



**EPIDEMIOLOGY OF SEXUALLY  
TRANSMITTED DISEASES  
IN ESTONIA IN 1990–2000**

**ANNELI UUSKÜLA**



DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS

71

**EPIDEMIOLOGY OF SEXUALLY  
TRANSMITTED DISEASES  
IN ESTONIA IN 1990–2000**

**ANNELI UUSKÜLA**



TARTU UNIVERSITY  
PRESS

Department of Dermatovenerology, Clinic of Dermatology, University of Tartu

The dissertation was accepted for the commencement of the degree of Doctor of Medical Sciences on August 29, 2001 by the Council of the Faculty of Medicine, University of Tartu, Estonia

Opponent: Professor Timo Reunala University of Tampere

Commencement: November 27, 2001

© Anneli Uusküla, 2001

Tartu Ülikooli Kirjastuse trükikoda  
Tiigi 78, Tartu 50410  
Tellimus nr. 787

# CONTENTS

LIST OF ORIGINAL PUBLICATIONS .....	6
ABBREVIATIONS .....	7
INTRODUCTION .....	8
REVIEW OF THE LITERATURE .....	9
AIMS OF THE STUDY .....	18
MATERIALS AND METHODS .....	19
RESULTS .....	23
DISCUSSION .....	42
CONCLUSIONS .....	43
ACKNOWLEDGEMENTS .....	44
REFERENCES .....	49
SUMMARY IN ESTONIAN. Sugulisel teel levivad infektsioonid Eestis aastatel 1990–2000, epidemioloogiline uuring .....	49
PUBLICATIONS .....	57

## LIST OF ORIGINAL PUBLICATIONS

The dissertation includes the following articles referred to in the text by their Roman numerals:

- I Uusküla A, Silm H, Vessin T. Sexually transmitted diseases in Estonia: Past and present. *International Journal of STD & AIDS* 1997; 8, 1–5.
- II Wilson TE, Uusküla A, Feldman J, Holman S, DeHovitz J. A case control study of beliefs and behaviors associated with STD occurrence in Estonia. *Sexually Transmitted Diseases* 2001; 28: 624–9.
- III Uusküla A, Plank T, Lassus A, Bingham JS. Sexually Transmitted Infections in Estonia — syndromic management of urethritis in a European country? *International Journal of STD & AIDS* 2001; 12: 493–49.
- IV Uusküla A, Kalikova N, Zilmer K, Tammai L, DeHovitz J. The role of injecting drug use in the emergence of HIV in Estonia. *International Journal of Infectious Diseases* 2002; 6: (accepted for publication)
- V Uusküla A, Nygård JF, Kibur M. Syphilis as a social disease: experience from post-communist transition period in Estonia (submitted).
- VI Uusküla A, Kibur M, Tamm A, Robinson NJ. HSV Seroepidemiology Multi-Centre Study Group. HSV-1 and HSV-2 seroprevalence study in Estonia. *International Journal of STD & AIDS* 2001; 12 Suppl 2: 152 (abstract).

Published and accepted papers are reproduced with the permission from the publisher.

## **ABBREVIATIONS**

<b>AIDS</b>	acquired immunodeficiency syndrome
<b>HIV</b>	human immunodeficiency virus
<b>HSV</b>	herpes simplex virus
<b>IDU</b>	injecting drug use
<b>STD</b>	sexually transmitted disease
<b>UNAIDS</b>	the United Nations joint program on HIV and AIDS
<b>WHO</b>	the World Health Organisation

## INTRODUCTION

Sexually transmitted diseases (STDs) have been recognised as a major public health problem for a number of years. Regardless to medical advances, STDs continue to pose a threat to the health and welfare of individuals. Human immunodeficiency virus (HIV) and STDs epidemics are having remarkable social, demographic and economic consequences.

There has been a dramatic increase in the reported STD incidence in East-Europe and Central Asia. Despite the underreporting of cases and decline in mass screening an epidemic has been documented.

In Estonia the STD incidence rapidly and substantially increased during the early 1990s and started to decline after 1994. Regardless to the rapidly and substantially increasing STD rates the epidemic of HIV infection was held during the decade until year 2000.

Epidemiology of sexually transmitted diseases concerns the incidence, distribution and trends in STD and related complications. The incidence and distribution of STDs show considerable variation across space and time, which reflects the distribution and trends in their determinants. Factors affecting the transmission of STDs can be categorised into those acting at the level of individuals (e.g. biological and psychological-behavioural) and others at the level of the sociophysical environment. The factors of the sociophysical environment associated with the community STD rates are economic, geographic, structural, technological and sociocultural, as well as the prevalence of disease in the population.

The two main sources of information on the prevalence and incidence of STDs are case-notification reports and epidemiological studies. In Estonia, the surveillance of HIV infection and STDs is based on the mandatory universal notification of newly identified cases to the State Health Protection Service (with the same reporting principles in use throughout the period).



# REVIEW OF THE LITERATURE

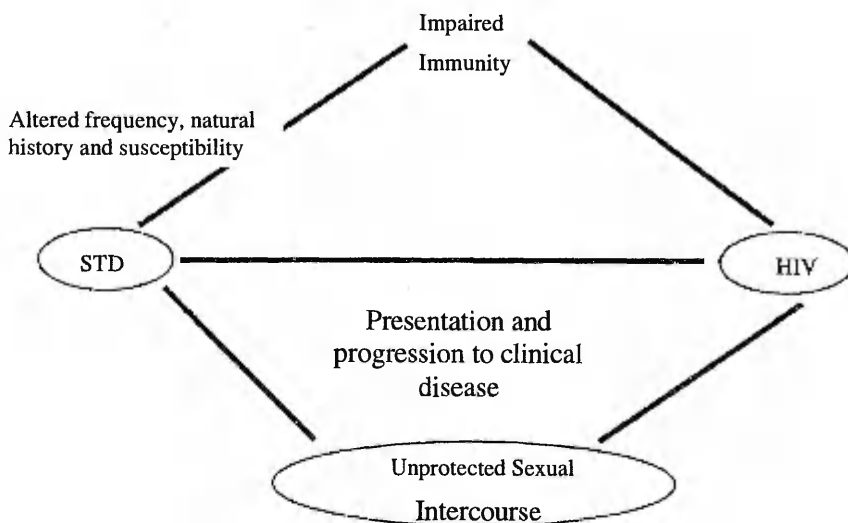
## 1. Sexually transmitted diseases

In the last decades there have been considerable development in the field of STDs. To a large extent, it has been conditioned by the HIV/AIDS epidemic, but also increased recognition of the range and severity of complications and sequelae that can be linked to these infections, and development of new case-management approaches should be noted. More than 30 bacterial, viral, and parasitic diseases have now been identified that can be transmitted by sexual route; however, only a minority have the sexual route as their dominant route of spread. STDs infect the reproductive tract as their primary site, with the transmission occurring during sexual intercourse or during pregnancy and childbirth. As a result, the greatest risk of infection is found among sexually active individuals and in infants born to infected mothers. Multiple infections within the same individual are also frequent, as is re-infection if partners have not been adequately treated.

The vast majority of the disease burden from STDs is a result of the complications and sequelae that may follow the infection<sup>1</sup>. For example, primary infection with gonorrhoea and chlamydia in women are usually asymptomatic. Untreated infections may migrate upwards from the lower genital tract and lead to pelvic inflammatory disease, chronic pelvic pain, ectopic pregnancies, and infertility. Additionally, untreated infections in pregnant women could result in fetal loss, stillbirths, low birth weight, or disease in newborn. Furthermore, STDs enhance HIV transmission<sup>2,3</sup>.

## 2. Interaction between STDs and HIV infection

Classic STDs promote HIV transmission via a variety of biological mechanisms by increasing either the infectiousness of the index case, the susceptibility of the partner, or both<sup>3,4</sup>. STD pathogens could disrupt mucosal tissues, and/or increase the number of cells receptive to HIV, and/or the number of receptors expressed per cell. Cohen with co-workers observed an eight-fold increase in secretion of HIV-1 RNA in semen of patients with urethritis in comparison to the control group without urethritis, with gonorrhoea and trichomoniasis having the most substantial effect<sup>5</sup>. Co-infection with HIV prolongs or augments the infectiousness of individuals with STDs, and if the same STDs facilitate transmission of HIV, these infections may greatly amplify one another ("epidemiological synergy")<sup>6</sup>.



### 3. Epidemiology of STDs

#### 3.1. Sources of information

The two main sources of information on the prevalence and incidence of STDs are surveillance systems (case-notification reports) and epidemiological studies. Nevertheless, the exact magnitude of the STDs burden is frequently unknown<sup>8</sup>. The data from the passive STD surveillance systems is not always reliable or complete. The quality and completeness of the available data and estimates depend on the quality of STD services, the extent to which patients seek health care, the intensity of case finding and diagnosis and the quality of reporting. The completeness is further affected by the STD's natural history since a large number of infections are asymptomatic. Moreover, only part of the symptomatic population seeks health care and even a smaller number of cases are reported. The social stigma that usually is associated with STDs may result in people seeking care from alternative providers or not seeking care at all. As a result, report-based STD surveillance systems tend to underestimate substantially the total number of new cases<sup>8</sup>.

In Estonia, the surveillance of STDs and HIV infection is based on the mandatory universal notification of the newly identified cases to the Counties Health Protection Bureaus, which in their turn send monthly reports to the Health Protection Inspectorate. Syphilis, gonorrhoea, trichomoniasis, chlamydial infection, genital herpes and anogenital wart virus infections, as well as HIV infection are all notifiable, and all physicians are compelled to report on them.

### 3.2. Global estimates for major STDs

The incidence and distribution of STDs varies across space and time<sup>7</sup>. In 1999, the WHO generated the global estimates for four major STDs. These estimates suggest that there were more than 340 million new cases of curable STDs in adults aged 15–49 years in 1999: syphilis (12 million cases), gonorrhoea (62 million cases), chlamydia (92 million cases), and trichomoniasis (174 million cases)<sup>8</sup>, with an estimated 22 million STD cases in Eastern Europe and Central Asia (syphilis: 100.000 cases; gonorrhoea 3.5 million cases; chlamydia 6 million cases; trichomoniasis 12.4 million cases)<sup>1,8</sup>. Geographically, the vast majority of these new cases occurred in the developing world (the Third World countries) (South and Southeast Asia, Sub-Saharan Africa, Latin America and the Caribbean), which reflects the global distribution of population.

Based on global serological evidence, even more incurable viral infections are transmitted each year via the sexual route<sup>9</sup>.

### 3.3 Specific STDs

#### 3.3.1. Syphilis

In Western Europe, syphilis prevalence has declined substantially since the peak after the World War II, with incidence rates below 5 / 100 000 in the majority of countries<sup>10,11,12</sup>. In contrast with the decline in rates observed in Western Europe, there has been an alarming increase of the rates in the newly independent states of the former Soviet Union since 1989<sup>13,14</sup>. In Estonia syphilis incidence has increased from 3.3 / 100 000 observed in 1990 to as high as 75.7 / 100 000 of population in 1998<sup>15</sup>.

#### 3.3.2. Gonorrhoea

In the years 1980–91, Western Europe experienced, a significant decline of incidence of gonorrhoea, which reached below 20 / 100 000 of population.<sup>10,17</sup>

However, since mid 1990s, an increase in cases of gonorrhoea has been observed in some countries (England<sup>18</sup>, Sweden<sup>19</sup>). An substantial increase in gonorrhoea rates has been detected in Eastern Europe, and in the new independent states of the former Soviet Union (with the highest rate in Estonia, Russia and Belarus)<sup>8</sup>.

