAID (N01-AI-40072).

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**F.22 (Vortrag)**

**A phase 1 study to evaluate the safety and immunogenicity of a recombinant adeno-associated virus HIV vaccine**


1University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 2National AIDS Research Institute, Pune, India, 3St. Pierre University Hospital, Brussels, Belgium, 4SGS Biopharma, Antwerp, Belgium, 5University Clinic, Bonn, Germany, 6Targeted Genetics Corporation, Seattle, United States of America, 7The Children’s Hospital of Philadelphia, Philadelphia, United States of America, 8IAVI, New York, United States of America, 9IAVI, New Delhi, India

**Background:** Delivery of HIV genes within recombinant adenovirus vectors is a potent inducer of both HIV-specific antibodies and T-cell responses in animal studies. A rAAV-based vaccine (tgAAC09), consisting of single-stranded DNA from Clade C HIV-1 genes for the gag, protease and part of the reverse transcriptase proteins enclosed within a rAAV2 protein capsid, was developed as a potential component of a HIV vaccine.
**Objective:** To evaluate the safety and immunogenicity of tgAAC09 in healthy, HIV-uninfected adult volunteers at low risk for HIV infection.

**Methods:** In this dose-escalation study, 80 healthy, HIV-uninfected volunteers received a single intra-muscular injection of tgAAC09 at different doses: 3x10^9 DRP (n=16), 3x10^10 DRP (n=23), 3x10^11 DRP (n=25) or placebo (n=16). In addition, 21 of 50 volunteers received a boost vaccination of tgAAC09 at a dose of 3x10^11 DRP or placebo. T-cell responses were assessed by IFN-γ ELISPOT assay, anti-AAV2 neutralizing titers (NT) by a cell-based assay, and vaccine shedding by PCR.

**Results:** The vaccine was well-tolerated after both initial and boost vaccination. Mild-to-moderate local and systemic reactogenicity was experienced by app. 15−20% of volunteers. No vaccine-related SAE’s were reported. The proportion of reactogenicity and AE’s were evenly distributed among the different dose groups and placebo. There was no evidence of vaccine shedding. At baseline, 48% of European and 97% of Indian volunteers had detectable NT against AAV2. The proportion of volunteers with four-fold or greater rise in anti-AAV2 NT increased with higher doses and after boost vaccination. HIV-specific T-cell responses were detected in 9/64 vaccinees, with 24% (6/25) of volunteers in the highest dose group responding. All responses were to gag epitopes and the magnitude was moderate (38-385 SFC/106 PBMC). No induction of antibody to HIV was observed.

**Conclusions:** Vaccination with tgAAC09 appears to be safe and well-tolerated. Immunogenicity data indicated a moderate response at the highest dose, directed to gag. Future clinical trials will focus on higher doses of tgAAC09, the optimal interval for boost vaccination, the effect of pre-existing immunity to AAV2, and evaluating prime-boost regimens.

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**F.23 (Poster)**

**Induction of neutralising antibodies after immunisation with the transmembrane envelope proteins p15E of gammaretroviruses:** Implication for the development of an HIV vaccine

*Fiebig U. 1, Langhammer S. 1, Behrendt R. 1, Kurth R. 1, Denner J. 1*

1Robert Koch-Institut, Berlin, Germany

**Objective:** Neutralising antibodies specific for the membrane-proximal external region (MPER) of the transmembrane envelope (TM) protein gp41 of HIV such as 2F5 and 4E10 have been isolated from infected patients. These antibodies are broadly neutralising and decreased the HIV load in clinical trials. However, many attempts to induce such antibodies failed so far.

To study the mechanism of induction and the efficacy of neutralising antibodies directed against the retroviral TM proteins, the TM proteins p15E of three different gammaretroviruses (porcine endogenous retrovirus, PERV; feline leukaemia virus, FeLV, and Koala retrovirus, KoRV) were used in immunisation experiments.

**Methods:** Recombinant p15E were produced; rats, goats and marmosets were immunised, neutralising antibodies were analysed in a real-time PCR based infection assay; ELISAs, Western blots and epitope mappings were performed, cells immunised with FeLVp15E were challenged with infectious FeLV.

**Results:** Antibodies neutralising PERV, FeLV and KoRV were obtained after immunisation with the corresponding p15E. Two epitopes, one located in the N-terminal part near the fusion peptide (designated E1), the other in the C-terminal MPER (E2) of p15E were found in all cases. The localisation of E2 corresponds to the localisation of the epitopes of 2F5/4E10 and despite the evolutionary difference of HIV and gammaretroviruses a limited sequence homology was observed. Neutralising antibodies specific for p15E of FeLV prevented in immunised cats an antigenemia, demonstrating their efficacy in vivo.

