

10th Alp-Danube-Adria Congress on STD and Skin Infections ADA 2004



Vienna
November 26 – 28 (first weekend in advent)
2004

FINAL PROGRAM

Welcome to Vienna

On behalf of the Study Group for STD and Dermatological Microbiology of the Austrian Society for Dermatology and Venereology and of the LBI for the Study of Venero-dermatological Infectious Diseases we cordially invite you to attend and actively participate in the

10th Congress of the Alp-Danube-Adria-Society for STD and Skin Infections.

Organized by

The Study group for Sexually Transmitted Diseases and Dermatological Microbiology (Chair: Angelika Stary) of the Austrian Society for Dermatology and Venereology and the Ludwig-Boltzmann-Institute for the Study of Venero-dermatological Infectious Diseases (Chair: Josef Söltz-Szöts, Erwin Tschachler)

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Aleksej Kansky

It is our great honour to organize this year's congress in Vienna and to celebrate the 10th anniversary of the Alp-Danube-Adria meetings.

In the course of this congress special lectures and symposia will cover the most important topics of sexually transmitted infections (STI). Prevention and control of venereal diseases have gained importance again since the number of bacterial infections has increased and may be influenced by the change of the political situation in the region. Exchange of experience in the field of viral STIs and HIV, which are still a major problem for treatment, is necessary. New data on preventive strategies, diagnostic procedure, and treatment options will be presented including the special field of tropical medicine.

The historic ambience of the Schönbrunn Castle which is located in walking distance of the congress venue and the special atmosphere during Christmas time with the most admired Christmas Market in front of the castle will make your stay a memorable one.

We look forward to welcoming you in Vienna for the anniversary meeting.

On behalf of the Local Organizing Committee

Angelika Stary / Chair of the congress

Josef Söltz-Szöts / Chair of the LBI

Scientific Program

Friday, November 26, 2004

- 16.00 – 17.00 Board Meeting of the Alp-Danube-Adria Society for STDs and Skin Infections
- 18.00 **Welcoming addresses**
A. Stary
H. J. Rauch
J. Söltz-Szöts
J. Lipozencic
A. Kansky
- 18.30 **Keynote lecture:**
Chair: J. Lipozencic, A. Stary
- 1 G. Stingl, Vienna:
Immunostimulation via the skin – a new approach for the treatment of inflammatory and neoplastic skin diseases
- 19.00 *Welcome reception at the Parkhotel Schönbrunn*

Saturday, November 27, 2004

- 8.30 – 9.00 **Case reports**
Chair: C. Heller-Vitouch, V. Varkonyi
- 2 V. Várkonyi, T. Somogyi, G. Veres, A. Horváth, Budapest:
Diagnostic problems with syphilis: recent cases
- 3 T. Gregurek-Novak, Zagreb:
Do we always think of syphilis?
- 4 E. Messeritsch, A. Geusau, Vienna:
Ocular manifestation in secondary syphilis
- 5 K. Chudomirova, V. Dosheva, S. Popov, V. Garov, Plovdiv:
Neurosyphilis – a case report
- 6 L. Richter, I. Heinrich, K. Rappersberger, Vienna:
Bowen's disease of the vulva – successful treatment with Imiquimod
- 7 C. M. Rudolph, R. R. Müllegger, H. Kerl, G. Ginter-Hanselmayer, Graz:
Systemic antifungal treatment of disseminated tinea corporis in late pregnancy. Report of two cases
- 9.00 – 10.45 Session I
Epidemiology of STIs in an expanding Europe
Chair: A. Horvath, S. Mayerhofer
- 8 **Plenary lecture**
K. Fenton, London:
Epidemiology of STIs in an expanding Europe

Scientific Program

Saturday, November 27, 2004

- 9 A. Horvath, Budapest:
Sociological relation of syphilis epidemic in Hungary
- 10 S. Mayerhofer, E. Vinzelj, M. Emri-Gasperlmair, Vienna:
Classical venereal diseases at the Viennese public health department
- 11 I. Kuklova, V. Kastankova, R. Pankova, H. Zakoucka, M. Drazdakova, R. Tryzna, J. Jedlicka, H. Malinova, R. Mak, Prague:
Outreach programme for female sex workers in Prague – the first results
- 12 I. Klavs, L. C. Rodrigues, K. Wellings, D. Keše, R. Hayes, Ljubljana/London:
Prevalence of genital *Chlamydia trachomatis* infection in the general population of Slovenia
- 13 B. Götz, E. Schuh, B. Sary, G. Gittler, A. Sary, Vienna:
Chlamydia screening in university students in Vienna
- 14 M. Potocnik, A. Godic, I. Bartenjev, Ljubljana:
STIs in Slovenia, what happened in the last decade?
- 10.45 – 11.15 *Coffee Break*
- 11.15 – 12.20 Session II
Viral STIs
Chair: A. Kansky, G. Stingl
- Plenary lecture:**
- 15 J. Paavonen, Helsinki:
HPV Vaccination: The beginning of the end of cervical cancer
- 16 B. Hönlinger, N. Romani, C.-P. Czerny, H. Huemer, R. Höpfl, Innsbruck/Göttingen:
Re-emerging animal orthopoxvirus infections in the light of potential bioterrorism
- 17 S. Ljubojevic, N. Ljubojevic, J. Lipozencic, M. Skerlev, L. Zele-Starcevic, Zagreb:
Peniscopy in diagnostic procedure of subclinical *human papilloma virus* infection
- 18 J. Pec, I. Chromej, J. Kliment, S. Urbancek, Martin:
Squamous cell carcinoma of the penis and STD. Situation in the central region of the Slovak Republic

Scientific Program

Saturday, November 27, 2004

- 12.30 – 13.45 Lunch Symposium (sponsored by Digene)
HPV-Diagnosis
Chair: M. Skerlev, J. Söltz-Szöts
- 19 H. Ikenberg, Bad Münders:
HPV testing as a routine method in the prevention of cervical cancer
- 20 J. Tarra, K. Straka, A. Stary, Vienna:
HPV genotyping in STI patients
- 21 C. Heller-Vitouch, J. Söltz-Szöts, Vienna:
Interpretation and consequences of HPV diagnosis
- 22 M. Skerlev, Zagreb:
Problem warts and problem patients in the male HPV-world
- 14.00 – 15.30 Session III
HIV
Chair: K. Nagy, E. Tschachler
- Plenary Lecture:**
- 23 M. Youle, London:
Update on AIDS and HIV
- 24 A. Rieger, Vienna:
The acute retroviral syndrome
- 25 E. Tschachler, Vienna:
New insights into Kaposi's sarcoma pathogenesis
- 26 K. Nagy, Budapest:
Characteristics of HIV/AIDS epidemic in Hungary
- 15.30 – 16.00 *Coffee Break*
- 16.00 – 17.00 Session IV
Tropical Infections of the Skin
Chair: G. Klein, J. Lipozencic
- Plenary Lecture:**
- 27 B. Naafs, Munnekeburen:
Skin infections in the tropics
- 28 R. Moser, Eisenstadt:
Cutaneous leishmaniasis
- 29 G. Klein, Linz:
Regional dermatological training centre in Tanzania: experiences and challenge
- 20.00 *Social Dinner at the "Lusthaus"*
(departure of buses from the Parkhotel Schönbrunn at 19.15)