### 3.3.3. Chlamydiosis

Genital tract infection caused by *Chlamydia trachomatis* is a common cause of pelvic inflammatory disease with subsequent risk for infertility. The higher prevalence of chlamydia observed among female adolescents (24.1%–27%)<sup>20,21</sup>, and the association with young age<sup>22</sup> highlights the important role that screening of sexually active female play in the prevention of infertility. In Europe, prevalence of chlamydia infection amongst pregnant women ranges from 2.7% in Italy to 8% in Iceland, with low prevalence and incidence rates in the Nordic countries, following a wide scale screening programmes in the 1970s<sup>23–27</sup>. Prevalence data regarding the former Soviet Union countries is limited or missing.

### 3.3.4. Trichomoniasis

In spite of the fact that trichomoniasis is the most common of STDs, the data on its prevalence and incidence are limited. High rates of *Trichomonas vaginalis* infection have been found in the developing countries<sup>28,29</sup> and in the industrialised countries<sup>30,31</sup>. Recently published findings suggest that, even in the industrialised countries, diagnostic evaluation and empirical treatment of older men with non-gonococcal urethritis<sup>32</sup>, and partner management in both sexes should include treatment for *Trichomonas vaginalis*<sup>32,33</sup>.

In Estonia, trichomoniasis is the most prevalent non-viral STD, with high incidence over decades<sup>15,16</sup>.

**Table 1.** STD incidences per 100 000 of population in different countries in 1998

	Syphilis	Gonorrhoea	Chlamydiosis	Trichomoniasis
<b>Estonia</b> <sup>16</sup>	75.7	137	237	267
<b>USA</b> <sup>102</sup>	2.6	133	237	–
<b>Russian Federation</b> <sup>103</sup>	235	130	114	317
<b>United Kingdom</b> <sup>104</sup> *	0.4	28	96	–
<b>Finland</b> <sup>105</sup>	3.6	5.2	207	–
<b>Latvia</b> <sup>106</sup>	106	50	–	–
<b>Lithuania</b> <sup>106</sup>	63	40	–	–

\* 1999

### 3.3.5. Genital herpes

Genital herpes is one of the most common STDs worldwide and is associated with serious morbidity with a chronic course with unpredictable occurrence of recurrences<sup>34,35</sup>. Genital herpes continues to be epidemic throughout the world<sup>34,35,36,37</sup>. The HSV type-specific serological tests have revealed varying

patterns of HSV infection around the world, with HSV 2 infections being far more common than previously suspected<sup>34</sup>, and that HSV 2 seroprevalence is rising in many developed countries<sup>36,38,39</sup>.

Epidemiological studies of HSV-2 infections have been conducted in several countries including the United States, the United Kingdom, Germany, France, Italy and Scandinavia<sup>36,37,40-44</sup>. HSV-2 seroprevalence ranges from 10 to more than 20% in most of the studies and is higher among the patients in STD clinics. The data describing increasing incidence of primary HSV 1 infection, suggest that seroprevalence studies based on HSV-2 type-specific assays underestimate overall prevalence of genital herpes<sup>45</sup>.

### 3.3.6. HIV infection

The human immunodeficiency virus (HIV) that causes AIDS has caused a global epidemic far more extensive than what was predicted even a decade ago. The UNAIDS and the WHO now estimate the number of people living with HIV or AIDS stands at 36.1 million at the end of the year 2000. The regions most affected by HIV epidemic are Sub Saharan Africa (adult — 15 to 49 years of age — prevalence rate 8.8%), Caribbean (adult prevalence rate 2.3%), and South and South-East Asia (adult prevalence rate 0.56%)<sup>46</sup>.

Taking into account the continuing expansion of the epidemics in Russian Federation (more new HIV infections registered than in all previous years) and the Ukraine, by the UNAIDS and the WHO estimates, the number of adults and children living with HIV or AIDS in Eastern Europe and Central Asia would be 700 000 by the end of the year 2000 (adult prevalence rate 0.35%), compared with 420 000 just a year ago<sup>46</sup>. Injecting drug use has played a major role in the spread of HIV in Europe. Several countries in Western Europe have reported declining HIV incidences among the drug users during the last decade<sup>47</sup>. In contrast, the dramatic increase in HIV incidence in the countries in Eastern Europe and in the Russian Federation can be attributed primarily to injection drug users<sup>48,49</sup>. Until the end of 1999, Estonia and Turkmenistan were the only successor states of the Soviet Union, where almost no HIV infections among injecting drug users (IDU) had officially been reported<sup>49</sup>. In year the 2000 Estonia dropped out of the “league of successors” with the HIV epidemic among IDUs.

The data from epidemiological surveys show that within countries and between countries in the same region, the prevalence and incidence of STDs may vary widely between urban and rural population, and even in similar population groups<sup>8</sup>. In general, the prevalence of STDs tends to be higher in urban residents, in unmarried individuals, and in young adults. STDs tend to occur at a younger age in females than in males, which may be explained by differences in

patterns of sexual activity and in the relative rates of transmission from one sex to the other<sup>8</sup>.

These differences reflect a variety of social, cultural, and economic factors, and also differences in the access to the appropriate treatment.

#### **4. Factors affecting the transmission of STDs**

Determinants of STD incidence have been described at the individual and population level analysis. At the individual level in epidemiological studies, various sociodemographic characteristics and sexual, health and substance abuse behaviours emerge as risk factors or risk markers for being infected with STDs. At the population or community level various economic, demographic, organizational, and sociocultural characteristics of populations may correlate strongly with STD incidence. At the individual and community level, determinants of STD risk tend to be strongly associated with one another and reinforcing and magnifying mutual effects<sup>50,51</sup>.

##### **4.1. Individual level factors: behavior as risk factors for STD**

Individual-level factors affecting health can be categorised as biogenic (e.g. immunologic competence), psychological (e.g. self-esteem) and behavioural<sup>51</sup>.

###### **4.1.1. Sexual behaviours**

The dimensions of sexual behaviour that increase risk for infection with STD include: early age at sexual debut, large numbers of lifetime and current sex partners, nondiscriminating sex partner recruitment patterns, high-risk characteristics of sex partners, specific sexual practices, such as anal intercourse and dry sex, frequency and timing of the sexual intercourse, sexual abuse during childhood<sup>50</sup>.

###### **4.1.2. Health behaviours**

Several health behaviours affect a persons risk for STD. Either decreasing risk (consistent and proper condom use, male circumcision, timely health care seeking, compliance with therapy and behaviour recommendations, including abstaining from sexual intercourse while having STD symptoms) or increasing it (unprotected sex, vaginal douching)<sup>50</sup>.

### 4.1.3. Substance abuse

Drug use in general constitute a risk factor for sexual transmission of STD. Drug use is associated with anonymous sex and sex exchange for drug and money; it also reduces the likelihood that safe sex will be practiced. Substance abuse (including alcohol abuse) increases the risk having STDs independently from the effects of age, race, age at sexual debut, and number of partners<sup>50,52</sup>.

In general, risk behaviours tend to occur together.

## 4.2. Community level factors related to STDs

Research on the epidemiology of STDs has dealt predominantly with individual-level factors. The awareness of the importance of other factors beside individual level factors that contribute to the disease rates is growing (“Syphilis as a barometer of community health”)<sup>53,54</sup>.

The environmental factors affecting health are geographic (e.g. rurality), structural and technological (e.g. availability of a vaccine or cure), sociocultural (e.g. social support)<sup>51</sup>, as well as economical. Considerable variations in the incidence of STDs assert the social pattern of these diseases<sup>55-58</sup>.

The factors of the sociophysical environment associated with the STD community rates are geographic (urban areas, proximity to major motorways), structural and technological (the availability of treatment services and the provision of treatment, number of physicians, disease prevention programs, STD outreach programs, needle the exchange programs among injecting drug users, social marketing and condom distribution, expenditures for education), sociocultural (gender subordination, nationality/race relations, rate of violent crime, birth rate) and economic (mean income, unemployment rate)<sup>55-58</sup>.

The origins of public health and public order overlap to a great extent and they are embedded in the security and stability of personal, domestic and community networks and other institutions. Disruption of such networks will lead to increase of violence, sexuality, substance abuse and general criminality<sup>80,92</sup>. Social disintegration has shown to exacerbate epidemics of other infectious diseases beside STDs, including tuberculosis<sup>59</sup>.

## 5. The management of STDs

The effective management of STD is one of the cornerstones of STD control, as it prevents the development of complications and sequelae (including infertility, fetal wastage, ectopic pregnancy, anogenital cancer, premature death, neonatal and infant infections), decreases the spread of these diseases in the community

and offers a unique opportunity for targeted education about HIV prevention. Appropriate treatment of STD patients at their first encounter with a health care provider is, therefore, an important public health measure<sup>60-64</sup>. The individual and national expenditure for STD care can be substantial.

### **5.1. STD case management**

STD case management is the care of a person with an STD-related syndrome or with a positive test for one or more STD. The components of case management include: history taking, examination, correct diagnosis, early and effective treatment, advice on sexual behaviour, promotion and/or provision of condoms, partner notification and treatment, case reporting and clinical follow-up as appropriate. Thus, effective case management consists not only of antimicrobial therapy to obtain cure and reduce infectivity, but also comprehensive care of the patient's needs for reproductive health.

### **5.2. Standardized protocols for management of STDs**

The use of appropriate standardized protocols is recommended in order to ensure adequate treatment at all levels of the health service. Such standardized treatment also facilitates the training and supervision of health providers, delays the development of antimicrobial resistance in sexually transmitted agents such as *Neisseria gonorrhoeae* and *Haemophilus ducreyi*, and is an important factor in rational drug procurement<sup>60-64</sup>.

### **5.3. STD management approaches: aetiological and syndromic**

Aetiological approach (i.e. identification of microorganisms prior to the treatment), although correct, avoiding over-treatment and unwanted adverse drug reactions is expensive in terms of laboratory costs and it may lead to delayed diagnosis and treatment, and might carry the risk of stigma if the clinic is designated as an STD clinic<sup>61,62</sup>.

To overcome the limitations and the expense of aetiological management of STDs, the WHO emphasises an integrated primary care approach using syndromic management<sup>61,62</sup>. Syndromic management is based on the identification of consistent groups of symptoms and easily recognized signs (syndromes), and the provision of treatment that will deal with the majority or most serious organisms responsible for producing a syndrome<sup>61,62</sup>. In order to maximise the value of the syndromic approach, the prevalence of the various STDs and their susceptibility to antibiotic treatment need to be known<sup>61,65</sup>.



Estonia has traditionally, managed STDs on an aetiological basis (laboratory-based system of diagnosis). Economic difficulties, market reforms and political restructuring have had a detrimental impact on the healthcare system. Medical services have not received sufficient financial support<sup>4,5</sup>. Limited resources have led to a situation where specialist STD services are of limited availability, and external quality control for laboratory services is absent. STD management is further complicated by the lack of consensus between different specialists (dermatovenerologists, gynecologists, urologist, general practitioners) who deal with STD related problems.

## 6. Diagnosis of STDs in Estonia

Syphilis is diagnosed both clinically and in the case of a primary chancre or secondary mucosal lesions by dark ground examination of secretions from the lesion for identification of *Treponema pallidum*. All cases, whether associated with clinically manifested infection or not, are confirmed using serological tests. Blood is screened using either the Rapid Plasma Reagin (RPR) test or the Venereal Diseases Reference Laboratory (VDRL) test. Confirmation is with the *Treponema Pallidum* Haemagglutination Assay (TPHA) and/or the Fluorescent Treponemal Antibody-Absorbed (FTA-Abs) test or by immuno-blot testing. Antigen detection methods (Enzym immuno assay, Immunofluorescence assay) for diagnosing of chlamydial infections became available in 1990 and *Chlamydia trachomatis* culture a few years later. Detection of chlamydial infection with the help of DNA amplification tests (Polymerase chain reaction — PCR) is not widely available. Gonorrhoea is diagnosed on microscopy of a Gram stained smear of genital secretion and by culture on a selective medium. Trichomoniasis is identified on microscopy of a wet preparation and by a culture that is, taken from urethra or vagina. Availability of cultural and DNA-based diagnostic methods is limited to the bigger medical institutions with the suitable laboratory back up.