**Conclusion:** These data show that the E2 domain represents a highly vulnerable target for neutralisation of retroviruses. Since by us (WO 2005/021574) and others a E1 domain was identified in gp41 of HIV, immunisation with proteins containing these domains may induce broadly neutralising antibodies of the type 2F5 and 4E10.

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**F.24 (Poster)**

**A novel gene therapeutic strategy against HIV-1 infection using the suicide protein tBid**

*Hülsmann P.M. 1, Hofmann A.D. 1, Rauch P. 1, Wolff H. 2, Berens C. 3, Metzner K. 1*

1University of Erlangen-Nuremberg, Institute of Clinical and Molecular Virology, Erlangen, Germany, 2GSF-Helmholtz Research Center for Environment and Health, Institute of Molecular Virology, Neuherberg, Germany, 3University of Erlangen-Nuremberg, Chair of Microbiology, Microbiology, Erlangen, Germany

**Objective:** Specific elimination of human immunodeficiency virus type 1 (HIV-1) infected cells by HIV-1 LTR driven suicide genes presents a promising strategy in gene therapy of HIV-1. Clinical applications of this approach depend on a fast and effective suicide gene which is exclusively expressed in HIV-1 infected cells. These preconditions have not yet been fulfilled and, thus far, success of suicide approaches is limited. It was recently shown that expression of truncated Bid (tBid), a human pro-apoptotic protein, rapidly and efficiently induces apoptosis. Thus, we tested tBid in the context of a novel HIV-1 LTR-based, Tat- and Rev-dependent transgene expression vector as a new potential suicide strategy in the gene therapy of HIV-1.

**Methods:** tBid was cloned into the HIV-1 LTR-based Tat- and Rev-dependent expression vector pLRred2xINSR replacing dsRed. The effects of tBid were then analyzed in the presence or absence of the HIV-1 proteins Tat and/or Rev in transiently and stably transfected 293T and HeLa cells. Cell death was determined 24 hours after transfection by PI-staining. The original vector pLRred2xINSR was used as control and dsRed expression determined by FACS and fluorescence-microscopy.

**Results:** tBid, expressed by the strong constitutive CMV promoter, was highly efficient in inducing apoptosis in both 293T and HeLa cells in less than 24 hours showing that tBid is effective in these cell lines. When expression of tBid was driven by the HIV-1 LTR promoter, induction of apoptosis was not observed in both cell lines in the absence of co-factors showing that this system is not leaky. Coexpression of Rev alone did not lead to induction of apoptosis, but coexpression of Tat alone moderately induced apoptosis. This effect was strongly enhanced by the co-expression of Tat and Rev. Cell death was rapidly observed within 24 hours. Equivalent results for dsRed expression/fluorescence were obtained using the control vector pLRred2xINSR.
Conclusion: Our results demonstrate that expression of tBid under the control of the HIV-1 LTR promoter preferentially induces apoptosis in Tat- and Rev-positive cells suggesting that this suicide vector has the potential for effective use in a gene therapy to exclusively eliminate HIV-1 infected cells.

**F.25 (Poster)**

Induction of immune responses by Human Immunodeficiency Virus Type-I (HIV-1) Pr55Gag virus-like particles (VLP) and the impact of the producer system upon activation of innate immune responses


1Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Molekulare Mikrobiologie und Gentherapie, Regensburg, Germany

**Objective:** HIV-1 Pr55Gag virus-like particles (VLP) produced in the baculovirus expression system have been shown to represent strong inducers of the humoral and CMI in mice and non-human primates. This study aimed towards investigating the molecular mechanisms underlying the strong immunogenicity and adjuvantivity of such VLP.

**Methods:** Pr55Gag VLP were produced (i) using the baculovirus (BV) expression system and (ii) mammalian 293T cells coexpressing the BV envelope protein gp64. Cytokine production (release of gIFN, IL5, others) from splenic cells of naive mice and human monocyte derived DC (huMDDC) and the upregulation of costimulatory molecules (CD40, 80, 83, HAL DR, CCR7) on the surface of huMDDC were used as a measure for the activation of innate immunity by VLP antigens.

**Results:** Ex vivo studies on huMDDC clearly demonstrated that VLP of BV origin, but not VLP produced in mammalian cells triggered MDDC maturation, activation and cytokine secretion. This lack of mammalian cell derived VLP to activate huMDDC could not be rescued by pseudotyping these VLP with BV gp64. Comparable results were obtained when murine splenic cells were used for the ex vivo studies. However, splenic cells from TLR9 knockout mice could be stimulated neither by mammalian, nor by BV produced VLP. Conclusion: These results clearly indicated that the potency of VLP to induce innate immune responses is not an intrinsic property of VLP rather than mediated by BV or insect cell derived components. The BV Env protein gp64 is clearly not contributing to TLR triggering, may however play a beneficial role in uptake of VLP by APC.