Scientific Program

Sunday, November 28, 2004

8.30 – 10.30

Session V

Bacterial STIs – Diagnosis and Treatment

Chair: M. Potocnik, A. Stary

- 30 K. Nagy, B. Kemeby, V. Varkonyi, A. Horvath, Budapest:
Molecular screening of syphilis by PCR
- 31 G. Veres, V. Várkonyi, S. Illniczky, I. Horváth, K. Nagy, A. Horváth,
Budapest:
Early neurosyphilis. Symptoms and management
- 32 S. Wöhr, A. Geusau, Vienna:
Neurosyphilis is unlikely in patients with late latent syphilis and a
negative blood VDRL

Plenary Lecture

- 33 A. Pöder, Tartu:
Impact of IUSTI on STI surveillance in Estonia
- 34 P. Komericki, M. Akkilić, M. Haller, L. Teodorowicz, W. Aberer, A. Stary,
Graz/Vienna:
Increasing failure of gonococcal culture on a selective medium
- 35 A. Zore, M. Petrovec, D. Keše, E. Ružič-Sabljić, M. Potočnik, M. Gubina,
Ljubljana:
Ciprofloxacin resistant strains of *Neisseria gonorrhoeae* in Slovenia
from 2001 to 2004
- 36 M. Haller, A. Bilina, P. Fuhrmann, C. Heller-Vitouch, A. Kuchinka-Koch,
L. Teodorowicz, A. Stary, Vienna:
Neisseria gonorrhoeae: resistance profile from 1999 to 2003

A. Stary, Vienna:

Presentation of the Austrian Guidelines for the Treatment of STIs 2004

10.30 – 11.00

Coffee Break

11.00 – 12.00

Session VI

Treatment issues of Fungal Infections

Chair: G. Ginter-Hanselmayer, G. Trevisan

- 37 W. Weger, G. Ginter-Hanselmayer, S. Pitzl, A. Paulitsch, P. Komericki,
M. Akkilić, W. Buzina, Graz:
Vaginal yeast isolates – do we need species identification?
- 38 A. Uthman, M. Dockal, J. Söltz-Szöts, E. Tschachler, Vienna:
Fluconazole upregulates *sconC* expression and inhibits sulphur
metabolism in *Microsporium canis*
- 39 F. Kokelj, G. Trevisan, Trieste:
Side effects and drug interactions of modern oral antimycotic drugs

12.00 – 12.15

Closing Remarks

General Information

Congress Venue

Parkhotel Schönbrunn, Hietzinger Hauptstrasse 10-20, A-1130 Vienna

Official Language

English

CME Credits

Information for Austrian participants: The Austrian Medical Association has certified the "ADA Meeting 2004" for the CME Program with 19 hours credits.

Congress Fees

Regular fee:	€ 150.-
Reduced fee for residents:	€ 80.-
Accompanying persons:	€ 50.-

Day tickets

Saturday, November 27, 2004:	€ 90.-
Sunday, November 28, 2004:	€ 60.-

Payment

Please see attached registration forms.

Registration forms can also be downloaded from the ADA 2004 website:

<http://www.medacad.org/ada2004/>

Opening hours of the registration desk at the Parkhotel Schönbrunn

Friday, November 26, 2004:	15.00 – 19.00
Saturday, November 27, 2004:	8.00 – 17.00
Sunday, November 28, 2004:	8.00 – 12.15

Social events

Welcome reception at the Parkhotel Schönbrunn: Friday, November 26, 2004, 19.00

Social Dinner at the "Lusthaus" (Wiener Prater): Saturday, November 27, 2004, 20.00
(included in the registration fee)

Departure of buses from the Parkhotel: 19.15

General Information

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Technical Exhibition

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Abstracts

00

JUDA AND TAMAR

A recently observed portrait in Slovenia

Aleksej Kansky, Dept Dermatology, Zaloška 2, 1525 Ljubljana, Slovenija.

The legend on Juda and Tamar as referred in the Bible (1) seems to be the oldest notice on the problem of prostitution. Our interest for this interesting topic was aroused by the excellent article of the late W. Kopp and S. Mayerhofer (2). By chance a large portrait labeled as Juda and Tamar was observed in a small Slovenian gallery. As there was no detailed information on the portrait at the moment, an inquiry was started to find more information on the author and the history of the portrait.

References

(1) Bible. Moses 1; Genesis 38: 14-23 .

(2) Kopp W., Mayerhofer S.. Commercial sex- past and present. Acta Dermatoven APA 2003;12 (2): 47-52.

DIAGNOSTIC PROBLEMS WITH SYPHILIS: RECENT CASES

Várkonyi V, Somogyi T, Veres G, Horváth A, Budapest

The authors present two cases of recent syphilis. In the first case, circumcision was performed on the patient in order to cure his primary chancre and phimosis at an urology department. Upon relying on the positive serology, bilateral lymphadenopathy and classic history this operation could have been avoided. The sexual partner of the previous patient was also seen with clinical manifestations of secondary syphilis. Her symptoms included erosive syphilitic condylomas at each corner of her mouth, at the genitoanal region and interdigitally on the right foot. The authors wish to remind all practicing physicians that syphilis needs to be considered and excluded when the classic signs of the disease are seen in both typical and unusual localizations.

DO WE ALWAYS THINK OF SYPHILIS?

Teodora Gregurek-Novak

Department of Dermatoveneorology, Clinical Hospital «Sestre milosrdnice», Zagreb, Croatia

In January in year 1999 – a woman patient born 1955 – was send to me for examination from our Clinic for Neurology. She was in wheelchair. From her patients history she told us that one year before weekness in lower limbs appeared. She was unsure in going. Slowly changes became stronger and about 3 months before coming to us, she was unable to go alone. First signs of hand weekness also appeared. Before coming to Clinic for Neurology she was examined twice in local Neurological Department in her native town and on one Clinic for Neurology in capital town-Zagreb and diagnosis was: multiple sclerosis. Serological reactions in blood were for the first time make in Clinic for Neurology in our hospital and they were all positive. I recomended examination of spinal fluid – serological one, and it was also positive. Patient then remembered that six years ago she had some sort of allergic reaction which quickly dissapeared under antihistamines. We called her husband who just admitted us that about 6 years before he was treated privately because of siphylitic infection, but he never told it to his wife and during therapy they had sexual contact. Both are parents of two children.

We immedately started a specific therapy with Extencillin injections during lo weeks – once weekly 2,400.000 units and because of slow response we repeated the same therapy 4 times - at first two therapies together with corticosteroid protection because of possibility of Jarisch-Herxheimer reaction. After this 4 cures our female patients received still for one months Erythromicin capsules – 2 grams daily. Husband was not necessary to heal because his serological examinations showed only signs of old infection (only TPHA positive in low value). Our patient already after first treatment was walking. She stayes under control and now is quite free of all symptoms and serological reactions in blood and spinal fluid are steady (only TPHA low positive). Children were not infected. She call me some-times and is living normally with his family.

