

Abstracts from the 12th Annual Meeting of the IHMF®

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In this section of the *Herpes* journal the abstracts of plenary and poster sessions from the 2005 IHMF® Annual Meeting are published. Readers should note that these have not been submitted to the journal's standard demanding peer review and editorial quality control processes and, subject to only minor modifications, they appear as originally submitted to the IHMF®. Views and factual claims expressed are those of the authors of each abstract and are not necessarily endorsed by the Editors, Advisors, Publisher, Distributors or Grantors of the journal.

Plenary Abstracts – Keynote Lectures

01: CMV vaccine potential

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Congenital CMV infection may be the leading cause of sensorineural hearing loss in children and can lead to mental retardation, cerebral palsy and impaired vision. Because congenital CMV infection is relatively common and rarely fatal, it is an important cause of disability, which impacts its victims and their families over a lifetime and has significant economic impact on the health care system. A special committee of the National Academy of Sciences that reviewed priorities for vaccine development in the US concluded that a vaccine aimed at prevention of congenital CMV infection should be a top priority.

Although there is concern about the ability of the host immune response to

prevent re-infection with CMV and even to prevent disease, there is substantial evidence that maternal immunity prior to conception will decrease both the frequency and severity of fetal infection. What is now needed is a vaccine candidate that will safely stimulate an immune response that will either prevent or modify maternal infection so that fetal infection and disease are prevented. Several vaccine candidates are now in various phases of preclinical and clinical testing in humans and large-scale efficacy trials will likely occur in the foreseeable future.

02: Topical anti-herpes therapies

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Topical therapies offer some advantages over systemic therapies especially for patients who are reluctant to use oral medications. Because current recommendations do not include the use of topical therapy for primary herpes disease or for recurrent genital herpes the presentation will concentrate on therapy for recurrent herpes simplex labialis. The major focus will be a review of the data for the three most common topical therapies for recurrent herpes labialis, 5% acyclovir cream, 1% penciclovir and 10% docosanol. To place these therapies in perspective the results of these trials will be compared to the simplest of oral

therapies, one-day treatment with high-dose oral valacyclovir. As will be shown all four therapies have been shown to reduce the duration of lesions by about 0.5–1.0 days and also reduce the duration of pain. The remainder of the discussion will review the rationale and potential use of immunomodulators and combination therapies with antivirals and anti-inflammatory agents for HSV infections. Current therapies for recurrent herpes labialis can reduce the pain and time to healing but the effects are less than optimal and improvements should be sought.

03: Martin Wood Memorial Lecture

The implications of new data from ongoing varicella vaccine trials

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Universal immunization of children in the USA has greatly reduced the incidence of varicella and its complications. However, there are two major concerns: 1) the appearance of breakthrough varicella in 8–15% of exposed childhood vaccinees implies that their future protection against varicella as adults will be suboptimal; 2) the vaccine-induced decline in varicella will remove the environmental boosting that may be essential to prevent herpes zoster (HZ) in our current elderly population. Thus, it is suggested that the age-specific incidence of HZ will increase as a result of childhood immunization. The administration of a second

dose of varicella vaccine to children is discussed as a solution to the first concern. The solution to the second concern, as well as to the growing problem of HZ in our aging population, is likely to be a vaccine to prevent or attenuate HZ in this high-risk group. A high dose live varicella vaccine, approximately 18 times more potent than the childhood vaccine (but the same virus), safely reduced the frequency of HZ (by 50%) and the pain and suffering (including post-herpetic neuralgia) by >60%. The rationale for administration of this vaccine and the potential issues raised by its use are discussed.

04: Combating VZV disease

Guidelines – session 1

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The goal of this presentation is to review new data related to antiviral therapy of varicella (chickenpox) and herpes zoster (shingles). We will focus on published data from randomized, controlled clinical trials that have become available since the last IHMF VZV management guidelines were published in 2001. Acyclovir remains the drug of choice for treatment of varicella in immunocompetent and immunocompromised patients. The pharmacokinetic profiles of famciclovir and valacyclovir suggest that these drugs will also be effective for chickenpox, but published data are limited. Treatment approaches for HIV-positive persons and for immunocompetent patients with complicated chickenpox (including pregnant women) remain based on anecdotal data. No large clinical trials addressing varicella therapy have been published since 2001. The efficacy of acyclovir, famciclovir, and valacyclovir for uncomplicated herpes zoster in the immunocompetent host has been well documented. New information

demonstrates that famciclovir is effective at doses from 250 mg 3 times daily to 750 mg once daily. Data published since 2001 also indicate that brivudin (BVDU) is an effective antiviral drug for shingles. Brivudin appears to be as effective as acyclovir or famciclovir for herpes zoster, although potentially serious drug interactions have prevented the approval of the drug in some countries. Intravenous acyclovir remains the drug of choice for treatment of herpes zoster in severely immunocompromised persons, although recently published data suggest that oral antiviral drugs (acyclovir and famciclovir) can be safely used in selected patients. Management of complications of herpes zoster (for example, encephalitis) remains based on clinical experience, not prospectively collected data. Revisions to the IHMF Guidelines open to discussion include the addition of brivudin as a recommended treatment for herpes zoster in the normal host.

Guidelines – session 2

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The majority of patients developing shingles will suffer no more than a few days of inconvenience and discomfort. A very significant minority however, particularly the elderly, will experience the start of a prolonged period, sometimes lifelong, of misery. All diseases have biological, psychological and social influences and the pain following herpes zoster (HZ), postherpetic neuralgia (PHN), is no exception. Although a definition for PHN is now almost universally accepted (significant pain or painful abnormal sensation 120 or more days after HZ rash appearance), the precise causative pathology varies between individuals

as does the detail of the symptoms.

Ideally management of a neuropathic pain such as PHN should be both mechanism based and evidence based. Despite significant advances in the understanding of mechanisms for PHN, treatment remains somewhat empirical. There have also been advances in the development of pharmacological tools for neuropathic pain management but few have been satisfactorily tested for more than short term administration. Efficacy of combination therapy has hardly been investigated at all.

Current knowledge indicates that established PHN may respond to tricyclic antidepressants (e.g. amitriptyline, nortriptyline), alpha-2-delta ligands (e.g.gabapentin, pregabalin) and opiates (e.g. morphine, oxycodone) with similar frequency. However, an individual with PHN may respond to one treatment but not others. Combination therapy, particularly of an alpha-2-delta ligand and an opiate, may be synergistic allowing greater benefit with reduced doses of both classes of drug and reduction of side effects. Adjunctive therapy with topical agents such as lidocaine may provide significant additional benefit. The results of a recent Systematic Review of PHN therapy will be presented.

To provide optimal management, thorough assessment, painstaking advice and surveillance with willingness to pursue pain alleviation over time, are necessary. Despite perseverance, some PHN patients will not gain satisfactory relief and Cognitive Pain Management Programmes may be considered. For HZ

patients with significant risk factors for PHN (greater age, severe acute pain and/or rash or prodromal pain), it may be that prophylactic administration of an alpha-2-delta ligand and opiate may afford protection although this has still to be convincingly demonstrated in humans. Antiviral drugs, particularly those with good bioavailability (famciclovir, valaciclovir, brivudin) remain an important preventive therapy reducing the incidence of PHN by approximately 50%.