The diagnosis of genital herpes is frequently made clinically by exclusion of other reasons for genital ulcers. Antigen detection is restricted, so far, to a few centres and identification by culture method is not available in Estonia. Detection of HIV antibodies in Estonia is done by a uniform use of internationally accepted ELISA kits (*Abbott*, USA; *Ortho Clinical Diagnostics*, USA; *BioRad*, France) and positive results are verified by immuno-blot method (*Ortho Clinical Diagnostics*, USA; *BioRad*, France; *Innogenetics*, Belgium).

## AIMS OF THE STUDIES

The general aim of these theses was to elucidate the epidemiology of sexually transmitted diseases in Estonia, with the emphasis on the post-communist transition period (1990–2000). Specifically, the aims were:

1. to evaluate the situation with STDs in Estonia: incidence trends, aetiology (Papers I, III, IV, VI); including the secondary aim to define whether infection with *Trichomonas vaginalis* is common enough to include its management in a syndromic management protocol (Paper III)
2. to identify the individual level risk factors and community level factors that may account for the increase in the incidence of STDs — for possible implication for disease prevention and control (Papers II, IV, V)
  - to delineate factors sexual / health behaviour and substance (alcohol, narcotics) abuse contributing to the STD epidemic in Estonia (Papers II, IV)
  - to study the community-level associations and incidence rate of syphilis in Estonia during the post-communist transition period (Paper V)

# MATERIAL AND METHODS

## 1. Data collection on STDs

The data on STDs number of cases and incidence were obtained from the national STD case surveillance register; HIV, syphilis, gonorrhoea, trichomoniasis, chlamydial infection, genital herpes and anogenital wart virus infections cases are reported to the Health Protection Inspectorate (reporting in obligatory for the physicians according to the decrees nr. 25 from 12.06.97 and nr. 59 from 07.01.99 of the Ministry of Social Affairs of Estonia). (Papers I, III, IV, V)

Until 1998 the data included a patient's personal identification number. We used this to find out people with several concomitant infections and/or persons with frequently diagnosed STDs. (Paper III)

The county syphilis rates were calculated with the Statistical Office of Estonia population count estimates<sup>66</sup> (1991 through 1999) as the population denominator. (Paper V)

## 2. Settings, subjects and study designs

### Paper II

Study activities took place at the Tartu University Clinic of Dermatovenerology.

A case control methodology was used.

Between 9/1996 and 6/1998, 301 men and women over the age of 18 were recruited.

*The cases* were composed of all the participants who presented for care to the Tartu University clinic of Dermatovenerology with a diagnosis of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Treponema pallidum* infections. Of the 229 clinic registrants approached for study participation, 189 enrolled as cases.

*The controls* were selected at random from the regional population registry. The selected participants were sent a letter describing the study and requesting them to contact study representatives at Tartu University Clinic of Dermatovenerology. A total of 1,100 letters were sent from the registry, and 112 persons responded and were enrolled as the controls. The controls were further divided as a function of their STD status at the time of enrolment.

*The procedures.* After providing informed consent for their participation, all the patients who engaged in the study were asked:

(1) to complete a self-administered questionnaire.

Participants were asked to report on their lifetime history of STD diagnosis prior to study entry, drug use, and of paying for sexual activity. The prevalence

of alcohol-related problems was determined via the four-item CAGE questionnaire<sup>67</sup>. Respondents also answered to a series of questions on behaviour in the last 3 months, including whether they had been sexually active, had had more than three sexual partners, had used condoms consistently (always or almost always), had engaged in sexual activity while drunk, had offered money to someone in exchange for sex, had had a casual sexual partner, had been engaged in anal sex, and whether they had used illicit drugs. Additional questions focused on whether respondents believed that their current sexual partners had had other sexual partners in the last 3 months and whether they had travelled outside Estonia in the past year. Finally, ratings were conducted on beliefs regarding STD prevention. The perceived efficacy of different activities, such as washing the genital area after having sex, urinating after sex, condom use, douching after sex, and using birth control pills, in preventing the transmission of STD was assessed on three-point scales (ineffective, effective, don't know).

(2) to participate in an examination in which cervical or urethral cultures were obtained for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (Thayer-Martin medium, Nouva Aptaca SRL, Italy; McCoy cell monolayers, European Collection of Cell Cultures, Salisbury, UK), and venous blood was drawn to determine syphilis serologic status (Rapid Plasma Reagin test with fluorescent treponemal antibody test for confirmation).

**Statistical analysis.** Demographic and behavioural variables were compared across groups (i.e., cases, controls with STD, controls without STD) using the Fisher exact test for dichotomous variables and t-tests for continuous variables. Beliefs about STD transmission were compared across groups using likelihood ratio chi-square tests. Odds of having an STD associated with engaging in a series of sexual risk behaviours were estimated among those who reported sexual activity in the last 3 months via logistic regression models, with group and sex included as main effects and a product term included to assess moderator effects. Demographic and behavioural factors that differentiated group memberships based on these analyses were selected for inclusion in a multinomial logistic regression model.

**Ethics.** All study procedures were approved by the Ethics Board at Tartu University and by Institutional Review Board at State University of New York Downstate Medical Center.

## **Paper V**

An ecological study methodology was used.

### ***Periods of post-Communist transition***

Lauristin et al. have divided the post-communist transition in Estonia into the three periods<sup>68</sup>.

I 1987–1991 — The liberation movements and political breakthrough.

II 1991–1994 — The restoration of the independent statehood involving radical political reforms.

III 1995–present day — The emergence of a stable democratic system, economic and cultural stabilization.

We chose the data of the last years of the first two periods (1991, 1994) and 1999 as the last year of the third period as for the samples in our statistical analysis.

***Sociodemography of counties.*** The data used in the analysis were provided by the Statistical Office of Estonia<sup>66,69</sup>. Administratively, Estonia is divided into 15 counties, the smallest with the population of approximately 12,000 and the largest of 535,000. The available sociodemographic characteristics of the counties were reviewed, and possible markers of socially disruptive situation; unemployment as a new phenomenon in post-communist countries; two basic demographic variables, and the tuberculosis incidence rate per 100,000<sup>15,16</sup> were selected for more detailed analysis. These characteristics were:

- (1) the percentage of the non-ethnic Estonians in the population
- (2) the percentage of urban population
- (3) the rate of homicides per 100,000
- (4) the unemployment rate per 100
- (5) the number of live births per 1000 females at age 15–49

### ***Statistical methods.***

The regression coefficients and the explained variance values were estimated by the ordinary least square regression. A five per cent significance level was chosen for the p-value of the regression coefficient. Pearson correlation coefficients were calculated.

## **Paper VI**

Study activities took place at the Tartu University Clinic of Dermatovenerology, Children Hospital, and Hospital of Obstetrics and Gynaecology, South Estonian Blood Centre and United Laboratories Tartu University Clinics.

A cross sectional methodology was used.

***Procedures.*** A consecutive series of altogether 2845 sera from 1,016 children (aged 1–12), 794 1st trimester antenatal women (aged 15–44) and 1,036 blood

donors (aged 18–66) whose serum samples had been submitted for serological analyses of non-HSV-related diseases were obtained during the first 5 months of year 2000.

Blood donation is voluntary and non-paid in Estonia; screening for blood-borne infections is mandatory. Blood samples from pregnant women are always drawn for screening of congenital infections before week 12 of gestation. Children sera were submitted from in- and out patient clinics for biochemistry testing.

**Laboratory methods.** Baculovirus expressed glycoprotein gG1 and gG2 were used as antigen in ELISA for detection of HSV-1 and HSV-2 IgG antibodies by using commercially available laboratory tests (MRL Diagnostics, Cypress, USA).

**Ethics.** The Ethics Board of Tartu University approved all study procedures.

This study was supported by GlaxoWellcome R&D.

# RESULTS

## 1. The post-communist transition period in Estonia

During the first ten years of independence, a decrease in agricultural and industrial production occurred, and the economy became more oriented towards provision of services. The role of industrial production declined from 39% to 31% in 1991-1995, and then it became stabilized. Approximately 6% of Gross Domestic Product (GDP) is spent on health care. The two main sources of revenue for health care provision in Estonia are the health insurance system and the state budget. The public health insurance embraces about 90% of the Estonian population; it is based on residency, not citizenship.

Basic general statistical data show that the health of Estonians has been deteriorating since 1990. The death rates due to cardiovascular diseases, accidents and poisonings have all risen. In 1994 life expectancy was lowest, being for men 61.1 years and for women 73.1, the former having declined from 66.5 and the latter from 74.9 in 1988<sup>66</sup>, however some signs of improvement have been noted in recent years.

The ethnic composition of the Estonian population has been stable in the past decade. Ethnic Estonians comprise about two thirds of the total population. There are two regions where the proportion of the non-ethnic Estonians in the population is considerably higher than in other places in Estonia: in Tallinn, the capital of the Republic of Estonia, non-ethnic Estonians make up nearly 50% and in the Ida-Virumaa County (in the North East of Estonia) 72% of the population. During the 1990s, the proportions of urban (~70%) and rural (~30%) population in Estonia were stable (Figure 1c).

The number of live births has continuously decreased in Estonia during this period. The decrease was more rapid in the first half of the 1990s. The decline in fertility slowed down in 1993, and a signs of rise in the birth rate began in 1999 (Figure 1b).

A clear trend can be seen while studying the data on homicides in Estonia over the 1990s. The number of homicides began to increase at the beginning of the decade. In first period, the homicide rate was more than 8.7 / 100 000. The worst year was 1994, with 365 homicides, a rate of 24.4. In the third period, the rate of homicide was less than 14 / 100 000. The places of the highest crime levels were Tallinn, Narva and Ida-Virumaa County.

Unemployment was virtually non-existent during the years of socialism. After the collapse of the Soviet Union, unemployment maintained a steep and steady growth tendency. In 1996, the unemployment rate stabilized at about 8%, to start a new rise and reached 12.8% in 1999-2000 under the impact of the Russian economic crisis (Figure 1b).

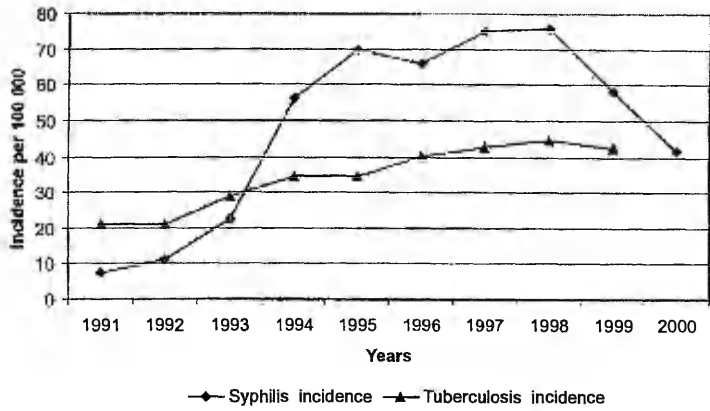


Figure 1a. Incidence of syphilis and tuberculosis in Estonia.



Figure 1b. Homicide, unemployment and birth rate in Estonia.