OCULAR MANIFESTION IN SECONDARY SYPHILIS

Eva Messeritsch, Alexandra Geusau

Department of Dermatology, Division of Immunodermatology, Allergy and Infectious Diseases (DIAID), Medical University of Vienna, Austria

We present a 29-year-old HIV-positive male patient who recently had acquired human immunodeficiency virus (HIV) infection. For the last 6 months, he had experienced patchy hair loss and a history of a self healing single skin lesion in the anogenital area. In addition, he had been under treatment of the ophthalmologists because of acute loss of sight on the left side. Ischemic papillitis was diagnosed and treatment with high dose systemic corticosteroids, 100mg prednisolon o.d. and acetyl salicylic acid was initiated. He improved and was admitted to our HIV-ward.

However, within the following week, his left-eyed visus deteriorated and he developed similar symptoms on the other side. On ophthalmologic examination there was swelling of the left papilla and central scotoma. The small vessels, arteries and veins, appeared normal; in particular, an occlusion could be excluded. T1-weighted magnetic resonance tomography (MRT) imaging of the brain revealed a left sided inflammatory swelling of the opticus nerve. A cerebral tumour or an inflammatory condition, e.g. multiple sclerosis could be excluded.

Other differential diagnoses of this inflammatory condition comprised infection or reactivation of neurotropic viruses such as varicella zoster and herpes simplex viruses, particular in HIV-positives. In addition, an infection with *Borrelia burgdorferi*, cytomegalovirus and *Cryptococcus neoformans* had to be excluded. On examination of cerebrospinal fluid (CSF), these conditions could be excluded as those viruses could neither be isolated nor detected by molecular biology. Finally, because of a positive syphilis blood serology and compatible CSF test results, the diagnosis **neuritis nervi optici in the course of early infectious syphilis**, could be established. The patient tested highly positive in the venereal disease laboratory (VDRL) test, a non-treponemal antibody test which correlates with disease activity (initial VDRL titer 1:512), and he showed reactivity in treponemal specific IgG and IgM antibody tests (*T.pallidum* particle agglutination (TPHA) and fluorescent treponemal antibody absorbed (FTA-Abs) tests, IgM solid phase haemadsorption assay (IgM-SPHA) 1:128, IgM-Elisa). The patient was also positive in the CSF-VDRL test (titer 1:2), and he met additional criteria for neurosyphilis such as a positive CSF-TPHA (1:640), pleocytosis, and a TPHA index of 96, which quantifies intrathecal production of *T.pallidum* specific IgG antibodies. In addition, the patient had lymphadenopathy, which might also been associated with his HIV-infection, and a restricted renal function as a possible involvement of inner organs.

According to the treatment guidelines of the Centers for Disease Control (CDC), patients who have syphilis and who demonstrate any neurological or ocular symptoms at any stage of syphilis infection and who meet the requested criteria upon CSF examination should be treated with a neurosyphilis regimen. The patient received aqueous crystalline penicillin G 24 million units per day, administered as 4 million units IV every 4 hours for 14 days, followed by benzathine penicillin G 7,2 million units total, administered as three doses of 2,4 million units IM each at 1-week intervals. Within a few days of treatment, the patient's sight improved dramatically and got normal with the end of the treatment, the same applied for the kidney function, and the VDRL titer dropped.

Neurological disease can occur during any stage of syphilis. Any patient who has clinical evidence of neurological symptoms including motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and symptoms or signs of meningitis should be tested for syphilis and CSF examination should be performed for all such patients to identify those with abnormalities. Syphilitic uveitis or other ocular manifestations may be associated with syphilis; patients with these symptoms should be treated according to the recommendations for patients with neurosyphilis.

NEUROSYPHILIS – A CASE REPORT

K. Chudomirova, V. Dosheva, S. Popov, V. Garov, Plovdiv

A 63-years old male patient with neurosyphilis – tabes dorsalis and general paresis is reported. The complaints began 8 years ago with an episode of vertigo and “loss of consciousness”. Other symptoms were gait disturbance, headache, hearing loss, forgetfulness, mood changes, ulceration on the right leg. The patient did not mention a history of syphilis. The clinical examination revealed papillary changes, anisocoria, positive Argyll-Robertson’s pupil sign, deafness, cerebral ataxia, positive Romberg’s sign, hypesthesia for light touch of the under extremities, loss of deep sensitivity, loss of the patellar and Achilles tendon reflexes, neuropathic arthropathy (radiographic and bone destruction), trophic ulcer on the right heel. The neuroimaging-X-ray computered tomography and the magnetic resonance showed leucoencephalomalacia in the basal ganglia of the brain, cerebrovasculitis, low-grade ventricular dilatation and degenerative changes of the spinal cord. Serological tests for syphilis (VDRL, TPHA, FTA-ABS) were positive in serum and CSF.

Central nervous system invasion by *Treponema pallidum* occurs may be in more than usually diagnosed patients with syphilis. Neurosyphilis is a significant medical problem and should be considered in differential diagnosis. Clinicians must approach this important condition using combination of clinical and laboratory findings and good understanding of the disease.

BOWEN`S DISEASE OF THE VULVA – SUCCESSFUL TREATMENT WITH IMIQUIMOD

Leo Richter, Ingrid Heinrich, Klemens Rappersberger, Vienna

Objectives: Topical anticancer therapy with imiquimod (IQM) and intralesional interferon-a (INF-a), non surgical approaches in the treatment of extensive, multifocal Bowen`s disease of the vulva i.e.: Vulvar Intraepithelial Neoplasia III (VIN-III).

Methods: Diagnosis was established by histopathology. The presence of bizarre keratohyaline granules and intranuclear inclusion bodies within epithelial cells were indicative of HPV-infection. Several HPV-smears revealed negative results of low/high risk papilloma viruses.

Results: Although gynecologists suggested vulve- and clitoridectomy we initiated a combination therapy consisting of topical imiquimod and intralesional interferon-a to first reduce tumor size and thus minimize further surgical procedure. 15 x 10⁶ units INF-a were injected intralesionally, every other day, five times, then the patient refused further injections because of pain. Simultaneously, topical IQM therapy was initiated, and applied three times per week. After seven days of combined treatment the patient started to display signs of severe inflammation and after 10 days the entire tumor became erosive. Despite severe local side effects such as pain, secretion, and bleeding we continued topical treatment, however, only after applying a topical anesthetic-gel (lidocaine), over three consecutive months. At that time several side effects have cleared and the mucous membrane of the vulva clinically appeared normal. Complete clearance of VIN III was proven by histopathology. The patient is now two years off therapy without any relapse. Her partnership is intact and she reportedly has a fulfilling sexual life.

Conclusion: Bowen`s disease of the vulva in most cases represents a multifocal tumor. So far the most common treatment modality was radical surgical excision or CO₂-laser. In the more recent past several non-surgical methods were employed to better preserve functional properties of the vulva: there already exist reports of successful treatment of VIN with photodynamic therapy (PDT) and intralesional bleomycine. Here we show complete regression of VIN III following topical treatment with imiquimod 5%. This type of treatment may represent an attractive alternative therapy and, moreover, assures an excellent preservation of the tissue and thus of functional properties.