Widespread adoption of child varicella vaccination programmes will ultimately eradicate varicella although paradoxically they may increase its incidence in the short and medium terms. After a generation or so, the pool of adults carrying latent VZ virus will be deceased and HZ will also be eradicated. In the meantime, preventive strategies for PHN should be strongly encouraged and the search for more effective therapy of established PHN should continue.

05: The continuing spread of HSV infection

Worldwide epidemiology

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HERPIMAX study was the first epidemiologic survey concerning HSV infection combining clinical and serologic observations in a community-based population carried out in France. The estimated prevalence of clinically probable genital herpes (CPGH) was 11.8% while the overall HSV2 seroprevalence was 17%. The prevalence of CPGH was lower in subjects who were infected with both HSV1 and HSV2 than in subjects infected only with HSV2, suggesting that HSV1 may have a protective effect on symptomatic expression of HSV2 infection. In Germany a survey conducted among the general population demonstrated a significant difference between former East Germany and former West Germany in HSV2 seroprevalence: 16.5% versus 12.6%, suggesting differences in sexual behaviour that warrant further investigation. The survey conducted in Estonia is one of the first in the newly independent Eastern European countries. HSV2 seroprevalences in women (24% in pregnant women and 21% in female blood donors) are higher than reported in similar populations in Europe and are similar to those reported from USA. In Switzerland a serosurvey demonstrated that HSV2 seropositivity was most strikingly reduced by HSV1 infection but only among women at the highest risk for HSV2 infection.

Epidemiology in developing countries: In Asia the example of Bangladesh illustrates the dramatic dissemination of HSV2 infection. In this country a survey conducted among female prostitutes shows a very high sero-prevalence of 94.6%. Condom use was very low and by chance no HIV infection was found. But one can imagine the situation when HIV will be introduced in this population. In Africa

the spread of the HSV2 epidemic continues to expand. A study among factory workers in Ethiopia found a 40.9% seroprevalence rate at enrolment. The transmission substudy performed in serodiscordant couples showed that the annual rate of infection from their partner was 21% for women and 5% for men findings which are quite the same than in USA. In Africa there is more evidence that genital herpes became the first cause of GUD (genital ulcerative disease). In Tanzania 82% of GUD was due to HSV2 while syphilis accounted for 6% of cases. In a mining community in South Africa HSV2 as a cause of GUD has increased from 17.2% to 36% between 1994 and 1998. The risk of neonatal herpes was never assessed in Africa. A study on genital shedding of HSV2 was conducted among childbearing-aged and pregnant women in Gabon. This study found a high prevalence (66%) of HSV2 seropositivity with a high proportion, 14%, of women harbouring HSV2 DNA shedding in their genital secretions, indicating that this female population is at high risk for HSV2 transmission during pregnancy.

HSV2 as cofactor for HIV transmission: In developed countries, a study conducted in France on HIV infected patients found a HSV2 seroprevalence over 50% which points out that interactions between HSV2 and HIV are not only a concern in developing countries. In Africa many recent studies (South Africa, Kenya, Uganda) confirm the dramatic role of HSV2 in both transmission and acquisition of HIV. This emphasizes the urgent need for the result of ongoing trials using acyclovir as an intervention treatment to reduce HIV incidence.

Frequency of HSV shedding as measured by PCR

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The epidemic of HSV-2 is driven by the ability of the virus to be transmitted during periods of asymptomatic or subclinical shedding. Most sexual and perinatal transmission of HSV occurs during asymptomatic viral reactivation. Our ability to measure the frequency of reactivation has been advanced with the development of HSV DNA PCR which is up to 4 times more sensitive than viral culture in detecting the virus on mucosal surfaces. Among HSV-2 seropositive persons, genital HSV shedding occurs on a median of 19% of days (range 0–96) and the spectrum of symptoms is also wide. This large variability in HSV-2 genital shedding rate as well as in the symptoms is poorly understood and appears

mostly determined by host factors. Viral type – HSV-2 vs. HSV-1 – and time since HSV-2 acquisition are the only known determinants of HSV reactivation. These factors, however, explain only a small portion of the observed variability. HIV infection increases the rate of genital HSV shedding both in frequency and in quantity. Highly active antiretroviral therapy ameliorates clinical HSV disease but has little effect on viral reactivation rates. Recent PCR-based studies of oral HSV reactivation show that HSV-2 shedding in the mouth is not infrequent among HIV infected patients.

Poster Abstracts

01-VZV: Clinico-epidemiological features of varicella in Romania

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Objectives: 1. To assess the epidemiological trends of varicella in Romania. 2. To compare the clinical and laboratory features of varicella in children versus adults.

Methods: 1. Analysis of the incidence of varicella, in Romania, between 1990 and 2004, according to Institute of Public Health national data. 2. Clinical and laboratory data-based study of 371 patients: 198 children (0–14 years old)/173 adults, admitted to the Infectious Diseases Institute "Prof.Dr.M.Bals", Bucharest, between 01.01.2003 and 01.12.2004.

Results: In Romania, the incidence of varicella (cases/100 000 inhabitants) increased from 122.8 in 1990 to 369.3 in 1995. Then, the incidence decreased slightly (242.2 in 1996, 220.3 in 1998, 206.3 in 2000), but remained higher than in 1990. In 2001, there was a sharp increase of the incidence of varicella (310.4). Afterwards, the incidence maintained over 200, reaching 315.5 in 2004. Age distribution among the patients hospitalized for varicella in our institute between

2003 and 2004 showed 2 peaks of incidence: first decade (35.57 % of cases) and third decade (26.13%). Mean age=15.41 years old (median=13). There were 53.27% patients with at least one complication, especially children ($P<0.05$). Comparative evaluation of complications in adults versus children is shown in Table 1.

Conclusions: Varicella is still considered a benign disease of childhood. Therefore, routine vaccination remains controversial. Incidence peak tends to move from children to adults, leading probably to a higher risk of complications and costs. Although our study suggests the utility of the routine varicella vaccination, this policy is not yet a priority in Romania, considering our socio-economical conditions.

Table 1: Comparative evaluation of varicella complications in Romania (adults versus children)

Clinical and laboratory findings	Adults No. (%)	Children No. (%)	Statistics
Skin bacterial infections	15 (8.67)	58 (29.29)	$P<0.05$
Pharyngitis	4 (2.31)	60 (30.3)	$P<0.05$
Interstitial pneumonia	10 (5.78)	35 (17.67)	$P<0.05$
Encephalitis	1 (0.57)	0	$P>0.05$
Cerebellar ataxia	1 (0.57)	0	$P>0.05$
Myelitis	1 (0.57)	0	$P>0.05$
Thrombocytopenia, of which	23 (13.29)	8 (4.04)	$P<0.05$
Purpura	0	1 (0.5)	$P>0.05$
Hepatocytolysis	6 (3.46)	4 (2.02)	$P>0.05$

2-VZV: Knowledge of shingles symptoms, risks and treatments low among adults: widespread shingles education efforts may reduce long-term complications

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Objectives: Herpes zoster, or shingles, is a common infection that can lead to long-term severe pain (postherpetic neuralgia), particularly in the elderly. An international survey was conducted to gauge existing knowledge of shingles, its symptoms, risk factors and treatment options in order to understand better the limitations of current shingles education efforts.

Methods: A total of 1808 telephone interviews were conducted with approximately 300 adults aged 55 and older in each of the six countries (Australia, Canada, Italy, Spain, United Kingdom, and United States). The sampling error for each country's population was ± 6 percentage points and was higher among sub-groups.