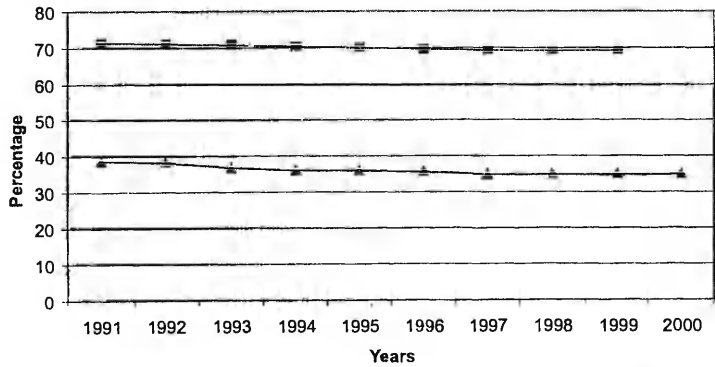


Figure 1c. Percentage of non-ethnic Estonian and urban population in Estonia.

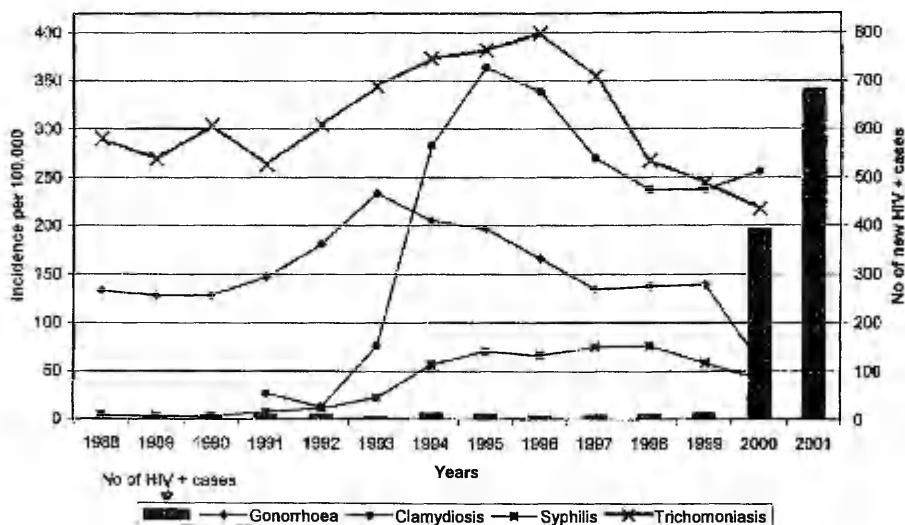
Figure 1. Selected sociodemographic factors, 1991–2000.



The incidence of tuberculosis rose from 21.5 per 100 000 in 1991 to 42.3 per 100,000 in 1999. The majority of the infected were men (approximately 70%), and the most affected age group was those between 35–55 (Figure 1a).

## 2. STDs in Estonia in 1990–2000: incidence trends, aetiology (Figure 2)

The syphilis incidence increased from 3.3 per 100 000 in 1990 to 75.7 in per 100 000 in 1998, a decline in incidence is observed thereafter (also Figure 1a). The available data reporting the ratio of male to female new cases of syphilis during the period is quite constant, not exceeding 2:1. Syphilis is most prevalent in young adults: in 1992 35% of the infected women were younger than 20 and 67% of women and 52% of men were younger than 25 years of age. After many decades, congenital syphilis was again diagnosed in 1993. Syphilis is focally distributed in Estonia; with the striking local differences in the incidence rates. There are two counties of the highest syphilis (STD) rates: Tallinn, the capital of the Republic of Estonia and Narva, the 3rd largest city situated in the North – East of Estonia, near the Estonia’s border with the Russian Federation



**Figure 2.** Incidence of reported STDs and absolute numbers of HIV positive cases in Estonia, 1988–2000.

In Estonia the incidence of gonorrhoea is high and almost doubled from 128 / 100 000 in 1990 to 233 / 100 000 in 1993, but a decreasing thereafter (60 / 100.000 in 2000). The male to female ratio has remained stable, and as for syphilis not exceeding 2:1. The majority of affected individuals of both sexes were younger those than 30 years of age. The difference between the two sexes could only be observed in the age group under 20, in which approximately 40 % more females than males were reported e.g. in 1991 and 1992.

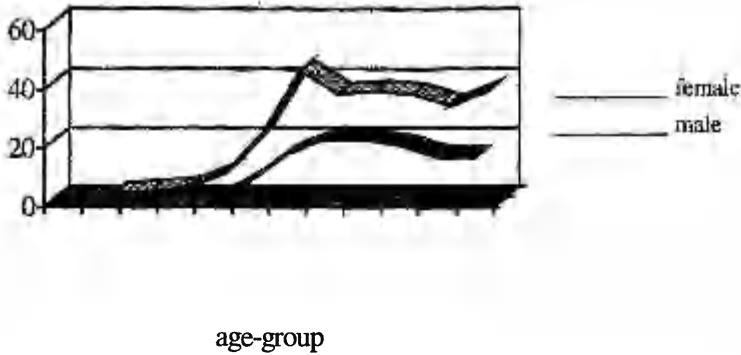
***Chlamydia trachomatis***. Almost two thirds of the reported cases were males in 1991 and 1992 (the testing was primarily done by dermatovenerologists in symptomatic cases). With increased screening of contacts and asymptomatic individuals the pattern has completely changed. In 1993 and 1994 over 80 % of reported new cases were females. Beginning from 1994 chlamydial genital infections outnumbered the reported new cases of gonorrhoea.

According to reported data ***Trichomonas vaginalis*** infections are the most prevalent STD in Estonia. The increase in incidence started in early 1990s (303.8 / 100 000 in 1990), and is followed by decrease since 1996 to 217 / 100 000 in 2000. In 1996, the reported incidence was 399.5 / 100 000, being the leading STD for men, and frequent cause of male urethritis (Figure 4). Nevertheless, approximately 75 % of the reported patients were females and the most affected age group is that of individuals between 20–24 years.

***Genital herpes*** has been a reportable disease since 1991, with an increasing incidence over the last 10 years (0.9 / 100 000 population in 1991, 23.9 / 100 000 in 2000). The magnitude of genital herpes problem is unknown, and the increasing trend in current context is most likely indicative of wider recognition of the disease by doctors and patients, availability of diagnostic possibilities, and less reliable in describing actual epidemiological situation.

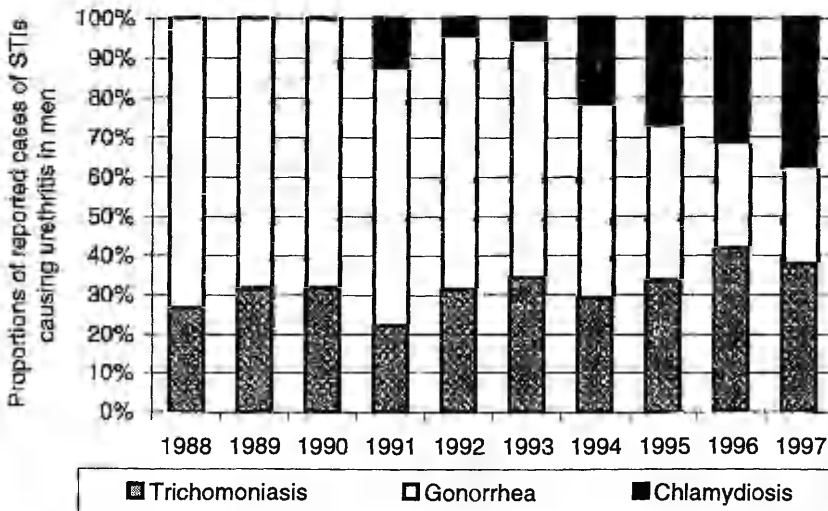
According to the study results, seroprevalences for HSV-2 among children, pregnant women and blood donors were 0.5%, 23% and 16%, respectively. A sharp increase in HSV-2 seroprevalence was detected among subjects of 15–40 years of age; but at higher magnitude for women (Figure 3). We found a statistically significant difference ( $p < 0.0002$ ) in HSV-2 seroprevalence among male blood donors (11%) and female blood donors (21%). A similar increase in HSV-2 seroprevalence by age was found among blood donors and pregnant women.

Starting with 1987, the total number of reported HIV seropositive cases has been 1169 with the male/female ratio of 914 / 255. The numbers of HIV infections have remained very low until recently, even when a considerable rise in the incidence of sexually transmitted diseases, especially syphilis, was recorded over those years. After the first HIV positive case was recorded in 1988, there were 96 cases by 1999. In 2000, a dramatic increase in HIV cases occurred: 357 new HIV positive cases were reported during the last 4 months of the year 2000, and additional 683 cases during the first 5 months of the year 2001. The available data on the transmission categories of HIV testing single out groups in



**Figure 3.** Proportions of seropositives to HSV-2 antibodies by age and gender.

Estonia with a high HIV incidence — STD patients, sailors, and the sexual contacts of HIV-positive persons. According to the data of 2000, we have to add a new main transmission category group at risk to those mentioned above — the injecting drug users (IDU). Before 1999, only one out of 96 HIV+ cases was categorized as an illegal drug user. The cumulative data, including the information recorded on HIV testing forms and clinical records testify to the fact that IDU was a factor in nearly 90% of the new HIV cases reported in the year 2000. The majority of new HIV+ cases (797 (74%)/1037) in 2000 and 2001 are reported to be the residents of the North-East of Estonia, and this epidemic is clearly driven by injection drug use.



**Figure 4.** Proportions of reported cases of STDs causing urethritis in men in Estonia 1988–1997.

### **3. Analysis of STD data reported to the Health Protection Service in Tartu district**

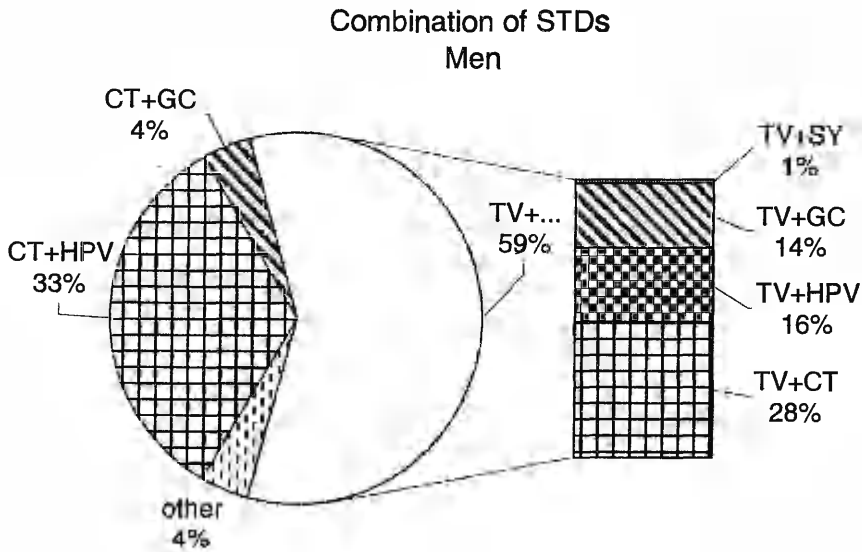
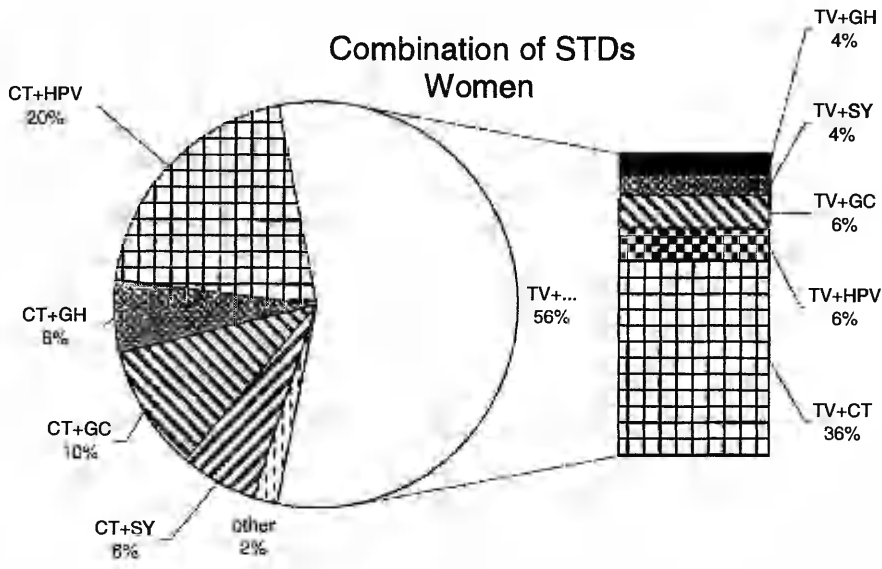
In 1998, in Tartu city and its district, 1558 cases of STDs were reported from 19 different medical facilities. The male to female ratio was 41:59. There were 61 cases of syphilis, 92 cases of gonorrhoea, 386 cases of trichomoniasis, 673 cases of chlamydial infection, 90 cases of genital herpes and 256 cases of anogenital wart infection. Of those 1558, 1387 cases (1219 individuals) were eligible for further analysis of concomitant infections. In 1998, 46 females (5.8%) and 74 males (17.6%) were reported to have co-infection with at least two different STDs during the same clinical episode. The most frequent combination in women was, co-infection with *Chlamydia trachomatis* and *Trichomonas vaginalis* (36%). In women with more than one infection, *Trichomonas vaginalis* was found in 56% of the cases (Figure 5). In men, *Trichomonas vaginalis* infection was accompanied by chlamydial infection in 28% of the cases and by genital wart virus infection in 16% of the cases. In men with more than one infection, *Trichomonas vaginalis* was found in 59% of the cases (Figure 5).