SYSTEMIC ANTIFUNGAL TREATMENT OF DISSEMINATED TINEA CORPORIS IN LATE PREGNANCY. REPORT OF TWO CASES

C. M. Rudolph, R. R. Müllegger, H. Kerl, G. Ginter-Hanselmayer, Graz

To discuss the indication and safety of systemic antifungal treatment of tinea corporis in pregnancy.

Patient 1: A 25y-old primigravida presented at 36 weeks gestation with rapidly extending erythematous lesions over her neck, face, and trunk from which *Microsporum canis* was cultured. The widespread manifestation with involvement of both breasts close to delivery and intention to breastfeed suggested systemic treatment. The patient received fluconazole (150mg on each day, 1 and 5) orally and isoconazole nitrate cream topically. 17 days later, when the patient gave birth to a healthy boy, all lesions had cleared completely. Patient 2: A 29y-old primigravida had been treated with topical steroids and UVB-light since early pregnancy for suspected pityriasis rosea. By 33 weeks gestation, the rash had become widespread involving the trunk, arms and legs. The initial scraping at that point was negative, but by 37 weeks gestation, the culture grew *Microsporum canis*. The patient was started on itraconazole (200mg daily for 1 week) orally and econazole nitrate shampoo, and tioconazole cream topically. At term, she gave birth to a healthy son. The lesions were still weakly visible, but further scrapings and culture were negative.

Systemic antifungal treatment in pregnancy is usually restricted to severe generalized mycotic infections. Certain conditions, such as widespread dissemination of skin lesions with involvement of potential contact areas with the baby during intended breast-feeding may require systemic treatment also for tinea corporis. Currently, there are no guidelines for systemic treatment of superficial mycosis in pregnancy. Although terbinafine is categorized in the FDA pregnancy category B, and both, fluconazole and itraconazole in category C, no studies support the use of terbinafine. Data on Fluconazole are controversial. In contrast, a prospective cohort study of pregnant women exposed to oral itraconazole supported the hypothesis that its use is safe.

In conclusion, topical treatment of tinea corporis in pregnancy is usually sufficient. If the extension of skin lesions or the intention to breastfeed require systemic treatment, the drug of choice would be itraconazole. However, the risk-benefit ratio for both, mother and child, must always be carefully considered.

OUTREACH PROGRAMME FOR FEMALE SEX WORKERS IN PRAGUE – THE FIRST RESULTS

*Kuklova, I., Kastankova, V., Pankova, R., Zakoucka, H., Drazdakova, M., Tryzna, R.,
Jedlicka, J., Malinova, H., Mak, R., Prague.*

In December 2003 a pilot Czech-flemish /ESO/ programme to enable free vaccination against hepatitis B virus for female sex workers started in Prague.

The study took place at the Department of Dermatovenerology of the 1st Faculty of Medicine, the Bliss without Risk NGO and its mobile ambulance.

Leaflets were designed describing the risks of sex work and giving the addresses of vaccination sites. The vaccination scheme was 0, 1, 6 months.

Over 4 months /from January till April 2004/, 145 female sex workers were vaccinated. Out of them 78,6% were of Czech nationality, 9% Slovak, 6% Ukrainian, 2,7% Bulgarian, 1,3 % Belarusian. The average time of their practice as sex workers was 2 years.

Their drug experience was the following: 9% marihuana, 6,8% pervitin-sniffs, 2% pervitin i.v., 2,7% ecstasy, 1,3% cocain, 0,6% heroin, 0,6% LSD.

Gonorrhoea was diagnosed in two cases, chlamydial infection in three cases, naturally acquired HBV was found in 8 cases, one person was positive for HBsAg, HCV was found in 7 cases. Six sex workers had syphilis in their history.

The aim of the project is to establish contacts with the sex worker community in order to develop and maintain prevention activities such as HIV and STI-screening and hepatitis B vaccination aiming at lowering the risks of sex work.

Grant support

The development of health, social and educational services for the sex workers in the Czech Republic according to a Flemish model (TSJ/ 004/ 03)

IGA MZ 8091-3: Serologic methods in syphilis diagnostics.

PREVALENCE OF GENITAL *CHLAMYDIA TRACHOMATIS* INFECTION IN THE GENERAL POPULATION OF SLOVENIA

Klavs I(1), Rodrigues LC(2), Wellings K(2), Keše D(3), Hayes R(2). (1)Institute of Public Health of the Republic of Slovenia, Ljubljana, Slovenia; (2)London School of Hygiene and Tropical Medicine, London, UK; (3)Institute of Microbiology and Immunology, Medical Faculty, University of Ljubljana, Ljub

Objectives: Studies of convenience samples in Slovenian health care settings reported prevalences of genital *Chlamydia trachomatis* from 6% to 16.5% among asymptomatic women and from 2.7% to 3.2% among asymptomatic men. These estimates, although subject to selection bias, suggest that the low reported incidence rate (12 per 100000 population in 2002) based on mandatory notification of diagnosed cases substantially underestimates the true burden. The low reported incidence may also result from the low estimated rate of testing for *C trachomatis* (217 tests in public health laboratories per 100000 population in 2002). One of the objectives of the first national survey of sexual lifestyles, attitudes and health in Slovenia was to estimate the prevalence of and risk factors for genital *Chlamydia trachomatis* infection in Slovenian adults aged 18-49 years.

Methods: Data were collected during 1999-2001 from a probability sample of the general population by a combination of face-to-face interviews and anonymous self-administered questionnaires. Respondents were invited to provide a first void urine (FVU) specimen for polymerase chain reaction testing for *C trachomatis* infection.

Results: 1447 individuals contributed FVU specimens (82.6% response among survey respondents, 55.3% among eligible). *C trachomatis* infection was diagnosed in 3.0% of men and 1.6% of women. Prevalence was highest in men and women aged 18-24 years (4.1% for both). Individuals who reported first heterosexual intercourse before the age of 16, unprotected sexual intercourse with at least one heterosexual partner during the preceding year, a concurrent heterosexual relationship during the preceding year, and five or more lifetime heterosexual partners had a higher prevalence of genital *C trachomatis* infection. The association was statistically significant only for five or more lifetime partners (adjusted OR 3.0; 95% CI 1.3-6.9; $p=0.01$).

Conclusions: A relatively high prevalence of genital *C trachomatis* infection among 18-24 year old Slovenians, in contrast with relatively low-risk sexual behaviour and low reported incidence rates of chlamydia infection, suggest that there may be serious gaps in diagnosing and treating the condition. The results provide strong support for the introduction of chlamydia screening in Slovenia.

CHLAMYDIA SCREENING IN UNIVERSITY STUDENTS IN VIENNA

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Objectives

The majority of chlamydia infections in women are asymptomatic and often remain undiagnosed. It is recommended that young sexually active individuals should be screened for *C. trachomatis* in order to detect infection before damage to the reproductive tract has occurred.

The aim of the study was to determine the infection rate in a young female population and to evaluate the reliability, practicability, and acceptance of selfsampling for chlamydia screening.

Patients and methods

Between March and August 2004 603 female university students aged between 18 and 25 years were recruited at the University of Vienna in order to inform them on selfsampling of vaginal swabs and to provide them with a study sampling pack and information on chlamydia screening. Of all recruited students, 248 delivered vaginal and urine samples and were asked for a second selfcollected vaginal swab at the laboratory.