In all six countries combined, 91% were aware of shingles. Awareness of shingles was high among respondents in the US (96%), Canada (89%), Italy

(95%), UK (98%), and Australia (92%). In Spain, where the recorded incidence of chicken-pox among children is relatively low, awareness of shingles was 34%. Of respondents aware of shingles, more than 60% know little or nothing about the condition and only 25% are aware of the connection between chicken-pox infection and adult risk for shingles. A considerable proportion of those aware of shingles believe they are at low or no risk of getting the condition [U.S. (56%), Canada (67%), Italy (37%), Spain (42%), UK (63%), Australia (66%)]. A majority either is unaware of or falsely believes there are no prescription medications available to treat shingles [US (61%), Canada (72%), Italy (65%), Spain (68%), UK (67%), Australia (70%)]. Moreover, those aware of a prescription medication are unaware that the medication can reduce the risk of long-term complications.

03-CMV: Virus-specific cytotoxic T lymphocytes in congenital CMV infection

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Investigations into human cytomegalovirus (CMV)-specific cellular immunity are important to the better understanding and management of CMV infections. CMV phosphoprotein pp65 is thought to be a major antigen for CMV-specific cellular immunity.

Flow cytometric analysis of CD4(+) and CD8 (+) T cells specific to CMV was undertaken in seven patients with congenital CMV infection, six healthy infants who had acquired infection, and six seropositive adults. Intracellular cytokine assays showed that 0.03–2.23% of CD4(+) T cells were found in seropositive

healthy infants and adults. In contrast, CD4(+) T cells were almost undetectable in circulating lymphocytes of the patients with congenital infections. Tetrameric MHC complex/peptide analysis demonstrated pp65-specific CD8(+) cells to be present in healthy individuals, but almost absent in the patients with congenital infection.

Thus, for management of CMV infections, monitoring of CMV-specific cellular immunity could be very important.

04-CMV: The effect of acute rejection on EBV and CMV reactivation in renal allograft recipients

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Objectives: Rejection can be associated with activation of some infections. This may be due to injury induced by alloantigen-driven inflammation or intensification of the immunosuppressive regimen in the course of rejection therapy. On the other hand, viral infections may induce rejection. This notion is based on the hypothesis that during the initial stage of viral infection interferon- γ (IFN- γ) production becomes activated. IFN- γ increases expression of MHC molecules in the graft, which makes the graft more vulnerable to effector mechanisms and may initiate local rejection. IFN- γ activates cells (cytotoxic cells, macrophages) involved in the rejection so it may not only induce acute rejection but also exacerbate the ongoing sub clinical process.

Methods: We have investigated 68 recipients (43 male and 25 female) of renal allograft who were transplanted at the transplantation institute of the University of Medical Sciences. The immunosuppressive regimen consisted of cyclosporine (CsA), azathioprine (Aza), prednisone (Pre) and MMF. Serum samples were collected prospectively from all patients before transplantation and at 3, 6, 9 and 12 months after transplantation. The following tests were performed: VCA IgM, VCA IgG, EBNA IgG and CMV IgG and IgM. The levels of antibodies were determined using the ELISA method.

Results: Among 68 patients studied acute rejection was diagnosed in 16 recipients. The mean time of diagnosis of acute rejection is 3.78 ± 0.12 months post transplant. All of them received therapy with methylprednisolone pulses,

and 9 recipients with steroid-resistant rejection were treated with ALG. Fourteen recipients had serological markers of previous infection by EBV in sera collected before a rejection episode. At the moment of transplantation 14 recipients had serological symptoms of previous infection. In serum samples obtained before transplantation, two patients had serological markers of reactivation of EBV infection. In serum samples obtained after a rejection episode and therapy, 10 patients had serological markers of reactivation of EBV infection. Sixteen recipients had serological markers of previous infection of CMV in sera collected before a rejection episode. At the moment of transplantation, serological symptoms of previous infection were detected in 16 recipients. In serum samples obtained after a rejection episode and therapy, 12 patients had serological markers of reactivation of CMV infection and four recipients had serological symptoms of previous infection.

Conclusions: During the time of the study rejection episodes occurred in 23.5% of recipients. All of them received therapy with high doses of methylprednisolone and 10 patients with steroid-resistant rejection were treated with anti-lymphocyte antibodies. We found 50% reactivation of EBV and a 75% CMV reactivation rate in recipients undergoing acute rejection. Rejection episode as well as anti-rejection therapy affects the serological status of EBV and CMV infection. Also, there was an effect of ATG administration on EBV and CMV infection serological markers.

05-CMV: Coincidence of Epstein Barr virus reactivation, cytomegalovirus infection in renal transplant recipients

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Objectives: Viral infection is the single greatest cause of infectious disease morbidity and mortality in transplant recipients. Both human herpes viruses, Epstein Barr virus (EBV) and cytomegalovirus (CMV), usually persist in a latent state after primary infection. CMV is the most important opportunistic infectious agent in immunosuppressed organ transplant recipients. Reactivation of chronic EBV infection sometimes results in clinical symptoms and eventually may lead to uncontrolled proliferation of B cells terminating in post-transplant lymphoproliferative disease (PTLD). The probability of PTLD is further increased by concomitant use of antilymphocytic antibodies and infection with cytomegalovirus.

Methods: We have investigated 68 recipients (44 male and 25 female) of renal allograft who were transplanted at the transplantation institute of the University of Medical Sciences. The immunosuppressive regimen consisted of cyclosporine (CsA), azathioprine (Aza), prednisone (Pre) and MMF. Ten patients underwent induction therapy with antibodies, eight patients with antithymocyte globulin (ATG), and two patients with monoclonal antibodies (OKT3). Serum samples were collected prospectively from all patients before transplantation and at 3, 6, 9 and 12 months after transplantation. The following tests were performed: EA IgM, EA IgA, EBNA IgG and CMV IgG and IgM. The levels of antibodies were determined using the ELISA method.

Results and Conclusion: Reactivation or primary infections were a common complication occurring during the post transplant course. Before the surgery 92.3% of recipients had latent infection with CMV, and only 1.5% of recipients had serological symptoms of CMV reactivation immediately before transplantation. During 12 months after transplantation reactivation of CMV infection developed in 13.8% of recipients. All patients were treated with gancyclovir. At the moment of transplantation, 78.5% of kidney recipients had serological symptoms of previous EBV infection, 13.8% were detected with reactivation of EBV and primary EBV infection occurred in 4.6% of patients. During the first year after transplantation, primary infection with EBV developed in 6.15% of recipients and EBV reactivation occurred in 27% of recipients. Since CMV infection causes a transient immunosuppression which may exacerbate EBV replication, analysis of the relationship between CMV and EBV infection was carried out. Among patients who had reactivation or primary infection with CMV, serological markers of EBV reactivation and replication developed in 56% recipients. Fifty-six recipients did not have reactivation of CMV infection after transplantation. Among them, 10 patients experienced the incidence of EBV reactivation as assessed by the presence of IgM EA antibodies. This difference is almost statistically significant ($\chi^2=3.22$) $P=0.068$ and it may suggest that CMV infection may play a role in the reactivation of EBV infection.