Co-infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* was found in only 9 patients (0.7% of all patients) and the detection of more than two STDs, simultaneously, was very rare (13 patients, 1.1% of all persons with STDs). Of those with more than two infections 85% were men. 2.9% of the patients with proven STDs had repeated episodes within the same year.

Finally, underreporting of STD cases is obvious. All medical facilities are supposed to report their data to the Health Protection Service. In spite of that, in Tartu city and its district, 98% of the cases of syphilis, 90% of the gonorrhoea cases and 97% of those notified with genital wart virus infection were reported from the University Clinic of Dermatovenerology (STD Clinic). Furthermore, 96% of the cases of trichomoniasis in men and 97% of the cases of chlamydiosis in men were reported from the University STD Clinic.

### **4. Factors sexual / health behaviour and substance (alcohol, narcotics) abuse contributing to the STD epidemic in Estonia**

Participant characteristics. Of the total study participants, 225 (74.7%) tested positive for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Treponema pallidum*. Of the 189 cases, 71% were positive for chlamydia, 24.1% for gonorrhoea, and 25% for syphilis, 15 were positive for gonorrhoea and chlamydia, 11 for syphilis and chlamydia, 1 for syphilis and gonorrhoea, and 1 for all STDs. Of the 112 controls, 36 (32.1%) were positive for at least 1 STD; 33 for chlamydia, 2 for gonorrhoea, and 1 for gonorrhoea and chlamydia. No



(abbreviations: CT — chlamydia, TV — trichomoniasis, HPV — anogenital HPV infection, GC — gonorrhea, GH — genital herpes, SY — syphilis).

**Figure 5.** Combination of STDs.

controls were positive for syphilis. The controls with STD were more likely to test positive for chlamydia than the cases (94.4% versus 71.0%,  $p < .05$ ), and less likely to test positive for gonorrhoea (8.6% versus 24.1%,  $p < .05$ ).

Respondents' age ranged from 18 to 57 (Mean = 26.5, SD = 6.4). A small majority of respondents were female (56.7% versus 43.3% male). The cases tended to be younger than the controls; 67.5% of those fell below the median age of 25, as opposed to 50.0% of the controls who presented with an STD, and 36.6% of controls who were not positive for any STD ( $p < .05$ ). Approximately half (54.0%) of the participants included in the study were either married or living with a sexual partner. The majority (80.7%) reported that they were Estonian, and 15.9% reported a Russian background. A history of drug use was reported by 15.1% of the entire sample, with 6.6% reporting a drug use in the past 3 months. The drugs reported by those who had used in the past 3 months included marijuana ( $n = 6$ ), cocaine ( $n = 4$ ), and amphetamines ( $n = 6$ ). Injection heroin use was reported by 1 respondent, who also declared using ketamine. The prevalence of a clinically significant CAGE score was 35.2% across the entire sample.

There were no statistically significant differences between the cases, the controls with STDs, or the controls without STDs in terms of sex, marital status, employment rates, drug use history, or CAGE scores.

Beliefs about STD prevention. Both the cases and the controls held misperceptions about methods for preventing the transmission of STDs, although there were no statistically significant group differences in terms of level of knowledge. Across the entire sample, 65.2% believed that washing the genital area after sex is an effective means for preventing STDs (6.3% reported that they did not know), 25.7% believed that urinating afterwards is effective (35.8% did not know), 35.5% believed that douching is effective (43.8% did not know), and 19.5% believed that using birth control pills is effective (22.2% did not know). Most of the participants believed that condoms are effective for STD prevention (94.5%); 3.1% claimed that they were unsure about their efficacy.

Univariate behavioural associations with group membership (Table 2). Across all groups, the respondents reported that they had recently engaged in a series of sexual behaviours (Table 1). In logistic regression models, there was a main effect of group membership after controlling for sex across several behaviours, including the proportion who reported (1) having a previous STD diagnosis (58.1% cases; 26.5% controls with STDs; 40% controls w/o an STD), (2) having three or more sexual partners in the last 3 months (21.0% cases; 5.7% controls with an STD; 8.5% controls without an STD,  $p < .05$ ), (3) having a casual sexual partner in the last 3 months (43.0% cases; 20.6% controls with an STD; 20.3% controls without an STD,  $p < .05$ ), and (4) engaging in sexual

**Table 2.** Univariate logistic regressions predicting behavior as a function of group and sex

	Cases (%) (N = 189)			Controls w/o STD (%) (N = 76)			Controls w/ STD (%) (N = 36)		
	M	F	Total	M	F	Total	M	F	Total
Lifetime history of STD*	55.2	60.6	58.1	29.0	47.7	40.0	27.3	26.1	26.5
Lifetime history of drug use †	24.4	12.0	17.7	19.4	6.8	12.0	18.2	4.0	8.3
CAGE score indicative of alcohol problems †	56.8	19.8	37.0	64.5	18.2	37.3	36.4	16.0	22.2
Travel outside Estonia in the last year ‡	46.0	32.0	38.5	16.1	31.8	25.3	45.5	36.0	38.9
Abstinent last 3 months	9.3	9.0	9.1	20.7	16.7	18.3	27.3	12.5	17.1
Three or more sexual partners last 3 months*†	34.9	9.0	21.0	20.7	0.0	8.5	18.2	0.0	5.7
Sexual relationship with a casual partner last 3 months*†	56.3	31.3	43.0	40.0	6.8	20.3	36.4	13.0	20.6
Sexual activity while intoxicated on alcohol last 3 months *†	77.4	58.5	67.4	50.0	38.5	43.1	54.5	45.5	48.5
Believes partner(s) had other sexual relationships last 3 months	17.7	20.2	19.2	9.5	15.8	13.6	0.0	21.1	15.4
Paid for sexual intercourse last 3 months †	13.1	0.0	6.0	3.4	0.0	1.4	9.1	0.0	3.0
Always used condoms last 3 months	18.8	21.3	20.1	.2	18.4	12.9	0.0	15.0	10.7

\*  $p < .05$  main effect of group membership

†  $p < .05$  main effect of sex

‡  $p = .07$  interaction of sex \* group

activity while intoxicated from alcohol (67.4% cases; 48.5% controls with an STD; 43.1% controls without an STD,  $p < .05$ ). In turn, the respondents who reported engaging in sexual activities while intoxicated were more likely to report that in the last 3 months they had been inconsistent condom users (86.3% versus 76.4%,  $p = .055$ ), to have had three or more sexual partners (25.9% versus 6.4%,  $p < .05$ ), to report a casual sexual relationship (52.6% versus 19.6%,  $p < .05$ ), and to have solicited sexual activity (7.8% versus 1.1%,  $p < .05$ ). There were no group differences detected in the proportion reporting lifetime drug use, a high CAGE score, travel outside the country in the last year,

abstinence in the last 3 months, a belief that the respondent's sexual partners had concurrent sexual relationships in the last 3 months, paying for sexual activity in the last 3 months, and always or almost always using condoms in the last 3 months.

There were main effects of sex after adjusting for group membership for (a) lifetime drug use (22.7% males; 9.5% females,  $p < .05$ ), (b) CAGE scores denoting alcohol problems (56.9% males; 18.8% females,  $p < .05$ ), (c) three or more sex partners in the last 3 months (30.2% males; 5.4% females,  $p < .05$ ), (d) the prevalence of a casual sex partners in the last 3 months (50.8% males; 22.3% females,  $p < .05$ ), (e) being intoxicated during sexual activity (69.4% males; 51.6% females,  $p < .05$ ), and (f) paying for sex in the last 3 months (10.5% males, 0% females,  $p < .05$ ).

Product terms were computed between sex and group membership for each behaviour. The interaction predicting travel outside of Estonia in the last year approached statistical significance ( $p = .07$ ), males with STDs were more likely to report travel in the past year (46% cases, 45.5% controls with STD) than were those without STD (16.1% travel for controls without STD). These differences were not seen among women (32% cases, 36% controls with STD, 31.8% controls without STD). Sexual relationships with new partners while travelling in the last year were reported by 16.1% of the male cases, while none of the controls reported this behaviour.

Multivariate behavioural associations with group membership (Table 3). A multinomial logit model was conducted to assess for group differences as a function of age, STD history, travel, casual sexual partners, having three or more sexual partners, sexual activity while intoxicated, and sex (Table 2). A product term representing the interaction of sex and travel significantly increased the fit of the model, and was also included ( $\chi^2$  difference = 6.9,  $df = 2$ ,  $p < .05$ ). The resulting equation was statistically significant ( $\chi^2 = 53.1$  (16),  $p < .05$ ), with age, lifetime history of an STD, sexual intercourse while intoxicated, and the product term of sex and travel differentiating the groups. In terms of age, those less than the median age of 25 were significantly more likely to have an STD than were the controls without an STD (OR = 3.3, 95% CI = 1.7 – 10.0), and the controls with an STD (OR = 3.3, 95% CI = 1.5 – 10.0). The individuals who reported an STD diagnosis prior to the study entry were over four times more likely to be the cases than to be the controls with an STD (OR = 4.2, 95% CI = 1.6 – 11.2). The only sexual behaviour that differentiated group membership after controlling for other factors in the model was whether the respondent had been engaged in a sexual intercourse while intoxicated. Those engaging in this behaviour were three and a half times more likely to be the cases than to be the controls without an STD (OR = 3.5, 95% CI = 1.6 – 7.6). Finally, after controlling for all other variables in the multivariate model, there was a statistically significant interaction detected between having travelled outside Estonia concerning the sex of the respondent for the comparison of the cases versus the controls without STD (OR = 0.1, 95% CI = 0.0 – 0.7), and a



trend toward statistical significance for the comparison of controls with STD versus controls without STD (OR = 0.1, 95% CI = 0.0 - 1.0). These interactions reflect the greater odds of STDs among the males who travelled (OR = 4.4, 95% CI = 1.5 - 16.0).