Of 261 symptomatic high risk women, urine and a selfcollected vaginal swab were obtained in addition to routine STD screening by the medical doctor. All participants were asked to provide basic demographic and epidemiological data and information on clinical symptoms. Altogether 1,266 urine and vaginal samples were tested by using COBAS Amplicor. Discordant samples were retested in a second run, sent to the French Chlamydia Reference Laboratory in Bordeaux, and were tested by real time PCR using primers directed to the cryptic plamid.

Results

In all 248 university students only 3 infected individuals (1.2%) were detected. The infection rate with *Chlamydia trachomatis* was higher in STI risk persons with a prevalence of 10.7% (28/261).

The performance characteristics for vaginal swabs were 100% for the specificity, sensitivity, and for the predictive values of positive and negative results, respectively. For urine swabs the corresponding data were 83.3%, 99.8%, 96.2%, and 99%, respectively. Although the concordance between urine samples and self-taken swabs was 98.7%, swab samples showed a higher detection rate when compared with urine.

Conclusions

A high acceptance and practicability of selfsampling could be observed in asymptomatic university students. Furthermore, self-taken swabs showed a high reliability and an excellent performance profile and can therefore be recommended as a noninvasive specimen type in order to test asymptomatic individuals.

STIs IN SLOVENIA, WHAT HAPPENED IN THE LAST DECADE?

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Objectives: Slovenia, an independent state since 1991 and member of the EU since 2004, has very reliable data on classical STIs (syphilis, gonorrhoea, chancroid and lymphogranuloma venereum) since 1951, when reporting them was compulsory by law. Notification of HIV was made mandatory since 1986 and that of chlamydial infections since 1987.

Results: During the past 30 years, the incidence of syphilis and gonorrhoea in Slovenia followed the trend in Western Europe. In 1994 the incidence increased to 1.82/100,000. This trend continued in the following years, but since 2001 the incidence is 0.05/100,000 and it is still decreasing. The most recent case of juvenile congenital syphilis was registered in 1986.

Gonorrhoea reached its climax in 1975 and then declined steadily. The incidence in the last 10 years was about 2.5/100,000.

Genital chlamydial infections appear to be on the increase in the last decade.

From 1986 to March 2004, there have been 110 patients with AIDS and 118 HIV positive persons registered, with men who have sex with men prevailing.

Discussion: The highest incidence of syphilis was in the capital of Slovenia. Most infections were imported directly or indirectly from the states of the former Eastern bloc. Gonorrhoea has been decreasing steadily since 1975. Due to not always exact diagnostic procedures, not strict reporting of cases and the use of antibiotics by population at large, the data are not completely reliable.

Genital chlamydial infections appear to be on the increase. AIDS and HIV epidemic is still in its early stage, the data indicate a slowly increasing trend.

Conclusions: The decreasing incidence of syphilis in the last years is presumably the consequence of the counselling of the general population and information about STIs in media. Because of the known reasons the data of gonorrhoea and genital chlamydial infections are not completely reliable. AIDS and HIV epidemic is still in its early stage.

The current epidemiological situation of STIs in Slovenia warrants strict surveillance of STDs by our medical services and close cooperation with the health authorities in all the neighbouring states.

RE-EMERGING ANIMAL ORTHOPOXVIRUS INFECTIONS IN THE LIGHT OF POTENTIAL BIOTERRORISM

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Objectives: After cessation of routine smallpox vaccination on May 8, 1980, various animal orthopoxvirus (OPV) species start to enter the niche, vacated in unvaccinated young people. These potential unrecognised diseases are too little recognised. Most recently, interest in rapid identification of animal OPV manifestations has increased following outbreaks of monkeypox in the United States.

Method and Result: A case with generalised cowpox infection after exposure to a rat is presented. A 16-year-old otherwise healthy boy developed fever and a generalised pustular eruption. Negative stain electron microscopy from lesion material revealed brick-shaped OPV particles, indistinguishable from the virions of variola. The surface of OPV consists of fine ridges, while parapox virus particles show spiral protrusions. As anamnestic investigation led to the suspicion of virus transmission by a pet rat, different molecular diagnostic methods were engaged, particularly to exclude monkeypox, which has been transmitted by imported pet rats in the USA most recently. Molecular typing could assign the virus to the species of cowpox viruses. The tyrolean isolate was most similar to the german strain OPV91-1 isolated from a cat in Southern Bavaria, supporting the concept of different clusters of OPV in geographically defined reservoirs. Rather cowpox specific antibodies were also found, this would suggest, that serological methods might be able to give a hint towards rapid determination of OPV species. The generalised rash in our immunocompetent patient was misleading, since cowpox infections usually lead to localised ulcerative nodules. Differential diagnoses in these cases includes herpes, anthrax and parapox manifestation such as orf. The later, however, does not show vesiculation and anthrax eschars grow more rapidly and are destructive. Dissemination of OPV is described in immunocompromised individuals or in patients with atopic eczema. Such generalised varicelliform eruptions may even mimic variola vera. For OPV no specific treatment has been established but various drugs have been considered, and especially cidofovir holds promise for treating severe cases.

Conclusion: Health authorities (including the Federal Ministry of Health in Austria) have recently implemented poxvirus alarm plans - the presented case highlights, that rapid differential diagnosis and awareness of re-emerging animal orthopox virus manifestations in humans is important

PENISCOPY IN DIAGNOSTIC PROCEDURE OF SUBCLINICAL HUMAN PAPILLOMA VIRUS INFECTION

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Background: Genital human papilloma virus (HPV) infections have risen dramatically over the past 30 years, and are now the most common courses of viral sexually transmitted disease (STD). Man are usually reservoir of the virus, which lives in latent form on genital mucous membranes, which as subclinical, asymptomatic infections can be oncogenic factor(s) in development of cervical cancer in female. Although penile skin hosts HPV frequently, cancer develops very rarely. However, sometimes they can develop penile intraepithelial neoplasia (PIN) lesions

Introduction: Human papillomavirus (HPV) is known to induce three different manifestations: clinical, subclinical, and latent infection. Clinical anogenital lesions are defined as those visible to the naked eye, without any enhancing techniques. They include a spectrum of diseases, from benign verruca vulgaris, condylomata acuminata, to malignant cervical, vulvar, anal or penile cancer. Using peniscopy, subclinical lesions can be classified as flat (at skin level), papular (raise slightly above the surface in circumscript area), papillary (obvious protrusion above the surface, forming papillary growth or papilloma), and classic condylomata (grossly recognizable protuberance with finely pointed epithelial excrescences). Latent infections are defined by presence of HPV DNA in areas with no clinical or histologic evidence of HPV infection.

Aim: of the study was to establish the frequency of HPV infection in asymptomatic male partners of women with cervical intraepithelial neoplasia (CIN).

Material and methods: The study included 30 male partners of females with known CIN grade 3, which was previously diagnosed by cytological tests (PAPA smears), done by their gynecologists. All male partners were unaware of or denied the presence of a genital sites. Exfoliated cells from predilection sites of the external penile surface (corona glandis, frenulum, preputium, sulcus) and urethral meatus were obtained and analyzed by Dygene Hybrid Capture II method (2001 Digene, Gaithersburg, USA). for the presence of HPV DNA. The peniscopy with previous use of 5% acetic acid, applied for 5-10 minutes was performed in all male sexual partner.