06-CMV: Treatment of CMV infection or disease in solid organ transplant patients with valganciclovir (VGC)

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Background: VGC has proved successful for prophylaxis against CMV in high risk transplant recipients yet is not tested for treatment of CMV infection or disease.

Method: Fifteen transplant recipients (10 kidney, two heart, three lung) have been enrolled. CMV serostatus was D+/- ($n=11$), D+/R+ ($n=3$), and D-/R+ ($n=1$). Six

patients were treated for CMV infection and nine for symptomatic CMV disease (retinitis $n=1$, gastro-intestinal $n=3$, pneumonia $n=1$, CMV syndrome $n=4$). VGC was administered for 2–3 weeks followed by 2–4 weeks of secondary prophylaxis at reduced dosage. Viral load monitoring was performed using quantitative rapid

culture and/or quantitative real time PCR assay. Recently, we added pharmacokinetic studies of ganciclovir blood levels.

Results: Clinically, all nine symptomatic patients responded to treatment. Virologically, treatment with VGC turned blood cultures negative for CMV within 2 weeks in all patients, and was associated with a >2 log decrease in blood CMV DNA within 3 weeks in 9/9 tested patients. With a follow-up of 6 months, asymptomatic recurrent CMV viraemia was noted in six cases, and CMV syndrome in one case. VGC was clinically well tolerated in all patients.

07-HHV-6: Reactivation of the herpes 6 virus in bone marrow transplant recipients

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Human herpesvirus 6 (HHV-6) infection occurs worldwide in the majority of infants under 3 years of age. Its reactivation is mainly associated with immunosuppression in bone marrow transplant (BMT) recipients, where it may lead to graft versus host disease (GVHD). In order to establish a correlation between the observed clinical aspects and the presence of the viral agent, 13 patients were monitored during pre- and post-BMT stages and their peripheral blood

Laboratory abnormalities were observed in three patients: increase in transaminases, isolated thrombocytopenia and pancytopenia (one each), all three reversible after VGC dose reduction.

Conclusions: Our experience suggests that VGC is safe and effective to treat CMV in organ transplant recipients. Validating the present model of pharmacokinetic and pharmacodynamic studies of valganciclovir may expedite the validation process of this therapeutic or prophylactic approach in new indications.

08-HSV: Neonatal herpes simplex virus infection

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Herpes simplex virus infection in neonates can be a devastating disease. Transmission of the HSV-1 and HSV-2 viruses often occurs during vaginal delivery. It has been shown that primary HSV infection of the mother is associated with most cases of infection acquired during birth. We report a neonatal infection that resulted in neurological sequelae. The mother went into premature labour and assisted delivery using Simpson's forceps was necessary. The child was born with APGAR 0,1,1,2 and was admitted to the Neonatal Intensive Care Unit. On the eighth day of life it presented with vesicles spread over the body and the result of the Tzanck test was positive. HSV-1 infection was confirmed by serological

mononuclear cells (PBMC) were tested using polymerase chain reaction (PCR). Three samples were found to be positive for HHV6 DNA (23%); two of these were pre-BMT and one was post-BMT. All the samples came from different patients aged between 2 and 3 years. Each patient presented with some kind of clinical symptom. We conclude that HHV6 reactivation has important implications for bone marrow transplants and should therefore be analysed carefully.

diagnosis and acyclovir treatment was adopted. The child developed viral encephalitis, pulmonary alterations and hepatic enzyme levels were altered, resulting in sequelae in the form of cerebral paralysis. Although the mother had not presented a clinical picture of labial or genital herpes at any stage in her life, she was HSV-1-positive. According to the literature, 70% of cases of transmission during delivery occur in asymptomatic women, making it important to identify the risk factors for herpes virus infection in the mother. Prevention during gestation and prior diagnosis of HSV infection in the neonate are the main means of reducing the morbidity-mortality of this illness.

09-HSV: Detection of viral herpesvirus DNA-emia in bronco-alveolar lavage of immunocompromised patients

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Human herpesvirus infections are frequent complications in immunocompromised patients. These patients are at high risk of viral pneumopathies. In this study, the diagnostic yield of broncoalveolar lavage (BAL) was evaluated by PCR and classic detection methods.

Methods: Fifteen specimens of BAL from 15 patients (10 had haematological disorders, three were renal transplant recipients and two had pulmonary adenocarcinoma) were analysed. Human cytomegalovirus (HCMV) immediately and early antigen detection was performed by inoculation in human fibroblasts (MRC5 cells from BAL by the shell-vial technique) and by direct immunofluorescence, using monoclonal antibodies E13+2A2. HCMV was also detected by PCR. Herpes simplex virus (HSV) types 1 and 2 and Epstein-Barr virus (EBV), were only detected by PCR. In all PCRs the region amplified was the DNA

polymerase gene. In all patients, the detection of HCMV antigen pp65 was performed. **Results:** Five respiratory viral infections were detected (5/15): one by direct examination, cell culture and PCR, and four by PCR. HCMV was detected in three cases, one case with detection of antigen and DNA-emia, one with HCMV DNA-emia detection and one co-infection with EBV; HSV1 and EBV DNA-emia was detected in one case each. Ten specimens were negative for PCR and antigen detection. All patients were negative for HCMV antigen pp65, when BAL examination was performed.

Conclusion: Although we had detected five DNA-emias, in only one case can we suppose that there was a HCMV pulmonary infection, since virus replication was observed. The presence of viral DNA-emia, does not exclude the possibility that the real aetiological agent of the infection could have another origin.

10-HSV: Chronic genital herpes during acyclovir therapy as a source of a secondary recurrent whitlow by acyclovir-resistant/temperature-sensitive herpes simplex virus

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Acyclovir is the drug of choice for the prophylactic and curative treatment of herpes simplex virus (HSV) infection. The emergence of acyclovir-resistant HSV in transplant recipients is a major concern. HSV-2 recurred as a pubic ulcer in a 40-year-old allogeneic stem cell recipient and a secondary herpetic whitlow on his thumb appeared during 2 months of acyclovir therapy. They were caused by acyclovir-sensitive and -resistant/temperature-sensitive viruses, respectively. Six months later the whitlow alone recurred due to an acyclovir-resistant/

temperature-sensitive HSV, maintaining its pathogenicity and capability of reactivation. The temperature-sensitivity of the whitlow viruses may be an important element of pathogenicity in this case, allowing them to reactivate and cause lesions such as the whitlow on the thumb at a 33/34°C finger temperature. This is the first case with simultaneous and independent herpetic lesions caused by acyclovir-sensitive and -resistant HSV, indicating the importance of the chronic HSV lesion as a source of virulent acyclovir-resistant HSV infection.

11-HSV: Postherpetic itch

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In Japan, herpes zoster occurs with a peak in patients in their 20s and 50s. Herpes zoster commonly comprises rash and pain of relatively short duration. In some individuals, especially the elderly, herpes zoster is associated with complications and prolonged pain (post-herpetic neuralgia, PHN), whereas younger patients experience itch accompanying, or instead of, pain. The itch occurs probably prior herpes zoster. Some report severe disabling postherpetic itch. We experienced 10 patients with postherpetic itch recently. To clarify the mechanism and mediators involved in the pruritus of post herpes zoster, we measured serum histamine levels and plasma substance P levels, and the clinical effectiveness by oral olopatadine hydrochloride, a non-sedating H1-receptor selective anti-histamine that exhibits consistent efficacy and safety in the treatment of allergic rhinitis, urticaria and atopic dermatitis. Moreover, this drug inhibits the release of transmitters (substance P etc.) from sensory nerves. We analysed changes in the postherpetic itching before and during olopatadine hydrochloride treatment 5 mg

twice daily for 1 month. The primary efficacy endpoint was mean change in pruritus score from baseline. Patients reflectively recorded pruritus scores twice daily using a five-point scale (0 = none; 4 = very severe). Itch was quantified on a visual analogue ranging from 0 mm (no itching) to 100 mm (severe itching). Serum histamine levels (1.4 – 3.5 nmol/l, mean 2.2 ± 0.8 nmol/l) in patients with postherpetic itch are higher than normal ranges. Substance P levels (8 – 55 pg/ml, mean 30.5 ± 13.7 pg/ml) are variable.

