HPVs & OTHER STDs
IN CROATIA – current status

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HIV INFECTION

- HIV infection shows a relatively favorable trend with 8-16 AIDS patient annually in the last 12 years.
- AIDS in Croatia did not follow Western European models, as there have not been any explosive growth.

GONORRHOEA AND SYPHILIS IN CROATIA

- Syphilis and gonorrhoea.
- Since the mid-80s there has been a clear, very gradual downward trend.
- We owe this to:
  - a) the good organisation of the epidemiological service and clinical treatment services;
  - b) the existence of effective therapy;
  - c) the effect of a broad action of medical education measures ever since the early 80s, for the sake of preventing and suppressing AIDS;
  - d) a positive change in the behaviour of the population, because the same precautionary measures apply not only to AIDS but also to all other STDs;
  - e) AIDS shows a relatively favourable trend with from 2-16 (mainly 8-16) infected annually in the last 12 years.
CHLAMYDIASIS IN CROATIA

- Chlamydia urogenitalis also shows a stationary trend.
- The number of reported patients ranges between 200 and 300 per year.
- On the other hand, from laboratories that undertake microbiological diagnoses, we can learn that the number of positive findings is significantly higher.
- According to clinical experience, this is frequently a matter of asymptomatic infections.

Estimated new cases of chlamydial infections among adults (WHO 1998)

- 4 million
- 5 million
- 5 million
- 6.5 million
- 40 million
- 300,000
- Global total: 89 million
- 65,670,000
Chlamydial infection

- Approximately 75% of women and 50% of men are asymptomatic, not aware of the infection and not treated.
- Women infected with chlamydial infections are in 3-5 fold increased risk of acquiring HIV infection.

Chlamydial infection in Croatia

- Croatia
  - 10% females
  - 29% adolescents * (STD clinics data – Klaiceva and University policlinic)
- 65,000 estimated new cases in Croatia among adults
Consequences

- 40% of women will develop PID:
  - among them 20% will become infertile,
  - 18% will experience debilitating, chronic pelvic pain,
  - 9% will have a life threatening tubal pregnancy. Tubal pregnancy is the leading cause of first-trimester pregnancy related deaths in American women.

- Very often results in adverse outcomes of pregnancy: neonatal conjunctivitis (50%) and pneumonia (20%)
Azithromycin – first choice drug for uncomplicated urethritis/cervicitis:

**1g single dose**

because

single-dose treatment extremely enhance the likelihood of successful treatment (especially in adolescents) in comparison to commonly used 7-day oral medication

*(CDC, Sexually transmitted diseases treatment guidelines, 1998.)*

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**CDC recommendations**

- CDC recommendations for prevention and management of chlamydia for all providers of health care:
  - comprehensive screening is needed
  - treatment not only for women but also for men
  - single-dose treatment extremely enhance the likelihood of successful treatment (especially in adolescents) in comparison to commonly used 7-day oral medication

*CDC, National Centre for HIV, STD and TB Prevention, Division of Sexually transmitted Diseases*

[www.cdc.gov/nchstp/dstd/chlamydia_facts.htm](http://www.cdc.gov/nchstp/dstd/chlamydia_facts.htm)
Chlamydia Infection Now Linked to Cervical Cancer.

P. Koskela et al., *Int J Cancer*, 2000;85:35-39

**HEPATITIS B IN CROATIA**

- Hepatitis B, more of a parenteral and blood borne disease, and partially sexually transmissible, has shown for decades in Croatia a practically stationary low endemic trend with an average of 200-250 people infected per year. According to the most recent results available from the Transfusion Centre, this is annually below 1% prevalence of HbsAg positive persons.
AIDS IN CROATIA

- In Europe, Croatia occupies the 25th position for AIDS sufferers per one million inhabitants (a total of 125 infected in 1998, or 27 per 1,000,000 of the population, while some other countries in Europe have 800 per 1,000,000).
- At the moment, AIDS in Croatia will not follow Western European models, there being no explosive growth.
- In Croatia, AIDS has been smouldering in the last 12 years, ever since it entered the population (above mentioned sources).