**F.26 (Poster)**

HIV vaccine candidates in cross-validation on dendritic cells


1Universität Regensburg, Institut für Medizinische Mikrobiologie und Hygiene, Molekulare Mikrobiologie und Gentherapie, Regensburg, Germany, 2University Medical Center, Institut für Medizinische Mikrobiologie und Virologie, Kiel, Germany, 3Cornell University, Microbiology and Immunology, Ithaca, United States of America

**Objectives:** Recently we have generated a new HIV Vaccine candidate based on the Equine Herpesvirus 1 (EHV-1). The primary goal of the current study is to compare a clinical trial lot of a recombinant New-York-Vaccinia Virus based HIV vaccine candidate (NYVAC-C; expressing Gag/Pol/Nef) with a corresponding EHV-based vaccine construct (EHV-C) regarding their capacity to induce maturation of monocyte derived dendritic cells (MDDC).

**Methods:** A recombinant EHV-1 C-GagPolNef (EHV-C) was generated using BAC-technology and RED-Recombination. MDDCs were infected with EHV-C and NYVAC-C at different MOIs. Expression of the transgenes was monitored by FACS and Western Blot analysis. Maturation of MDDCs was determined by FACS analysis of differentiation markers and in ELISA assay measuring secreted proinflammatory cytokine levels. Furthermore, early/late gene expression and antigen expression of the HIV vaccine candidates was measured via RNA quantification.

**Results:** Depending on the used MOI a substantial fraction (~40%) of EHV-C infected MDDCs displayed expression of significant amounts of GagPolNef immunogens. MDDCs infected with EHV-C show various markers for DC maturation and activation as monitored by release of cytokines and surface expression of costimulatory signals. In contrast, MDDCs infected with NYVAC-C only weakly express HIV transgenes and do, upon direct infection, not support DC maturation or activation. NYVAC-C expresses very low amounts of a late gene F17R on MDDC, which could be interpreted as a block in the viral replication and responsible for the low transgene expression.

**Conclusion:** EHV derived vectors support efficient transgene expression and provide signals required for DC maturation & activation.

**F.27 (Poster)**

Detection of distinct mutants of TRIM5-alpha mRNA derived from SIV infected macaques and HIV-1 infected individuals


1HIV Research Laboratory, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 2Heinrich-Pette-Institute for Experimental Virology and Immunology, Hamburg, Germany, 3German Primate Center (DPZ), Dept. of Immunology and Virology, Gottingen, Germany

**Background:** Recently the tripartite motif protein TRIM5a was identified as an intracellular restriction factor against HIV-1. Although unmodified human TRIM5-alpha is not active against HIV-1, its restriction potential was significantly increased by different modifications in the SPRY domain of the protein, which was defined earlier as the region responsible for inhibitory activity. Thus certain mutated TRIM5a variants may exist, which play a role in the delayed disease progression of so called Long-Term-Non-Progressors (LTNP).

**Objective:** To study the genetic sequence of human and simian TRIM5a and its potential role in the restriction of HIV-1 and SIV infection.

**Materials and methods:** Cloning and sequencing of TRIM5a cDNA was performed in blood PBL from 10 subjects of either of the following groups:

a) LTNP or “slow progressors”, who maintain a viral load < 2000 copies/ml and CD4 counts > 500 cells/μl without any treatment for up to 10 years;
b) patients in various stages of disease progression and
c) HIV-1 negative individuals as normal controls. Moreover,
we started to sequence simian TRIM5a variants obtained
from 10 SIV-infected monkeys with LTNP characteristics
and compared the sequences to a group with rapid disease
progression.

**Results:** A TRIM5-a specific Nested-PCR was developed al-
lowing for the detection of sufficient amounts of TRIM5a
cDNA for cloning and sequencing. So far this was performed
for 10 LTNP macaques and 10 HIV-1 negative human con-
trols. In controls a total of 7 mutations compared to wild type
was found. As of yet the significance of these mutations can-
not be determined. Two distinct mutations in the SPRY region
were detected in 10/10 LTNP monkeys. Additional mutation
patterns were detected in different regions of the protein.
These mutations differed from the consensus sequence report-
ed so far but the clinical significance remains to be elucidated
as results from the group with progressive disease are still
pending.

**Conclusions:** Analysis of the LTNP macaques and normal
human controls showed mutations which differed from con-
sensus sequences. The analysis of all subjects is required in
order to assess the significance and relevance of these find-
ing.