In four of 10 patients, itching was significantly attenuated with olopatadine hydrochloride treatment. Their serum histamine levels were not changed. Postherpetic itch may be not associated with histamine and substance P. It seems that postherpetic itch happens by various mechanisms and is classified into two groups according to effect of olopatadine. These findings indicate a need for research on postherpetic itch.

12-HSV: Performance of the 2nd generation Focus HerpeSelect™ HSV-2 IgG ELISA on selected serum panels

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Background: The performance of a 2nd generation recombinant gG2-based ELISA was tested using sera with HSV-2 immunoreactivity determined by Western blot (WB) and HSV inhibition-ELISA. Included in the serum panels were sera that initially gave discordant results between the 1st generation ELISA and Western blot.

Methods: Three serum panels were used in the evaluation: Panel 1 consisted of 76 sera (from a study of >1100 sera) negative for HSV-2 by WB but initially positive by the current HerpeSelect™ HSV-2 ELISA, Panel 2 contained 80 sera with concordant WB and HerpeSelect™ HSV-2 results, and Panel 3 contained 20 sera from patients at low risk for genital herpes of which 12 reacted positive in the 1st generation HerpeSelect™ HSV-2 kit.

Results: In Panel 1, 29 of 76 sera (38%) proved to be positive by the HSV-2 inhibition assay and 23 of the 29 were positive in the 2nd generation

HerpeSelect™ HSV-2 ELISA with the remaining six sera being equivocal. Thirty-four sera in Panel 1 were confirmed as false-positive based on the inhibition assay results, and 24 of the 34 false-positive sera were negative on the 2nd generation assay with six being equivocal. The 13 remaining samples in Panel 1 were consensus negative or equivocal. For Panel 2, the 2nd generation ELISA gave concurrent results as the WB on 78 (98%) of the 80 sera. In Panel 3, seven (58%) of 12 initially positive sera proved to be false-positive as determined by both the inhibition assay and the 2nd generation HerpeSelect™ HSV-2 ELISA.

Conclusions: Of the 41 sera that were positive by HerpeSelect™ but negative by both WB and inhibition assays, 31 (77%) were negative and six (14%) were equivocal with the 2nd generation HerpeSelect™ HSV-2 assay. Thus, the 2nd generation HerpeSelect™ reduces falsely positive results.

13-HSV: Stigma, shame and genital herpes: results from Italy, France, the United Kingdom and the United States

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Objectives: This research hypothesizes a positive association between levels of social stigma and shame toward genital herpes and transmission-related behaviours because when individuals feel stigmatized and shamed, they are less likely to disclose a positive herpes status to potential partners. We hypothesize that after adjusting for potential confounding variables, stigma and shame will predict disclosure of infection status.

Methodology: A 39-question survey was administered at universities in the United States (in 2003), the United Kingdom (in 2003), Italy (in 2004), and France (in 2004) and resulted in 504 usable surveys. The survey instrument utilizes a scale for measuring stigma and shame identified by Fortenberry *et al*¹ and asks respondents to estimate how likely they are to disclose a positive herpes status to potential partners. It also measures the respondent's level of knowledge about how genital herpes is transmitted and asks about how that knowledge was obtained.

Results: After adjusting for the confounding effects of covariates (age, gender, religion, religiosity, parents' education), respondents' self-reported stigma and shame differed significantly among the four countries. In general, respondents who associate a greater sense of social stigma and shame with herpes were less likely to tell a casual sex partner.

Conclusions: One strategy for reducing the spread of genital herpes is for infected persons to disclose their infection status to potential partners and then to use safer methods of sex. We, therefore, conclude that public health authorities should mount public education campaigns targeted at reducing levels of stigma and shame toward genital herpes.

1. Fortenberry JD, McFarlane M, Bleakley A, Bull S, Fishbein M, Crimley DM, *et al*. Relationships of stigma and shame to gonorrhoea and HIV screening. *Am J Public Health* 2002;92:378-381.

14-HSV: Serological analysis for pathogenesis of female genital herpes simplex virus infection

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Objective: This study was conducted to elucidate the pathogenesis of female genital herpes simplex virus infection using type-specific antibodies to HSV-1 or HSV-2.

Methods: Type-specific antibodies to HSV-1 or HSV-2 using HerpeSelect™ ELISA were measured for sera obtained from 276 female patients with virologically proven genital HSV-1 or HSV-2 infection at their first visit. These patients were classified clinically as first or recurrent episode and analysed for pathogenesis by serological status.

Results: 1) Among 101 patients with HSV-1 first episode infection 72 were primary infection and 29 (23%) were first recurrent. Six patients had anti HSV-2 antibody. Two of 13 recurrent cases had no antibody to HSV.

2) Among 84 patients with HSV-2 first episode infection 38 were primary infection and 45 (54%) were first recurrent. Fifty-eight out of 78 recurrent cases had only anti HSV-2 and 19 both anti HSV-1 and HSV-2.

Conclusions: Among first episode genital herpes patients 23% of HSV-1 infected and 54% of HSV-2 infected patients were first recurrent respectively ($P < 0.01$).

Table 1:

Caused by	Clinical classification	Antibody against				
		HSV-1	–	+	–	+
HSV-1	First episode	101	72	23	3	3
	Recurrent	13	2	11	0	0
	Total	114	74	34	3	3
HSV-2	First episode	84	38	1	37	8
	Recurrent	78	0	1	58	19
	Total	162	38	2	95	27

15-HSV: Herpes simplex virus-2 and -1 seroprevalence in selected population groups in Hungary

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Background: No data are available on type-specific HSV-1 and HSV-2 seropositivity in Hungary.

Objective: To determine HSV-2 and HSV-1 seropositivity in representative samples of women and men in Hungary.

Methods: 1500 available samples (1045 women, 455 men) were included: 249 medical students, 153 abortion patients, 287 antenatal attendees, 46 *in-vitro* fertilization clients, 238 blood donors, and 527 health care personnel. Eligibility criteria included being over 15 years and residents of Southeastern Hungary. Participants were interviewed on demographic and life-style factors, and blood was

collected to determine HSV-2 and HSV-1 IgG antibodies (Focus Diagnostics ELISAs). **Results:** HSV-2 seroprevalence in study groups ranged from 6% (95% confidence intervals, CI: 3.4 – 9.7%) to 22.6% (19–26%), with generally higher positivity in older ages. HSV-1 seropositivity was detected in most population groups, ranging from 49.9% (43–56%) to 82.8% (77–87%).