COMMON CANCER

- Incidence
- Mortality

Cancer sites:
1. Breast
2. Stomach
3. Uterine cervix
4. Uterine body
5. Ovary
6. Colon
7. Bronchus and lungs
8. Rectum
9. Pancreas
CERVICAL CANCER

HYPOTHESIS

Drazancic et al. 1992
Committee for women health protection of the Ministry of Health Croatia

Women in Croatia > 15 years
(1991 national register)

2,010,000
1/3
670,000

Abnormal PAP smear 2.5%
Colposcopy 17,000
Biopsy / Conization 1/5

3,500 women
HPV TESTING

Number of women tested by PCR (N = 4,230)

HPV PREVALENCE

Croatian women with abnormal cytology (N = 4,230)
HPV TYPES

Study group (N=1977) from 1999 to 2002

HPV ACCORDING TO DIAGNOSIS

Study group (N=1977) from 1999 to 2002
HPV ACCORDING TO DIAGNOSIS

Study group (N=1977) from 1999 to 2002

HPV IN MEN

According to the Croatian guidelines for premalignant lesion associated to HPV infection, we include, recently male partner, in order to cut through both the "ping-pong" sexually transmitted HPV and chlamydial infection.
CONCLUSION

Young women (15-24 years) exhibited the highest rate of HPV infection and they are therefore, exposed to cervical cancerogenesis very early in life and their reproductive possibilities are endangered as well as it is by other STDs, such as chlamydia.

Larkin M. Easing the way to safer sex, The Lancet 1998; 351:964.

- New topical microbicides – bactericidal and virucidal intravaginal preparations for preventing of STD are promising, non irritating products, which are supposed to offer women safe, convenient and in some cases virtually undetectable protection:
  - PRO 2000 colourless, odourless naphthalene sulphonate polymer as a gel.
  - Acts against HIV-1, genital herpes, and possibly chlamydia trachomatis.
  - It has also contraceptive effect.
• “Invisible condom” also promising, thermoreversible unique product:
  – It is liquid at room temperature, but quickly sets to a transparent odourless gel at body temperature;
  – When applied as liquid it infiltrates the smallest mucosal folds;
  – When jellifies almost immediately it should adhere strongly to the mucosa and stay in place during sexual intercourse;
  – Alone acts as physical barrier to pathogen;
  – Mixed with microbicides form chemical barrier against pathogens.

CROATIAN CONSENSUS ON CIN TREATMENT

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Cytological examination according to modified Bethesda classification


In patients with abnormal cytology: colposcopy according to International classification (7th World congress of IFCPC, Rome 1990.)

Further treatment depends on

- age, parity and cytological signs of HPV infection.
- Before any therapy it is obligatory to cure bacterial vaginosis.
- After local therapy and proven antimicrobial therapeutic success:

In young nulliparous women

a) If there exists CIN I + minor colposcopic change:
   - follow up every 6 months during 2 years.

- If there is no regression then target biopsy, and in case of CIN I treat (ECG).
b) in the case of CIN I + HPV and minor colposcopic change:
   - HPV typisation (PCR)

c) in case of HPV 6/11 treat the same way as a)

d) in case of HPV 16/18:
   - target biopsy and treatment according to PHD of biopsy sample: (ECG) if PHD no greater than CIN II

e) in case of CIN I + major colposcopic change, or

f) in case of CIN I + major colposcopic change and low risk HPV:
   - follow up one year. In case of persistence: treat by ECG.

   In case of high risk HPV:
   - treat immediately and definitely by ECG.

   • Both after target biopsy no greater than CIN I.
g) in case of CIN II + above mentioned colposcopic changes and HPV presence of either low or high risk HPV:
- perform the definite therapy by ECG, although CIN II belongs to HGSIL group, but there we face young female population in whom we must definitely cure the lesion and conserve the procreation after CIN II on target biopsy.

- Between punch biopsy histology and definite therapeutic approach we can wait 4-6 months taking in the mind possible regression due to healing process, i.e. therapeutical effect of targeted biopsy.
h) in the case of severe displasya having in the mind that almost 95% of these lesions contain high risk HPV:
– colposcopy, targeted biopsy and LETZ cone after targeted biopsy which had proven dysplasia gravis.

• In the case of CIS in target biopsy specimen: cold knife conisation

In parous women

with or without HPV presence we treat
• persistent CIN I by ECG,
• CIN II by ECG,
• Severe Dysplasia by LETZ,
• Carcinoma in situ by cold knife conisation.

• Every operation is performed by colposcopical guide.
• In all cases the first cytological control after 3 months.
• In case of abnormal control cytology follow up:
  – perform colposcopy and HPV typisation taking in mind either the possibility of residual disease or reinfection
  – then if indicated perform target biopsy and further therapeutical approach which has to be as conservative as possible

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