**Table 3.** Multinomial logit model regressing group membership onto sexual risk behaviors.

	Chi-square (all df = 2)	Cases vs Controls w/o STD		Cases vs Controls w/ STD		Controls w/ STD vs controls w/o STD	
		OR	95% CI	OR	95% CI	OR	95% CI
Male	0.3	1.2	0.6-2.6	1.2	0.5-3.2	1.0	0.3-2.7
Age greater than 25	15.5 *	0.3	0.1-0.6	0.3	0.1-0.7	1.0	0.4-2.6
Travel outside Estonia in last year	1.4	1.5	0.7-3.2	0.8	0.3-2.0	1.8	0.6-5.1
Three or more sexual partners; 3 months	0.7	0.6	0.1-2.5	1.4	0.2-9.0	0.4	0.0-3.9
Sexual activity while intoxicated; 3 months	10.1 *	3.5	1.6-7.6	1.5	0.6-3.8	2.3	0.8-6.5
Sexual relationship with casual partner; 3 months	3.0	2.1	0.7-6.4	2.1	0.6-7.2	1.0	0.2-4.4
Ever been diagnosed with an STD	9.8 *	1.6	0.7-3.3	4.2	1.6-11.2	0.4	0.1-1.1
Travel * Male sex	6.9 *	0.1	0.0-0.7	1.1	0.2-6.8	0.1	0.0-1.0

\*  $p < .05$  for the overall parameter estimate.

### 5. The community-level determinants and incidence rate of syphilis in Estonia during the post-communist transition period

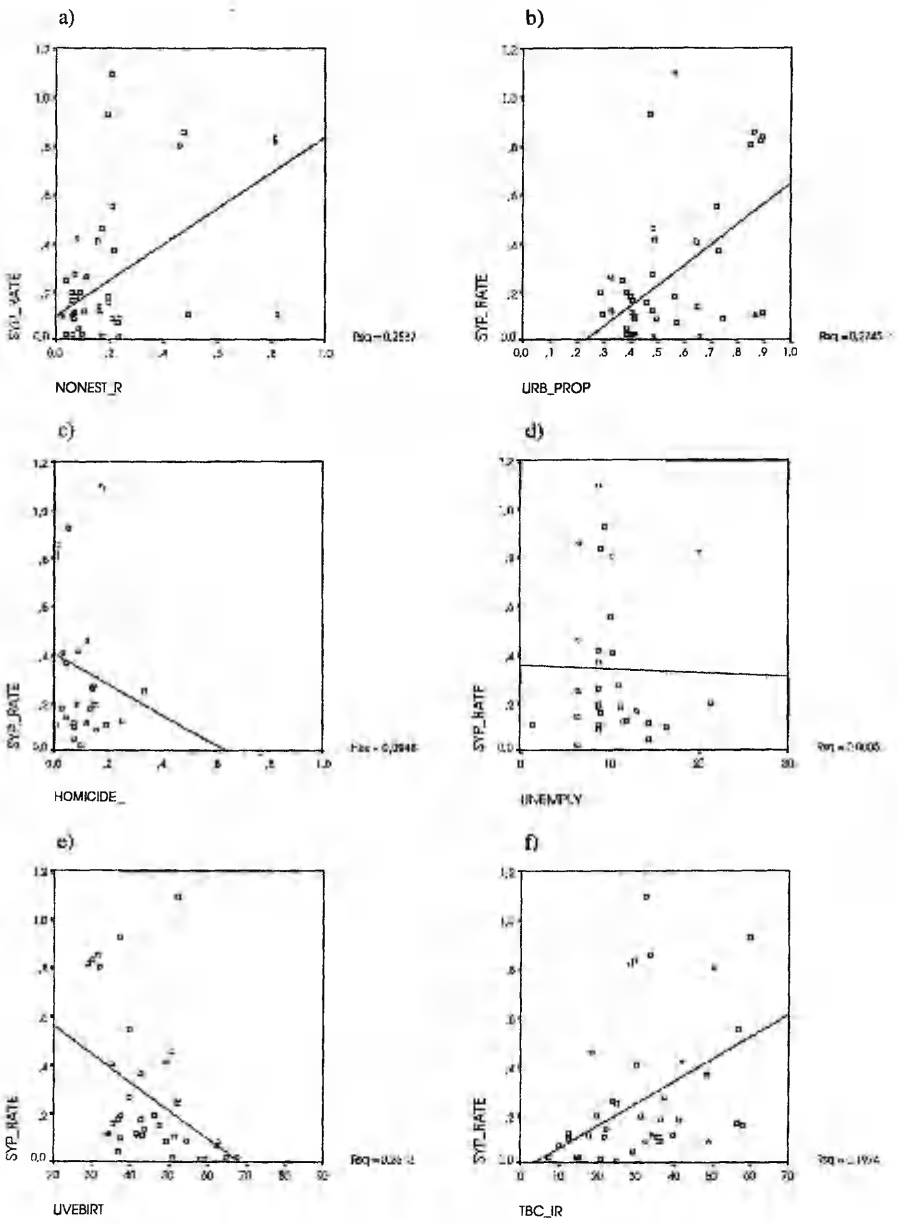
Statistically significant positive correlation was found between syphilis incidence rate and percentage of non-Estonian population (Pearson's  $r = 0.509$ ), urban population (Pearson's  $r = 0.524$ ), and tuberculosis incidence (Pearson's  $r = 0.444$ ), which explains 25.9 %, 27.5 %, and 19.7 % of the variation in syphilis incidence rates across the counties and the three time periods, respectively (Table 4).

**Table 4.** Explained variance, correlation and regression coefficient for the association between syphilis rate and six sociodemographic characteristics

	Explained variance	Regression coefficient	p-value of regression coefficient	Correlation coefficient
Non-Estonian population(percentage)	0.2587	0.738	0.000	0.509
Urban population (percentage)	0.2745	0.841	0.000	0.524
Homicides Rate (per 100,000)	0.0948	-0.632	0.118	-0.308
Unemployment rate (percentage)	0.0005	-0.002	0.909	-0.022
Live births (per 1000 females at age 15-49)	0.2513	-0.012	0.000	-0.501
Tuberculosis incidence rate (per 100,000)	0.1974	0.009	0.002	0.444

A statistically significant negative correlation was also found for syphilis incidence rate the birth rate (Pearson's  $r = -0.501$ ), which explains 25 % of the variance.

No associations between the syphilis incidence rate and the homicides rate and the unemployment rate were found (Figure 6, a-f).



(abbreviations: SYF RATE — syphilis incidence rate, NONEST\_R — proportion of non-Estonian, URB\_PROP — urban proportion, HOMICIDE\_ — homicides rate, UNEMPLY — unemployment rate, LIVEBIRT — live birth rate, TBC\_IR — incidence of tuberculosis)

**Figure 6.** Association of syphilis incidence rate with a) proportion of non-Estonian b) urban proportion c) homicides rate d) unemployment rate e) live birth rate f) incidence of tuberculosis.

## DISCUSSION

A marked increase in incidence of STDs in early 1990s, being most dramatic in new cases of syphilis, was observed in Estonia during the time period of the great changes in society — a shift from being a Soviet socialist republic to an independent country with a new developing market economy. While, the incidence of other reported bacterial STD (gonorrhoea, chlamydiosis) started to decline in 1994–1995, the trend toward stabilization and decline in incidence of syphilis is apparent from 1999<sup>15,16</sup> (syphilis is considered as the most reliably reported STD in former Soviet Union countries, including Estonia<sup>79,81</sup>).

This decline in the STD incidence has been observed not only in Estonia but also in the neighboring countries<sup>64</sup>, and has been attributed to a number of different factors. It has been interpreted as reflecting the peak values having been achieved among those socially disadvantaged and at risk, or related to changes in care seeking patterns, to implementation of symptomatic treatment without the verification of the causative agent, and incomplete case reporting<sup>69,74</sup>.

Passive report-based STD surveillance system underestimates the prevalent caseload since not all infections are reportable and many patients with STDs are asymptomatic and, therefore, do not seek care. Because of the continuing public perception of social stigma associated with the acquisition and treatment of an STD, many patients do not seek care at all. However, even if they do, as elsewhere in the world, misdiagnosis and underreporting obligation may occur. For example in 1998 in Tartu city and its district, 98% of cases of syphilis, 90% of gonorrhoea cases and 97% of those notified with genital wart virus infection were reported from the University Clinic of Dermatovenerology. Bearing in mind that many infections are asymptomatic, the diagnosis of STD may be completely overlooked (lack of expertise) or STD cases not reported to county's Health Protection Bureaus by other doctors (family doctors, gynaecologists and urologists) than dermatovenerologists.

In Estonia, trichomoniasis and chlamydial infections are the most prevalent non-viral STDs. In men, trichomoniasis has been associated with prostatitis, epididymitis and infertility with the strongest association being with non-gonococcal urethritis. Balanitis and posthitis have been described with trichomoniasis and, in severe cases, penile ulceration too<sup>70</sup>. In women, vaginitis and vulvitis are the main clinical conditions<sup>71</sup>. Recent studies have shown an association between trichomoniasis and low birth rate of babies (independent of HIV infection and other risk factors associated with low birth rate)<sup>72,73</sup> and pre-term labour<sup>73</sup>. As a classic STD, trichomoniasis may facilitate HIV transmission in both ways — increasing the infectiousness of and susceptibility to HIV infection<sup>74</sup>. Degradation of secretory leucocyte protease inhibitors (SLPI) is associated with trichomonal infection. SLPI is believed to limit the transmission of HIV infection by inhibiting virus entry into monocytes (*in vitro*)<sup>75</sup>. The data

from Laga and her colleagues show an association between trichomoniasis and acquisition of HIV infection in women, with estimated relative risks ranging from 1.8 to 3.0<sup>78</sup>. Urethral infection with gonorrhoea and trichomoniasis has been found to have a significant effect on HIV-1 RNA excretion<sup>76,77</sup>. Algorithms for the management of urethral discharge in men have been evaluated and proven to be valid and sensitive<sup>61</sup> but, with a caveat: that the chosen antimicrobial regimens should cover the major pathogens responsible for the syndromes in a specific region<sup>1</sup>. By ignoring trichomoniasis as a cause of urethritis in men in a setting where trichomoniasis prevalence is high, basic syndromic management targets might be missed: firstly, effective treatment of the genital tract at the first visit and patient satisfaction<sup>61,65</sup>. The first visit may be the only opportunity to treat and counsel as follow-up rates in men can be low<sup>65</sup>. In Estonia, trichomoniasis accounts for 35% of cases of male urethritis<sup>15,16</sup> and is found in 59% of men with mixed STDs (in a situation where major target of urethritis treatment in context of syndromic management — co-infection with *Chlamydia trachomatis* and *Neisseria gonorrhoeae* is rare). Thus, it might be reasonable to include metronidazole among the first line treatments for the urethral discharge syndrome in men. In Estonia, the management of STDs and control efforts are limited and a specialist service using full laboratory facilities is expensive and is in fact only accessible to urban residents near centres with laboratory support. In Soviet times, the healthcare system was centralised with STD care being mostly provided through dermatovenereology clinics which used a laboratory-based system of diagnosis. After independence in Estonia, while the centralisation of services is less, it may be appropriate, outside the main centres, to provide care for STDs within the primary healthcare system<sup>79</sup>. In the primary care setting, there would be considerable advantage to the use of syndromic STD management protocols, and in Estonia the inclusion of metronidazole amongst the medications used for the urethral discharge syndrome would be appropriate.