Conclusion: HSV-2 seroprevalence varied notably between different groups in Hungary, yet appeared to depend upon the study population's mean age. High HSV-1 seroprevalence was consistently found to be over 75% in adults. Data are needed on time trends of HSV-2 and -1 in Hungary.

Table 1:

Dates	Population group	Mean age (range) years	HSV-1 %	HSV-2 %
5–6/2004	College students	21.9 (18–53)	49.9	6.0
2–12/2004	Abortion patients	29.5 (14–46)	76.5	16.3
1–12/2004	Antenatal attendees	29.5 (16–44)	79.1	13.6
3–10/2004	<i>In-vitro</i> fertilization clients	32.3 (22–47)	80.4	17.4
1–12/2004	Blood donors	34.6 (18–69)	82.8	15.1
9–11/2004	Health care personnel	41.2 (18–79)	77.0	22.6

16-HSV: Effects of exogenous sex steroids on CD8+ T cell function in response to neurons latently infected with herpes simplex virus type 1
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Objectives: We have recently demonstrated that hormonal contraceptive use is a risk factor for genital tract shedding of herpes simplex virus type 2 (HSV-2). Since CD8+ T lymphocytes maintain HSV latency via interferon-gamma (INF- γ) production and lytic granule (LG) release, our objective was to evaluate the effects of exogenous sex steroids on these CD8+ T cell functions.

Methods: Corneas of 6–8 week-old female C57BL/6 mice were infected with 105 plaque forming units of HSV-1. At day 14 post-infection trigeminal ganglia (TG) were excised, collagenase treated, and dispersed into single cells. Single cell suspensions of pooled TG cells were cultured with DMEM containing 10% FCS and ethyl alcohol (control), norethindrone (NE), ethinyl estradiol (EE), or NE and EE (all at 10^{-4} M) for either 48 hours or for 6 hours in the presence of HSV-1 antigen-pulsed targets (to optimize stimulation). INF- γ production and LG

exocytosis were measured by flow cytometric analysis.

Results: Exposure to both EE and NE/EE significantly reduced INF- γ production by CD8+ T cells responding to latently infected neurons (Figure 1), and exposure to NE, EE, and NE/EE reduced both INF- γ production and LG exocytosis in CD8+ T cells responding to antigen-pulsed targets (Figure 2).

Conclusions: Exposure of CD8+ T cells to exogenous sex steroids commonly found in hormonal contraceptives (EE or NE) results in an inhibition of the mechanisms used by these cells to maintain HSV latency. Further work is necessary to determine if the inhibition of T cell function is associated with increased HSV reactivation from latency in *ex vivo* TG murine cell cultures or if this compromise of T cell function contributes to an increased frequency of HSV shedding among women using hormonal contraception.

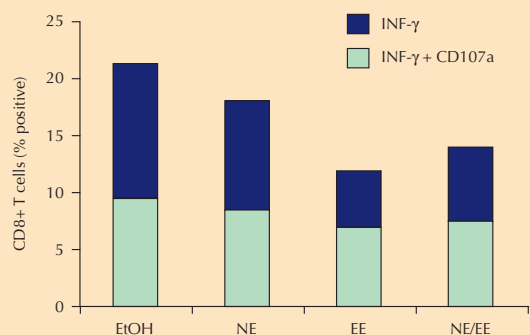


Figure 1:
Effects of Exogenous Sex Steroids on CD8+ T Cell Function
(48 Hour Exposure)

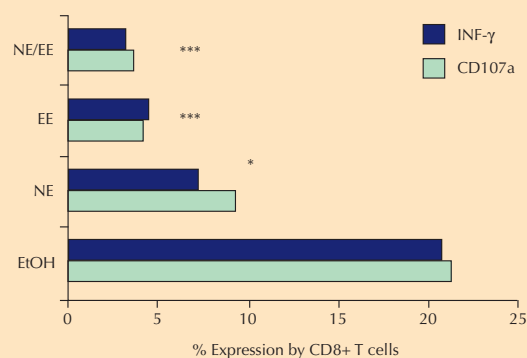


Figure 2:
Effects of Exogenous Sex Steroids on CD8+ T Cell Function
(6 Hour Exposure + HSV-1 Antigen-Pulsed Targets)

17-HSV: Evaluation of patients' preferences in genital herpes treatment

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Objectives: Genital herpes (GH) is a widespread, psychologically and physically disabling disease. It is characterized by episodic outbreaks of genital and perigenital vesicles and ulcers. The seroprevalence of herpes simplex virus (HSV) type 2 ranges from 4% to 40% in Europe, similar to the US. GH is often not adequately treated, with consequences on the patients' well being. GH patients play an important role in the decision-making for their management strategies, and their preferences can be crucial to maximise treatment outcomes. This study evaluated patients' preferences in GH treatment.

Methods: Preferences were elicited from 157 patients, recruited from the Harris Poll panel, who completed an online Discrete Choice Experiment (DCE) questionnaire. DCE data were analysed using multinomial logit regression models to estimate respondents' preferences for GH medical treatment.

Results: Respondents, from the US (87.9%) and UK (12.1%), had a median age of 43 years (21–65); 83.4% were women. Overall, respondents preferred medical treatment to no treatment of GH, with suppressive treatment preferred to episodic, all other things being equal. Generally respondents' preferences indicated that patients preferred the treatment they currently receive. Overall, more patients would choose to be treated with episodic or suppressive therapy (74.3%) than those actually treated (56.2%).

Conclusion: Patients prefer suppressive treatment of GH. Such preferences are influenced by experience, knowledge and awareness of available options. The estimated model suggests that more patients would consider receiving drug therapy than the number who are actually treated.

18-HSV: Herpes simplex virus testing in Quebec province: two surveys of microbiologists and microbiology laboratories

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Objectives: Decreasing the burden of herpes simplex virus type 2 (HSV -2) is an objective of Quebec's national public health program. Genital herpes is not only a common STI but also a major public health problem. Availability and efficient laboratory testing are necessary for diagnosis, counselling and epidemiologic surveillance. Our objectives were: conduct an inventory of virologic tests and survey microbiologists' opinions about HSV testing.

Methods: Two trans-sectional surveys of microbiologist-immunologists of Quebec

province were done in 2004: one by the provincial laboratory on inventory of testing and one by the genital herpes working group of the Quebec National Public Health Institute on opinion of microbiologists about HSV testing. The inventory survey was returned by 113/114 laboratories and 49 microbiologists filled the opinion survey. Subsequently, a descriptive analysis was done.

Results:	
Viral culture with typing	
Labs which offer	Labs which do not offer
<ul style="list-style-type: none"> • 17% of laboratories do viral culture with typing (19/113) • 5% anticipate to offer by 1 year 	<ul style="list-style-type: none"> • 72.7% said little demand • 90.9% said it is too expensive • 10% considered clinical diagnosis sufficient
100% believe that there is no validity issue for viral isolation	
Immunofluorescent testing	
14% (16/113)	
IN TOTAL	
21/113 laboratories offer at one or both viral identification tests by a direct method.	
Type specific serology	
Labs which offer*	Labs which do not offer
2/113	<ul style="list-style-type: none"> • 90% of respondents say that there is little demand • 70% think that is too expensive • 30% believe that the test validity is not good enough.
*mid-June 2005, there are now six labs offering type specific serology	
CDC 2002 STD guidelines	
90% agreed that clinical diagnosis should be confirmed by a lab test	
84% agreed that these tests should be available at clinics where patients are seen.	