Results: Nine out of 30 patients (30%) had positive HPV using Dygene Hybrid Capture method. Peniscopy showed various HPV associated changes (from condylomata plana to PIN lesions) in 28 (93%) patients. All 28 patients were properly treated.

Conclusion: Screening and treatment of male partners which sexual partners have CIN lesion are mandatory not only for the patient but also for epidemiological purposes, including prevention of carcinoma. Examination of the genitalia by colposcopic equipment (peniscopy) after application of 5% acetic acid has been claimed to be the most reliable method for the identification of subclinical HPV infection. Our data could confirm that importance.

HPV GENOTYPING IN STI PATIENTS

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Objectives

A persistent infection with Human Papilloma Virus (HPV) is shown to be the primary causal factor in the development of cervical cancer. The aim of the study was to examine the incidence of HPV high- and low-risk genotypes in women according to their age and cytological diagnosis of the PAP smear.

Patients and methods

Between 2001 and 2003 6,695 women visited the outpatients centre with the cytological diagnosis Pap III, IIID or IV were analysed for the presence of HPV. In comparison, HPV diagnosis was performed in an asymptomatic screening group of 2,627 women. Specimens were taken with the cytobrush from the os of the cervix. For HPV genotyping, the Digene Hybrid Capture HPV Test, a microplate nucleic acid hybridization assay with signal amplification, was used.

Results

In all 6,695 women examined, high-risk DNA HPV genotypes were detected in 1,998 cases (29,8%), in 767 individuals (11,5%) an infection with both types was diagnosed and low-risk HPV genotypes in 335 women (5%) respectively.. Most of the high risk infections were diagnosed in women between 25 to 30 years. In the age group of women over 55 years the percentage of negative results increased to over 70 %. Among the 1,356 women with the cytological diagnosis Pap IIID or IV, high-risk HPV infections were detected in 671 cases (49,5%) and in addition, a coinfection with high- and low-risk genotypes was diagnosed in 205 cases (15,1%). Only 60 women (4,4%) turned out to be infected with low-risk HPV. In comparison, in asymptomatic women with normal cervical cytology the prevalence of HPV was low with an incidence of high-risk and low-risk DNA as well as a coinfection of 13,2%, 4,2%, and 5,1%, respectively. The pattern of the age distribution was similar in all groups.

In 549 patients with a positive outcome of the first examination, repeated diagnosis procedures within the following 34 months were performed. The relation between negative and positive HPV results changed significantly in favour of negative results ($p < 0,001$), corresponding to the increasing interval between the first examination.

Conclusions

HPV-high risk genotypes were detected most commonly in women between 25 and 30 years. In patients with the diagnosis PAP IIID and IV HPV-high-risk infections were found 4 times more often than in the screening group. Routine screening for HPV high risk types should be recommended for persons with pathological cytology.

INTERPRETATION AND CONSEQUENCES OF HPV DIAGNOSIS

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Infection with Human Papilloma Virus (HPV) high risk type is the most important factor for development of neoplasia of the cervix. Cytological screening by Papanicolaou staining dramatically reduced the incidence of this malignoma, being the most successful cancer prevention program. Nevertheless, 200 000 women worldwide die of cervical carcinoma each year, part of them having been screened cytologically before.

Epidemiological studies could demonstrate that in cervical swabs of up to 85% of sexually active young women HPV-DNA could be detected. About two thirds of the women younger than 24 became HPV negative within 15 month, when observed for 5 years the clearance rate was 92%. The risk factors causing the progression of the infected cells to malignant forms are not completely known up to now. Viral factors such as pathogenic variants of the high risk types, host factors (HLA) and environmental factors as other STIs might be important.

As the absence of HPV high risk DNA means a very low probability for the development of cervical dysplasia, in some countries the lengthening of the cytological screening interval to 5-7 years in HPV negative women older than 35 is discussed. In the assessment of unclear cytological results (ASCUS) HPV detection is an important prognostic parameter. Up to now early recognition and surgical treatment of malignant lesions due to viral infection is the only therapeutic meaning in fighting the disease. Most promising for the future is the development of prophylactic vaccines to prevent HPV-infection.

MOLECULAR SCREENING OF SYPHILIS BY PCR

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Objectives: For molecular detection of *T.pallidum* a sensitive, semiquantitative nested PCR on whole blood has been introduced, comparing PCR results with syphilis serology and patients history.

Methods: *T.pallidum* genome encoding the 47 kD membrane protein was amplified. A positive control was a Condyloma lata (Syll) biopsy inoculated into rabbit scrota (RIT). For quantitation suspension of *T.pallidum* (Nichols) containing a known number of organisms was prepared. Seventy-eight persons were than tested: 70 young gay males, 3 Syll clinical cases and 6 HIV+ outpatients. DNA amplified by PCR was purified from whole blood. **Results:** The RIT scrotum *T.pallidum* inoculation test was PCR (+), as was the *T.pallidum* preparation. Among the 70 men, all were negative for RPR and TPHA. PCR detected *T.pallidum* specific DNA in 4 syphilis seronegative cases with a prevalence of 5.6%. Repeated syphilis serology in these men was negative except for one weak TPHA. Syll clinically diagnosed cases were positive in serology and PCR. One HIV+ case was also positive in *T.pallidum* PCR. No PCR positive case had a syphilis history except the three Syll clinical cases.

Conclusions: Syphilis remains a difficult target, and there is little doubt that it facilitates HIV aquisition, and progression of HIV disease. Antibody tests were insensitive for 4 latent syphilis cases in our small series. Other traditional technouques for direct detection of *T.pallidum* require expertise and/or costly, and/or not practical for mass screening. Our whole blood PCR can be used in amniotic fluid and CSF. We do not know if aggressive therapy for latent syphilis is detected only by PCR on whole blood. Are these cases partially immune suppressed, and more vulnerable to HIV? Are they infectious? We suggest a PCR test like this may help exclude latent syphilis in cases of HIV infection and AIDS, and should be considered as a screening tool.