Increased rates of STD in Estonia are associated with patterns of sexual risk behaviours. Factors contributing to increased rates of STD among men and women include risk factors typically associated with STD epidemics; these include the prevalence of multiple sexual partners, engaging in sexual relationships with casual partners, engaging in a sexual activity with new partners while travelling outside of the country, and engaging in sexual activity while intoxicated. In addition, an inaccurate understanding of STD transmission dynamics may further contribute to the STD occurrence.

The cases and the controls, in our study exhibited similarly high levels of misconceptions regarding methods for preventing disease transmission. Although this population was generally aware of condom use as an effective prevention tool, over 65% believed that washing the genital area is effective, and 20–33% of the population believed that using birth control pills, douching after intercourse, or urinating after intercourse are also effective. Incorrect knowledge regarding these issues may place individuals at increased risk for

HIV/STD if they rely on these behaviours for disease prevention; education regarding the efficacy of different modes of disease transmission and prevention is important in this population.

Those who indicated recent alcohol intoxication during sexual intercourse were more likely to be the cases than to be the controls testing negative for STD. Individuals reporting this behaviour were also more likely to have multiple and casual sexual partners, to have engaged in sex exchange behaviour, and were less likely to report using condoms consistently. These findings, when coupled with the fact that over a third of the population had a CAGE score that indicate alcohol-related problems, suggest that identification and treatment of alcohol addiction may be an important component of disease control in this population.

This study on individual factors associated with STD occurrence is limited by the low rate of response from the mail recruitment of controls; the assumption that this sample is representative of the general population should be taken with caution. It is possible that controls who responded to the letter may have done so in order to receive the STD examination and treatment that was included as part of study participation. For these reasons, some of the marked differences may be attributable to the sample selection, such that those with suspected conditions were more likely to respond. Provided that there were still statistically significant behavioural differences between the cases and controls, however, this supports rather than detracts from the contention that these two groups are fundamentally different. Furthermore, those individuals with STD in the control group were more likely to have chlamydia, and less likely to have had gonorrhoea or syphilis. Given that symptoms of chlamydia are often less noticeable than these other diseases, it seems justified to conclude likely that those individuals were probably unaware of their disease, rather than avoiding treatment for a suspected condition. The findings suggest that this population segment may benefit from the efforts aimed at greater outreach and screening, coupled with sexual risk reduction counselling.

Social disintegration has proven to exacerbate epidemics of infectious diseases, including AIDS, and tuberculosis, and behavioural pathologies such as substance abuse and violence<sup>80</sup>. The lack of economic equilibrium and insecurity have deepened in the society, and on the other hand, the freedom to make own decisions has increased without a simultaneous consciousness of responsibility. Especially in case of STDs, societal factors tend to influence risk behaviour and consequently the probability of being infected. First, society provides the context in which behaviours are shaped and conducted. Syphilis is a classical example of STD.

In our study on community level associations of syphilis incidence rate, constantly higher syphilis incidence rates were identified in Tallinn and Ida-Virumaa County, the regions with high percentage of non-ethnic Estonian population and unemployment rate. Syphilis rate was positively associated with the proportion of non-Estonian (Pearsons  $r=0.509$ ), but we found almost no

association with unemployment rate. The ethnic origin is not considered to be a biological risk factor for syphilis; ethnicity is probably a marker of interrelationships of ethnicity with other socioeconomic and demographic factors. Socially disruptive situation is a critical and unique environmental condition that may trigger syphilis epidemic<sup>82</sup>. Due to the language-based labour division during the Soviet period, changes in society had affected Estonians and non-ethnic Estonians in different ways. The Russian-speaking population is predominantly occupied in those branches of the economy, which have been deteriorating since the restoration of Estonia's independence, intensifying the problem with the unemployment.

The unemployment rate in our study did not correlate with the syphilis rate. There could be several explanations to this finding. The unemployment is the greatest problem in the North-East of Estonia (as there are too many oversized enterprises that were subordinated to centralized control from Moscow) and in the South of Estonia (mostly dominated by the enterprises of agriculture, fishing, forestry)<sup>83</sup>, yet the syphilis incidence in the two above-mentioned areas is different. Another region with a high STD rate is Tallinn with its good job opportunities and low unemployment rate.

The theories on STD transmission have drawn the readers' attention to importance of current prevalence of infection in population<sup>108</sup>, and to social networks<sup>89,90</sup>. The capital city of Ida-Virumaa county, Narva, is located on a cross-border motorway between Estonia and the Russian Federation, and connecting Tallinn with St Petersburg — an area with extremely high STD rates, especially syphilis incidence is also faced with serious STD problems. So in 1998, the incidence of syphilis in Estonia was 75.7 / 100,000 population, but in Narva it was 258.8 / 100,000 population<sup>15</sup> that is comparable to the syphilis incidence in the Russian Federation (234 / 100,000 population)<sup>91</sup>. Major motorways may serve as conduits for illegal drug trafficking. Drugs are known to have a potential of altering sexual mixing patterns<sup>88</sup>. The data assured also by our case-control study on sexual beliefs and behaviours determining that sexual behaviour on travel might contribute to STD rates.

Another marker of social integration is the rate of live birth, which in this study was inversely associated with county syphilis rate (Pearsons  $r = -0.501$ ).

Large population downturn (including decrease in birth rates) during transition period radical socioeconomic changes is also characteristic of other Eastern European countries<sup>84</sup>. During the last decade, Estonia lost 8% of its population compared to the pre-transition period (1989)<sup>66</sup>. This phenomenon is assumed to be the consequence of the drastic changes in political, economic and social conditions<sup>83</sup>. The rate of legitimate birth is continuously falling, and the mean age of women at child birth and the mean age of women at the birth of the first child were steadily increasing during the nineties<sup>66</sup>.

The high incidence rate of syphilis was observed in Tallinn, the capital of Estonia. Urban residence has been proven to be associated with high syphilis rates<sup>85</sup>, although there may also be a surveillance artefact, with better access to

medical care in urban areas,<sup>86</sup> resulting in higher rates of appropriate diagnosis and reporting syphilis cases. In this study, the proportion of urban population in the county was strongly associated with the county's syphilis rate (Pearson's  $r=0.524$ ). Age specific migration rates revealed that the growth of internal migration had mostly taken place on account of the decrease of non-registered changes of the place of residence of 15–34 year old males and 15–29 year-old females<sup>87</sup> — the age groups most vulnerable to STD related problems.

The disruption of public health and public order, instability of personal, domestic and community networks will lead to the increased levels of violence, sexuality, substance abuse and general criminality<sup>92</sup>. In Estonia a substantial increase of IDU began in 1994, and it is still escalating. According to the Estonian Health Statistics the number of patients admitted for care for psychiatric and behavioural disorders caused by the use of illegal drugs more than tripled during the late 1990s (24.5 / 100000 in 1995, 82.2 / 100 000 in 1998)<sup>107</sup>. Unfortunately, no verified data on the extent of drug abuse are available, but the number of IDUs in Estonia is estimated to be 10.000–12.000; the majority is Russian-speaking (90%) males, aged 15–25 (85%) heroin addicts<sup>93,94,95</sup>. The marked increase in HIV incidence in Estonia was preceded by an increase in the numbers of the registered cases of hepatitis B and hepatitis C<sup>15</sup>, which was considered to be associated with the spread of injecting drug use in Estonia<sup>93,96,97</sup>. The increase may also be the result of the change in the pattern of drug use<sup>93</sup>, from smoking drugs to injecting drugs. The period of 1994 to 1997, indicated an almost five-fold increase in the absolute numbers of the registered new cases of hepatitis B and C in the age group of 15–19 years old; 50% of hepatitis B and 52% of hepatitis C cases were diagnosed in this age group in the year 1997<sup>96</sup>. One of the interesting observations from the last decade of the 20<sup>th</sup> century Estonia is that the number of HIV infection cases remained relatively low, regardless of the rapidly and substantially increasing STD rates (syphilis in particular) (Figure 2). HIV epidemic began to develop only after it was introduced to the drug injecting community. In Estonia, the current data, including the information recorded on HIV testing forms<sup>98</sup> and clinical records<sup>93,99</sup> document the fact that IDU was a factor in nearly 90% of the new HIV cases reported in the year 2000.

The majority of new HIV+ cases (797 (74%)/1037) in the years of 2000 and 2001 are reported to be residents in the North-East of Estonia, and this epidemic is clearly driven by intravenous drug use<sup>93, 98,99,100</sup>.

In addition to STDs, social disintegration has shown to exacerbate epidemics of several other infectious diseases including tuberculosis<sup>59</sup>. We found that syphilis rate was positively associated with the tuberculosis incidence rate, which further supports the similar risk factors for these infections, e.g. social disintegration.

Our study on association between community level determinants and syphilis incidence rate is limited in several ways: we used data from passive STDs surveillance systems (as explained above), and so we could underestimate the



real burden of the disease; we only used the available county-level data. There is an absence of reliable national level data on sexual behaviour and alcohol/substance abuse. However, this ecological analysis used the unique social and political situation with radical changes in community in a very short period, and it demonstrated the important associations between community-level indicators and the rate of syphilis incidence. The results support the theory of syphilis as a social disease, with the considerable variation of the incidence of syphilis across space and time, asserting the social pattern of the disease.

## CONCLUSIONS

- The study results demonstrate high rates of sexual risk behaviour and inadequate knowledge regarding prevention of disease transmission.  
In a case-control study of beliefs on behaviours associated with STDs, across the entire sample, 65.2% believed that washing the genitals after sex is an effective mean for preventing STD; despite that almost all respondents (94.5%) were aware that condom use protects against STD, less than one-fifth reported always or almost always using condoms. These factors signify that basic health education and promotion efforts implemented across the entire population should be public health priorities.
- The 32% STD prevalence rate among those recruited as controls indicates that effective STDs identification and treatment is of utmost importance. The importance of effective measures in STD control is further emphasised in the light of the advent of HIV/AIDS epidemic in Estonia — the high rate of STDs (including infectious syphilis), indicate the country being susceptible to the possibility of the epidemic spread of HIV infection via heterosexual intercourse, into the general population.
- HIV infection appeared much later in Estonia than in many other parts of the world. The HIV outbreak was preceded by more than a decade of a “silent HIV infection” in our community. Rapidly increasing rates of HIV in Estonia require immediate efforts to promote risk reduction including behavioral intervention programs targeting IDUs and their sexual/drug using partners, syringe needle exchange and distribution programs, substitution pharmacotherapy, outreach to IDUs, peer education programs. The expertise of the other countries that confronted with the challenges of HIV earlier could be of great help and importance for Estonia.
- These results underline the importance of the socioeconomic and demographic factors, and the complex social dimensions of public health problems. We found statistically significant relationships between the syphilis incidence rate and such community level factors as the percentage of non-ethnic Estonians in the population (Pearsons  $r=0.509$ ), the percentage of urban population (Pearsons  $r=0.524$ ), the tuberculosis incidence (Pearsons  $r=0.444$ ) and the birth rate (Pearsons  $r=-0.501$ ). Our findings illustrate the same origins of the public health and public order, and emphasize the importance of establishing close ties between the health care sector and the other community resources to prevent sexually transmitted infections.

## ACNOWLEDGEMENTS

I wish to express my sincere gratitude to the following persons and organisations:

### My supervisors

Helgi Silm, for friendly advice and support throughout the years.  
Allan Lassus, for sharing his knowledge on everything about writing and publishing a scientific paper.

### Reviewers

Professor Raul Allan Kiivet, for sparing his time for critical reading of the thesis and for valuable comments.

### My co-authors,

James Bingham, Jack DeHovitz, Joe Feldman, Susan Holman, Nelli Kalikova, Allan Lassus, Mari and Jan Nygård, Toomas Plank, Helgi Silm, Lea Tammai, Toomas Vessin, Tracey Wilson, Kai Zilmer, for fruitful collaboration and stimulating discussions.