Conclusions: Evaluating the availability of viral testing and opinion allow defining the problem, planning strategies, and making concrete propositions to public health policy-makers and clinicians. Conjoint workshops between the STI division and the laboratory division, the Public Health Institute and the microbiologist association are being designed for better exchange between public

health authorities and the microbiologists and infectious disease specialists. Increased availability of type specific serology and viral identification techniques is of utmost importance in tackling the objective of reducing the burden of genital herpes for the Quebec population.

19-HSV: PRIISME: a Quebec province conjoint public health and private sector initiative about reducing the burden of genital herpes

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Objectives: Reduce the incidence and impact of genital herpes according to the objective of Quebec's national public health program 2000–2012.

Methodology: The Quebec National Public Health Institute has the mandate to implement Quebec's national public health program. A working group was created to advise the Institute on how best to reduce the incidence and impact of genital herpes. This group is chaired by a public health officer and a microbiologist and includes representatives of various groups and geographic areas. All of the appointed members have experience in genital herpes research and/or clinic.

Results: The working group objectives were centred

On surveillance

- Evaluate the prevalence and incidence of HSV infection in the general and high risk populations.

On care and services

- Circumscribe optimal diagnostic norms
- Circumscribe optimal therapeutic norms
- Define pre- and post-test counselling for serology testing

- Define adequate counselling for persons recently diagnosed
- Do an inventory of national laboratory resources
- Develop support material for health care professionals
- Prepare continuing health information
- Circumscribe unmet needs of the Quebec healthcare network

On prevention

- Circumscribe individual optimal preventative strategies
- Develop preventative messages to the general population, youths and high risk populations
- Propose transmission preventative measures to recently diagnosed persons
- Do an inventory of national prevention tools
- Develop support material for infected persons and their partners

On research

- Circumscribe specific national research needs
- Define populations for type specific serology screening pilot project

Conclusion: This project's objectives are being worked upon and will lead to a national formation program about reducing the burden of genital herpes.

Members of the working group			
Names	Actual position	Institution	Field(s) of expertise
Michel Alary	Physician, epidemiologist	INSPQ	Epidemiology of STI/HIV
Guy Boivin, co-president	Physician, microbiologist-infectious disease	CHUL	Herpes research (laboratory and clinic)
Louise Charest	General practitioner	Clinique L'Actuel	STI/HIV (clinic and public health)
Marc Dionne, ex-officio	Physician, community health	INSPQ	Director of the biological risk unit, vaccine research
Bernard Duval	Physician, community health	INSPQ	Vaccine research and director of the scientific group on vaccine
Robert Sabbah	Gynaecology-obstetrician	Hôpital Sacré-Coeur	Gynaecology-obstetrician and formation
Deana Funaro	Dermatologist	Centre hospitalier de l'Université de Montréal	Vulvar disease
Françoise Gendron	General practitioner	CLSC Sherbrooke	STI prevention in youth
Annie-Claude Labbé	Physician, microbiologist-infectious disease	Hôpital Maisonneuve-Rosemont	STI/HIV (clinic, laboratory and public health)
Michel Lassonde	Dermatologist	Private practice	Herpes vaccine and therapy research
Claude Laberge	General practitioner	Service de lutte aux ITSS, ministry of health	STI/HIV (public health)
Nicole Marois	Medical formation specialist	INSPQ	Head of formation, biological risk division
Stéphane Roy	General practitioner	INSPQ	STI/HIV (clinic and public health)
Katia Sénécal	Sexologist	Centre de ressources et interventions en santé et sexualité	Herpes counselling
Marc Steben, (President)	Family physician	INSPQ	Viral STI (clinic, research and public health)

HSV-20: Validation study comparing herpes simplex virus (HSV)-2 antibody detection using the Focus Diagnostics ELISA, Kalon ELISA, Western blot and inhibition test

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Background: In certain parts of Africa, type-specific HSV type-2 ELISAs may have limited specificity. To date, no validation study has been conducted using both the Western blot (Wb) reference standard and inhibition testing.

Objective: To validate Focus Diagnostics (FD) and Kalon type-specific HSV-2 ELISAs versus the Wb and versus the inhibition test among young men in Kisumu, Kenya.

Methods: A total of 120 HIV-seronegative men (aged 18–24 years) provided blood samples. HSV-2 IgG serum antibodies were detected using four different methods: (i) FD HSV-2 ELISA (n=120), (ii) Kalon HSV-2 ELISA (n=120), (iii) University of Washington Wb (n=101), and (iv) FD in-house inhibition test (n=93). Equivocal results were excluded from data analyses.

Results: HSV-2 seroprevalence differed significantly by HSV-2 detection method, ranging from 24.8% with the Wb to 69.7% with the FD ELISA assay. Using the WB as the reference standard, the FD ELISA had the highest sensitivity for HSV-2

antibody detection (100%), yet lowest specificity (40.8%). Similar results were obtained using the FD inhibition test as the reference standard. The sensitivity and specificity of the Kalon test were, respectively, 92% and 79% vs the Wb; and 76% and 82% vs the inhibition test. Using the inhibition test as the reference standard, the sensitivity of the Wb appeared low (49%). Further validation results will be presented testing the same sera panel with a second generation FD HSV-2 ELISA.

Conclusions: In HIV-seronegative men in western Kenya, the FD and Kalon type-specific ELISAs had high sensitivities yet limited specificities using the Wb as reference standard. Further understanding is needed for the interpretation of HSV-2 inhibition or ELISA test positive/WB seronegative results. Before HSV-2 seropositivity may be reliably reported in Africa, validation studies of HSV-2 serological assays in individual geographical areas are recommended.

Table 1:

	N tested	HSV-2 (%)	Western blot as reference standard (101 sera)		Inhibition test as reference standard (93 sera)	
			Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Focus/MRL	120	83 (69.7)	25/25 (100)	31/76 (40.8)	42/42 (100)	28/51 (54.9)
Kalon	120	46 (38.3)	23/25 (92)	60/76 (79.0)	32/42 (76.2)	42/51 (82.4)
WB	101	25 (24.8)			17/35 (48.6)	(39/41)(95.1)
Inhibition	93	42 (45.2)	17/19 (89.5)	39/57 (68.4)		

HSV-21: Rapid diagnosis of acute herpetic gingivostomatitis by using HSV type-specific LAMP method

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This study evaluated the reliability of herpes simplex virus (HSV) type-specific loop mediated isothermal amplification (LAMP) for rapid diagnosis of acute herpetic gingivostomatitis. The results of HSV type-specific LAMP were compared with those of real-time PCR. LAMP was carried out by using TERAMECS 200, which measures turbidity of samples. Reaction time was only 60 min. Swab samples (placed into 1 ml of sterilized water) obtained from the oral cavity were collected from 46 children with gingivostomatitis. DNA was extracted from 200 µl samples. HSV-2 DNA was not detected in any of the samples by either real-time PCR or the HSV type-specific LAMP method. Twenty-seven of 46 (58.7%) samples were positive for HSV-1 by real-time PCR (ranged between 32 and 8717903 copies/tube). Meanwhile, twenty-six of 46 (56.5%) samples were positive for HSV-1 by the HSV type-specific LAMP method. If real-time PCR was

used as the standard method, sensitivity, specificity, positive predictive value, and negative predictive value of the LAMP method were 88.9%, 89.5%, 92.3% and 85%, respectively. Additionally, we examined direct detection of viral DNA (amplified HSV DNA from the swab samples without DNA extraction) by HSV type-specific LAMP to obtain the results as soon as possible. Twenty-five of 46 (54.3%) samples were positive for HSV-1 by the direct detection method. Again, if real-time PCR was used as the standard method, sensitivity, specificity, positive predictive value, and negative predictive value of the direct detection method were 81.5%, 84.2%, 88% and 76%, respectively. Thus, HSV type-specific LAMP is likely to be a useful tool for rapid diagnosis of acute herpetic gingivostomatitis, which might lead to appropriate antiviral treatment.