EARLY NEUROSYPHILIS. SYMPTOMS AND MANAGEMENT

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Syphilis is a widespread infective disease all over the World, in certain regions – e.g. black Africa, Southeast Asia, USA, Eastern Europe, former Soviet Union – particularly common. It is rare in Hungary, but the incidence is rising – slowly from 1989, rapidly from 1997. Neurosyphilis is a well-known late manifestation. At the first half of the past century most patients treated at the psychiatric institutes had general paresis of the insane. Beside to this serious condition the so-called early neurosyphilis fell into the background, however the most frequent systemic manifestation in early syphilis. 40-50% of the early syphilis patients have meningeal symptoms, e.g. headache (occipital, at night), nausea and stiff neck. Probably all syphilitic patients have spirochaetae in the central nervous system, but early or late neurosyphilis develops in only limited number of patients. Meningeal, vascular and parenchymal disease can occur, the process generally starts with aseptic meningitis. The untreated disease heals (frequently with sequelae) or 4-40 (med. 25) years later evolves into late neurosyphilis; the two processes don't certainly correlate. We observed 3 homosexual male patients with early neurosyphilis. The 40 year-old man had macular syphilitid, hepatopathy and positive liquor serology. He got 24 ME crystalline penicillin for 10 days with total healing of the symptoms and improved liquor serology. However, 4 month later became HIV+. A 30 year-old man had typical 2nd stage syphilis: diffuse alopecia and papules. He got erythromycin, later azithromycin because of penicillin sensitivity. Suddenly visual problems developed and optic neuritis had been diagnosed. The diagnosis of neurosyphilis was based on the liquor serology. 4 months after iv. doxycyclin therapy, the visual problems and liquor serology improved. The 43 year-old man presented with patchy alopecia and positive syphilis serology. He got repeated azithromycin treatment because of penicillin sensitivity. The skin symptoms were resistant and tinnitus occurred. The liquor examination resulted elevated protein level and TPHA positivity. He also got iv. doxycyclin and healed without sequelae. Our cases demonstrate that early neurosyphilis is an existing problem and point towards three typical complications: hepatopathy, ocular and vestibular neuropathy. In case of attention the diagnosis rarely means difficulties. The treatment of penicillin sensitive patients can be problematic.

NEUROSYPHILIS IS UNLIKELY IN PATIENTS WITH LATE LATENT SYPHILIS AND A NEGATIVE BLOOD VDRL

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BACKGROUND

Patients with late latent syphilis should be evaluated clinically for tertiary disease and lumbar puncture (LP) may be performed to exclude neurosyphilis. The diagnosis depends on various combinations of reactive serologic test results, abnormalities of cerebrospinal fluid (CSF)-cell count or protein, or a reactive VDRL-CSF with or without clinical manifestations. LP, however, is an invasive procedure with side effects and should therefore be restricted to indicated cases. The aim of this retrospective study was to determine serologic parameters which can serve as criterion for the indication of LP in these patients.

METHODS

Between January 1988 and June 2004, CSFs from 710 patients were sent to our syphilis laboratory. After excluding the replicant estimates and patients, whose blood serology was either not available or had not been determined within 3 months of LP, 265 patients were retained for analysis. Each of the 265 patients (79 female / 186 male) tested positive in at least one treponemal specific antibody test (TPHA and/or FTA-Abs test) in peripheral blood, which together with the medical history and a clinical condition was indicative for late latent syphilis.

RESULTS

Forty-five of the 265 patients (16.9%) fitted the laboratory criteria of neurosyphilis; in detail, 39 of them fulfilled the CDC-criteria for neurosyphilis (reactive CSF-VDRL or CSF-pleiocytosis with >10 white blood cells mm^{-3} and elevated CSF-protein >0.50 g/l). Applying the criteria of the European STD guidelines we identified additional 5 patients (CSF-pleiocytosis, reactive CSF-TPHA, elevated IgG-index); one patient was included because of a solitary elevated CSF-TPHA-index of more than 70. Seventy-two of the 265 patients were HIV-positive, of whom 7 fulfilled the criteria for neurosyphilis. The mean age of the patients with neurosyphilis was 47 years \pm 16. There was not a single patient with neurosyphilis who exhibited a negative VDRL in peripheral blood, regardless of the HIV-serostatus, which was highly significant ($p < 0.01$, χ^2 -test). The median blood-VDRL titer was significantly higher in patients with neurosyphilis compared with those without (1:32 vs. 1:0; $p < 0.01$, T-test of means, 2-sided).

CONCLUSION

According to our results, neurosyphilis is very unlikely in patients with untreated late latent syphilis and a negative VDRL in peripheral blood. Therefore, the performance of LP in these patients is not recommended.

INCREASING FAILURE OF GONOCOCCAL CULTURE ON A SELECTIVE MEDIUM

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Objective: Culture of *Neisseria gonorrhoeae* is still the reference method for the diagnosis of gonorrhea in many countries. In the STD-clinics in Graz a decrease of sensitivity of culture with the selective Thayer-Martin medium by Heipha (TMH) down to 30% in the last 4 years compared to 100% in the first years of study period was observed.

The aim of the study was to compare the TMH with other routine media and to determine whether the concentration of antibiotics in selective media is the reason for the failure of culture.

Methods: Between April and September 2004 a two center study was conducted in Graz and Vienna. The growth of gonococcal strains on selective media (Thayer Martin medium by BioMerieux TMB and by Heipha TMH, modified New York City medium NYC) and non-selective media (Blood-GC-medium in Vienna, Chocolat PolyViteX Agar in Graz) was compared. In Vienna susceptibility testing with vancomycin, trimethoprim, and colistin was performed by Etest additionally. These antibiotics are supplemented in selective media for growth inhibition of non-gonococcal bacteria.

Results: In Graz specimens of 14 patients were included. All isolates grew on TMB (100%), 13 isolates also on the nonselective medium (92.9%). The routinely used TMH failed in 4 cases (71.4% positive).

In Vienna 48 isolates and one control strain were included. Three selective media (NYC, TMB, TMH) and one nonselective medium were used. The nonselective medium failed in culture for one isolate (2.1%), NYC for 3 isolates (6.3%), and TMB for 2 isolates (4.2%). On TMH failure of culture occurred in 42 cases (87.5%), which is significantly more often ($p < 0.001$) than on all other used media. In addition a control strain (ATCC 43069) which is recommended for quality control of culture of *N.gonorrhoeae* by the National Committee for Clinical Laboratory Standards was tested and showed excellent growths on all media except TMH. For 45% of the TMH culture negative isolates susceptibility testing with vancomycin and colistin revealed minimal inhibition concentrations (MICs), which may contribute to growth inhibition. The concentration of trimethoprim had no influence on culture.

Conclusion: The results of this study demonstrate that TMH agar seems to be no adequate medium for culture of *N.gonorrhoeae*. The concentration of vancomycin and in a lesser extent colistin may contribute to growth inhibition, but may not be the only reason for failure of culture which might be also due to deficiencies in nutritional supplements. Regarding the clinical and epidemiological importance of *N. gonorrhoeae* infections the use of both, selective and nonselective media is recommended to prevent culture failure.

CIPROFLOXACIN RESISTANT STRAINS OF *NEISSERIA GONORRHOEAE* IN SLOVENIA FROM 2001 TO 2004

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Objectives: Sensitivity of *Neisseria gonorrhoeae* to antibiotics is changing. First fluoroquinolone resistant strains of *N. gonorrhoeae* has been diagnosed in Slovenia in year 2002. The aim of the study was to find out the susceptibility of *N. gonorrhoeae* isolates from patients in Slovenia to antibiotics and to investigate genetic heterogeneity of resistant isolates.

Methods: In the four-years period (2001-2004) we isolated *N. gonorrhoeae* at 103 patients (94 males and 9 females) treated at the outpatient clinic of Dept. of Dermatology. Swabs of urethra and cervix were transported to laboratory in transport culture system. GC-Agar plates supplemented by Vitox (Oxoid) were cultured at 5 % CO₂, at 35 °C for 1-2 days. Isolated strains of *N. gonorrhoeae* were determined on minimal inhibitory concentrations to 6 antibiotics: penicillin, tetracycline, azithromycin, cefotaxime, ceftriaxone and ciprofloxacin by E-test (AB Biodisc). For quality control we used *N. gonorrhoeae* strain ATCC 49226. Genetic heterogeneity of fluoroquinolone resistant isolates were determined for gyrA gene and proC gene by sequencing of PCR products of those two genes.