HSV-22: Anti herpes virus 1/2 specific secretory IgA detected by Western-blot analysis in total ejaculates (HSV-1and/or HSV-2 PCR positive) of patients unaware of viral shedding

Mazzoli S, Rupealta V. *STDs Center, Ospedale S. Maria Annunziata, ASL 10, Firenze, Italy.*

Genital herpes (type 1 and type 2) infections result from contact with infected secretions at genital and oral mucosal sites. Mucosal anti-herpes 1/2 specific immunity plays a fundamental role in neutralizing or modulating the infections. Secretory IgA presence has been related to specific antiherpes virus immunization in women with untreated or recurrent infections or vaccine inoculation, both in women and animals, in the lower female genital tract. No investigations have been reported in the deep genital tract of males.

The objective of our study was to assess the presence of HSV 1/2 secretory IgA in total ejaculates of 21 males without symptoms of past or present HSV 1/2 infections, and who are unaware of HSV 1 and/or HSV 2 shedding, proved by a positive PCR test and selected from a wider 333-subject population.

All samples tested positive by two different PCR tests (AlphaWatch HSV 1/2,

Alphagenics-Diaco-Biotechnology and HSV 1/2 Genotype TechPlate, Diatech). Western blot (WB) analysis for sIgA was performed by a modification of the Herpesselect™ 1 and 2 Immunoblot IgG (Focus Diagnostics, USA); the test uses purified recombinant type-specific gG1 and gG2 antigens and native common antigens immobilized on nitrocellulose membranes.

Results: of the 21 herpes PCR+ ejaculates 85.7% tested positive for common antigens IgA confirming the infection; 71.4% for gG1, versus 95% by PCR, and 66.6% for gG2 IgA, versus 23.8% by PCR. HSV 2 specific IgA detected an additional 10 patients (ejaculates) testing negative for HSV 2 DNA. Secretory-specific IgA WB can be a test for detecting infection exposure, inapparent/asymptomatic infections, active infections, reactivations and viral shedding.

HSV-23: HSV-1 and HSV-2 shedding (PCR positive) in total ejaculates from patients with chronic prostatitis/CP/PS

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Chronic prostatitis represents one of the emerging infection problems in young males in Italy: mean age 37–40 years. STD microorganisms have been involved in the aetiology and pathogenesis.

HSV has been associated with leucocytospermia and is found in semen and spermatozoa of infertile males or is isolated in semen in the absence of discernible lesions.

The objective of our study was to evaluate the presence of HSV 1/2 DNA by PCR (HSV 1/2 Genotype TechPlate, Diatech) and the rate of asymptomatic shedding in total ejaculates from a population of 197 men affected by chronic prostatitis (April–May 2004). *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, HPV and the urogenital mycoplasmas were also investigated by PCR or culture.

Results: 39 out of the 197 screened patients were HSV 1 and/or HSV 2 PCR

positive (19.7%) in their ejaculates: 35 (17.7%) tested HSV 1 and nine (4.5%) tested HSV 2 positive: coinfection occurred in 5/197 (2.5%). Mainly associated STDs were HPV 23%, *Chlamydia t.* 23%, *Neisseria g.* 23%, *Ureaplasma u.* 5.7%.

All the patients (100%) were unaware of HSV genital or oral infection.

Our study shows HSV infection, replication and release/shedding in the upper genital tract organs of these males affected by prostatitis and demonstrates the potential role of ejaculates in infecting the sexual partner. The high association rate with other STDs proves the same risk factors. Finally, the concomitant presence of viral and bacterial inflammation and cancerogenic agents focuses on the importance to define better the role of these associations in prostatitis and prostate cancer.

HSV-24: Genital herpes in Turkish patients: HSV-1 or HSV-2?

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Introduction: The purpose of the present multicentric study was to review the relative proportion of HSV 1 and HSV 2 as the cause of genital herpes infections in Turkish patients and to determine the correlation between serology and the type of HSV in the lesion.

Materials and methods: We applied PCR for the detection of HSV 1, HSV 2 in active typical skin lesions and ELISA for detection of type specific antibodies in blood samples.

Results: Seventy cases of genital herpes infection were reviewed. Forty-two cases

were male (60%) and 28 were female (40%). HSV 1 accounted for 10 (16.7%) and HSV 2 accounted for 50 (83.3%) in skin lesion of 60 confirmed genital herpes patients. Infection rate was higher in women than in men for HSV 1 (30% versus 8%, $P=0.03$) In the first episode HSV 1 infection is higher than the recurrent infection and it is statistically significant for HSV 1 ($P=0.01$)

Conclusion: Our preliminary results show that HSV 2 is the major causal factor of genital herpes in Turkish patients. However, HSV 1 accounts for a high proportion of the females and first episode cases.

Table 1: Demographical data of the cases

	Female	Male	Total
Age	33.2 ± 11.8	38.6 ± 13.9	37.1 ± 12.7
Marital status (married)	54% (15/28)	64% (27/42)	61% (43/70)
Sexual partner>1	21% (6/28)	74% (31/42)	53% (37/70)
Education (university)	32% (9/28)	43% (18/42)	39% (27/70)
Episodes/year	6.8	8.3	7.5
First episode	35.7% (10/28)	1% (8/42)	25.7% (18/70)
Application date	4.0	3.3	3.6

Case Study 1: Sacral zoster with secondary dissemination and urinary retention in an immunocompromised patient

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A 52-year old patient with low-grade non-Hodgkin's lymphoma known since 2000 had received conventional chemotherapy until 2002. Upon lymphoma progression, he underwent five episodes of fludarabine/rituximab/cyclophosphamide chemotherapy from September 2004 to January 2005 that resulted in complete remission. Two months before admission, total lymphs were 456 cells/mm³, CD4+ 115 and CD8+ 228. Ten days before admission, a crop of painful vesicles appeared on the right buttock, in a S4 crescent distribution. A few days later, disseminated vesicles started to appear on the whole body. Oral valaciclovir was initiated but vesicles continued to appear which led to the admission of the patient 3 days later. Physical and neurological examinations

were unremarkable except for cutaneous findings. Blood cell count and chemistry were unremarkable. Aciclovir (2x10 mg/kg/d) was administered. Within 3 days, no new lesions were noticed, but the S4 right dermatome presented as a shallow confluent ulceration with a fibrinous exudate in the intergluteal area. Five days after admission, the patient presented a urinary retention that required urethral catheterization. Absent right achillean and patellar reflexes, and paraesthesias on the right thigh and buttock were observed. Retrospectively, he mentioned that he had had difficulties with micturition since the appearance of the vesicles. Urinary retention is a well described complication of sacral zoster. Published case reports suggest that in a majority of cases, bladder function recovers within a few weeks.