Results and Conclusions: 43 of 103 (42%) *N. gonorrhoeae* strains were resistant to ciprofloxacin. All ciprofloxacin resistant strains had point mutations in gyrA or parC genes. In year 2002 we determined first ciprofloxacin resistant strain of *N. gonorrhoeae* in Slovenia. In following years we detected increasing rate of isolated strains. Most of strains have in gyr A gene point mutations on location Ser-91 and Asp-95 and in par C gene the most common point mutation was on location Asp-86.

NEISSERIA GONORRHOEAE RESISTANCE PROFILE FROM 1999 TO 2003

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Objectives:

A global increase of gonorrhea and rising numbers of *Neisseria gonorrhoeae* isolates with resistance to fluoroquinolones have been noticed.

The aim of the study was to evaluate the prevalence of gonorrhea and the resistance patterns of the isolated gonococci as well as to confirm the reliability of disk diffusion method for susceptibility testing of *N.gonorrhoeae*.

Methods:

Between 1999 and 2003 a total of 137,302 men and women were examined for the presence of gonorrhea or other STDs. Cervical and/or urethral swabs were obtained to detect *N.gonorrhoeae* by Gram-stain and culture on modified NYC-medium. The resistance patterns were determined using disk diffusion method and additionally Etest for 69 isolates.

Results:

While numbers of patients remained almost constant, a significant increase of gonococcal infections from 52 (0.2%) in 1999 to 231 (0.9%) in 2003 was noticed, with a tendency to be diagnosed ten times more often in men than in women. During the investigation period increasing numbers of gonococcal isolates exhibiting antibiotic resistance were observed. While in 1999 only 3.1% of the *N.gonorrhoeae* isolates showed resistance to ciprofloxacin, this was the case for 63.5% in 2003. The number of penicillin resistant *N.gonorrhoeae* isolates has increased from 7 (13.5%) in 1999 to 186 (51.41%) in 2002. Furthermore, a higher number of penicillin and tetracyclin intermediately susceptible isolates was detected. No resistance to cephalosporines has been observed. Comparison of the results of disk diffusion method and Etest revealed excellent correlation for fluoroquinolones (>97%), penicillin G (89.9%), and tetracyclin (87.0%), respectively.

Conclusions:

The results of this study demonstrate the necessity of the microbiological examination including the gonococcal resistance profile for successful treatment of gonorrhea. Moreover, the study confirms that disk diffusion method represents an adequate antibiotic susceptibility test for *N.gonorrhoeae*.

According to the CDC's STD Treatment Guidelines 2002 cephalosporines (third generation) should be used as first-line treatment for gonorrhea. The recommendation of fluoroquinolones as alternative therapy has to be revised.

VAGINAL YEAST ISOLATES – DO WE NEED SPECIES IDENTIFICATION?

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Introduction

Vulvovaginal candidiasis (VVC) is found worldwide and during the childbearing period approximately 75% of all women will experience at least one episode of VVC.¹ 50% of these patients will have a second episode of VVC. Furthermore, in some 5% of cases, the disease develops a chronic course. 85-90% of all yeasts isolated from the vagina are *Candida albicans*. The remaining 10-15% comprise the so-called non-albicans *Candida* species and other yeasts. In recurrent cases an increase in these species (*C. glabrata*, *C. tropicalis*, *Saccharomyces cerevisiae*) has been discussed over the last few years.

Objective

The aim of the present study was to identify the different yeast species isolated from patients with VVC and to test the antifungal susceptibility of isolates in a subset of patients.

Patients and Methods

Vaginal smears were obtained from 168 VCC patients, who were seen at our department between January 2002 and July 2004. The Gram-stained preparations were investigated microscopically for the presence of yeasts. Fungal cultures were obtained using Sabouraud glucose agar (SGA). Furthermore, for specific yeast identification *Candida*-id (Biomérieux) and the colorimetric sugar assimilation test Auxacolor 2 (Bio-rad) were used. In a subset of patients yeast susceptibility to antimycotic treatment was tested by E-test (AB Biodisk) and ATB Fungus 2 (Biomérieux).

Results

The following yeasts were isolated from the vaginal smears: *C. albicans* 129 (76,8%), *Saccharomyces cerevisiae* 11 (6,5%), non-albicans *Candida* species 6 (3,6%), mixed cultures 3 (1,8%). In 11,3% of all smears the yeast species was not identified.

Conclusion

In contrast to the recent literature we could not find an increase in non-albicans *Candida* species (especially *C. glabrata*) causing VVC in our patients, whereas an increase in *Saccharomyces cerevisiae* was noted. In general, species identification of vaginal yeasts is not mandatory. Nevertheless, some cases of VVC are resistant to treatment. In these patients identification of the yeasts and their susceptibility to antimycotic treatment is of major importance, if other reasons for recurrence are excluded.

¹ Sobel JD. Vaginitis. NEJM 1997;337:1896-1903.

FLUCONAZOLE UPREGULATES SCONC EXPRESSION AND INHIBITS SULPHUR METABOLISM IN *MICROSPORUM CANIS*

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Azole derivatives such as fluconazole are mainstay of therapeutic agents for the treatment of fungal infections. Their action through alteration in the conversion of lanosterol to ergosterol is well established. We used differential display to detect gene regulations in dermatophyte (*M.canis*) treated with fluconazole. The regulated genes were isolated from cDNA library. Recently we reported that fluconazole downregulates the expression of the fungal metallothionein gene. Here we report the effect of fluconazole on the sulphur metabolism negative regulator gene (*sconC*) in *Microsporium canis*. Characterization of the *M. canis sconC* gene revealed that its ORF comprised 724 bp interrupted by four introns of 47-70 bp. Exposure of *M. canis* in suspension to fluconazole upregulates *sconC* mRNA level and protein expression as determined by Northern and Western blot analysis respectively. Upregulation of *sconC* was accompanied by the inhibition of sulphur metabolism of the fungus as e

videnced by a greatly reduce incorporation of radioactive labeled sulphuric acid into fungal proteins. These data establish that in addition to its action on ergosterol synthesis, fluconazole acts on other biological pathways in fungal cells.

SIDE EFFECTS AND DRUG INTERACTIONS OF MODERN ORAL ANTIMYCOTIC DRUGS

Franco Kokelj and Giusto Trevisan, Triest

In the last decades the common fungal infections have been well controlled by the new oral antimycotic drugs: ketokonazole, itraconazole, fluconazole and terbinafine.

All these drugs are quite safe and handleable. These characteristics induced an important increase in the use of this drug categories.


Moreover all these therapies present a series of sides effects, usually not particularly serious – such as gastrointestinal disturbance, nausea, abdominal pain, headache etc. – while others are more important, like heart involvement.

Another problem is that of the possible interactions of oral anti-mycotics with other drugs, and this must be well considered when we prescribe these therapies.

In our presentation we summarize the possible side effects of the different therapies and the drugs interactions and present our experience on this subject.

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