Professor Jack DeHovitz, for useful discussions and comments helpful in revision.

### My family

Mart, Rasmus and Rahel, my father and brother, Larissa and Mait, for love and support, and for always being there when I needed it most.

These studies were supported by the Estonian Science Foundation, by the Ministry of Education in Estonia through a doctoral student position in Clinic of Dermatology at University of Tartu, and Fogarty International Center, US National Institutes of Health.

## REFERENCES

1. Gerbase AC, Rowley JT, Mertens TE. Global epidemiology of sexually transmitted diseases. *Lancet* 1998; 351 (Suppl III):2-4.
2. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Inf* 1999; 75:3-17.
3. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. *Lancet* 1998; Suppl III:5-7.
4. Royce RA, Sena A, Cates W, Cohen M. Sexual transmission of HIV-1. *N Eng J Med* 1997; 336:1072-78.
5. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. *Lancet* 1997; 349:1868-73.
6. Wasserheit JN. Epidemiological synergy. Interrelationships between human immunodeficiency virus infection and other sexually transmitted diseases. *Sex Transm Dis* 1992;19:61-77.
7. Aral SO, Holmes KK. Epidemiology of sexual behavior and sexually transmitted diseases. In: Holmes KK, Mardh P-A, Sparling F, eds. Sexually transmitted diseases. New York: McGraw-Hill, 1990:19-36.
8. WHO/Global Programm on AIDS. Global prevalence and incidence of selected curable sexually transmitted diseases: overview and estimates. WHO/HIV\_AIDS/2001;02., WHO/CDS/CSR/EDC/2001;10:1-32.
9. Cates W, Dallabeta G. The staying power of sexually transmitted diseases. *Lancet* 1999;354 Suppl 4:62.
10. Kohl PK. Epidemiology of sexually transmitted diseases. *Sex Transm Dis* 1994;Suppl 1:81-83.
11. Garcia-Lechuz JM, Rivera M, Catalan P, Sanchez Carillo c, Rodriguez-Creixems M, Bouza E. Differences in curable STDs between HIV and non-HIV population in Spain. *Aids Patient Care & STD* 1999;13:175-7.
12. Paget WJ, Zimmermann HP. Surveillance of sexually transmitted diseases in Switzerland, 1973-1994: evidence of declining trends in gonorrhoea and syphilis. *Sozial and Praventivmedizin* 1997;42:30-6.
13. WHO/EURO Epidemic of sexually transmitted diseases in Eastern Europe. Report on a Who Meeting, Copenhagen, Denmark 1996, 13-15 May.
14. Renton AM, Borisenko KK, Meheus A, Gramyko A. Epidemic of syphilis in the newly independent states of the former Soviet Union. *Sex Transm Inf* 1998;74:165-66.
15. National Board of Health Protection. Communicable Diseases Statistics in Estonia, 1998: 24,26,30,61.
16. Health protection inspectorate. Communicable disease statistics in Estonia 2000;8:100-1.
17. De Schryver A, Meheus A. Epidemiology of sexually transmitted diseases: the global picture. *WHO Bulletin OMS* 1990;68:639-53.
18. Anonymous. The incidence of gonorrhoea in England and Wales is rising. *Communicable disease Report. CDR Weekly* 1997;7:217-20.
19. Berglund T, Fredlund H, Ramstedt K. Reemergence of gonorrhoea in Sweden. *Sex Transm Dis* 1999; 26:390-1.
20. Bunnell RE, Dahlberg L, Rolfs R, Ramsonm R, Gershman K, Farshy C, Newhall WJ, Schmid S, Stone K, St Louis M. High prevalence and incidence of sexually transmitted diseases in urban adolescent females despite moderate risk behaviour. *JID* 1999;180:1624-31.

21. Burstein GR, Gaydos CA, Diner-West M, Howell MR, Zenilman JM, Quinn TC. Incident Chlamydia trachomatis infections among inner-city adolescent females. *JAMA* 198;280:521-6.
22. Cook RL, St George K, Lassak M, Tran N, Anhalt JP, Rinaldo CR. Screening for Chlamydia trachomatis infection in college women with a polymerase chain reaction assay. *Clin inf Dis* 1999;28:1002-7.
23. Jonsdottir K, Geirsson RT., Steingrimsson O, Olafsson JH, Stefansdottir S. Reduced prevalence of cervical Chlamydia infection among women requesting termination. *Acta Obs Gynec Scand* 1997;76:438-41.
24. Munk C, Morre SA, Kjaer SK, Poll Pa, Bock JE, Meijer CJ. AJ. PCR detected chlamydia trachomatis infections from the uterine cervix of young women from the general population: prevalence and risk determinants. *Sex Transm Dis* 1999;26:325-8.
25. Kirkwood K, Horn K, Glasier A, Sutherland S, Young H, Patrizio C. Non-invasive screening of teenagers for Chlamydia trachomatis in a family planning setting. *Br J Fam Plann* 1999;25:11-2.
26. Deak J, Nagy E, Vereb I, Meszarons G, Kovacs L, Nyari T. Prevalence of Chlamydia trachomatis infection in a low-risk population in Hungary. *Sex Transm Dis* 1997;24:538-42.
27. Bavastrelli M, Midulla M, Rossi D, Salzano M, Calzolari E, Midulla C. Sexually active adolescents and young adults: a high risk group for Chlamydia trachomatis infection. *Journal of Travel Medicine* 1998;5:57-60.
28. Wawer MJ, McNairn D, Wabwire-Managen F, Paxton L, Gray RH, Kiwanuka N. Self-administered vaginal swabs for population-based assessment of *Trichomonas vaginalis* prevalence. *Lancet* 1995;345:130-31.
29. Passey M, Mgone CS, Lupiwa S, Suve N, Tiwara S, Lupiwa T et al. Community based study of sexually transmitted diseases in rural women in the highlands of Papua New Guinea: prevalence and risk factors. *Sex Transm Dis* 1998;2:120-7.
30. Sorvillo F, Kovacs A, Kerndt P, Stek A, Muderspach L, Sanchez-Keeland L. Risk factors for trichomoniasis among women with human immunodeficiency virus (HIV) at a public clinic in Los Angeles County, California: implications for HIV prevention. *Am J Trop Med Hyg* 1998;4:495-500.
31. Shuter J, Bell D, Graham D, Holbrook KA, Bellin EY. Rates of and risk factors for trichomoniasis among pregnant inmates in New York City. *Sex Transm Dis* 1998;6:303-7.
32. Joyner JL, Douglas JM Jr, Ragsdale S, Foster M, Judson FN. Comparative prevalence of infection with *Trichomonas vaginalis* among men attending a sexually transmitted diseases clinic. *Sex Transm Dis* 2000;27:236-40.
33. Niccolai LM, Kopicko JJ, Kassie A, Petros H, Clark RA, Kissinger P. Incidence and predictors of reinfection with *Trichomonas vaginalis* in HIV-infected women. *Sex Transm Dis* 2000;27:284-8.
34. Mindel A. Genital herpes — how much of a public-health problem? *Lancet* 1998;352 supp III:16-18.
35. Ashley RL, Wald A. Genital herpes: review of the epidemic and the potential use of type-specific serology. *Clin Microb Rev* 1999;12:1-8.
36. Fleming DT, McQuillan GM, Johnson RE, Nahmias AJ, Aral SO, Lee FK. Herpes simplex virus type 2 in the United States, 1976 to 1994. *N Engl J Med* 1997;337:1105-1111.
37. Nahmias AJ, Lee FK, Beckman-Nahmias S. Sero-epidemiological and -sociological patterns of herpes simplex infection in the world. *Scand Infect Dis* 1990;69 suppl:19-36.
38. Forsgren M, Skoog E, Jeansson S, Olofsson S, Giesecke J. Prevalence of antibodies to herpes simplex virus in pregnant women in Stockholm in 1969, 1983, and 1989: implications for STD epidemiology. *Int J STD AIDS* 1994;5:113-6.
39. Arvaja M, Lehtinen M, Koskela P, Lappainen M, Paavonen J, Vesikari T. Serological evaluation of herpes simplex virus type 1 and 2 infections in pregnancy. *Sex Transm Infect* 1999;75:168-71.

40. Janier M, Lassau F, Bloch J, Spindler E, Morel P, Gerard P. Seroprevalence of herpes simplex virus type 2 antibodies in an STD clinic in Paris. *Int J STD AIDS* 1999;10:522-526.
41. Vyse AJ, Gay NJ, Slomka MJ, Gopal R, Gibbs T, Morgan-Capner P. The burden of infection with HSV-1 and HSV-2 in England and Wales: implications for the changing epidemiology of genital herpes. *Sex Transm Inf* 2000;76:183-7.
42. Wutzler P, Doerr HW, Farber I, Eichhorn U, Helbig B, Sauerbrei A. Seroprevalence of herpes simplex virus type 1 and type 2 in selected German populations — relevance for the incidence of genital herpes. *J Med Virol* 2000;61:201-7.
43. Kibur M, Koskela P, Dillner J, Leinikki P, Saikku P, Lehtinen M et al. Seropositivity to multiple STIs is not common. *Sex Transm Dis* 2000;27:425-30.
44. Cusinis M, Cusan M, Parolini C, Scioccati L, Declava I, Mengoli C. Seroprevalence of herpes simplex virus type 2 infection among attendees of a sexually transmitted clinic in Italy. *Sex Transm Dis* 2000;27:292-5.
45. Lafferty WE, Downey L, Celum C, Wald A. Herpes simplex virus type 1 as a cause of genital herpes: impact on surveillance and prevention. *JID* 2000;181:1454-7.
46. [http://www.unaids.org/wac/2000/wad00/files/WAD\\_epidemic\\_report.htm](http://www.unaids.org/wac/2000/wad00/files/WAD_epidemic_report.htm). 12.07.2001.
47. Hamers FF, Batter V, Downs AM, Alix J, Cazein F, Brunet JB. The HIV epidemic associated with injecting drug use in Europe: geographic and time trends. *AIDS* 1997;11:1365-74.
48. Stephenson J. HIV/AIDS Surging in Eastern Europe. *JAMA* 2000;284:3113.
49. Dehne KL, Khodakevich L, Hamers FF, Schwartlander B. The HIV/AIDS epidemic in Eastern Europe: recent patterns and trends and their implications for policy-making. *AIDS* 1999; 13:741-9.
50. Aral SO. Sexual behavior in sexually transmitted disease research. *Sexually transmitted diseases* 1994;Suppl:59-64.
51. Stokols D. Establishing and maintaining healthy environments: toward a social ecology of health promotion. *American psychologist* 1992;42:6-22
52. Erickson KP, Trocki KF. Behavioral risk factors for sexually transmitted diseases in American households. *Soc Sci Med* 1992;34:843-853.
53. Aral SO, Holmes KK, Padian NS, Cates W. Individual and population approaches to the epidemiology and prevention of sexually transmitted infections and human immunodeficiency virus. *JID* 1996;174 Suppl 2:S127-33.
54. Wasserheit J, Syphilis as a barometer of community health. *Sex Transm Dis* 2000;27:311-2.
55. Thomas JC, Clark M, Robinson J, Monnett M, Kilmarx PH, Peterman TA. The social ecology of syphilis. *Soc Sci Med* 1999;48:1081-94.
56. Kilmarx PH, Zaidi AA, Thomas JC, Nakashima AK, St. Louis E, Flock ML. Sociodemographic factors and the variation in syphilis rates among US counties, 1984 through 1993: an ecological analysis. *Am J Publ Health* 1997;87:1937-43.
57. Potterat JJ, Rothenberg RB, Woodhouse DE, Muth JB, Ptatts CI, Fogle JS. Gonorrhea as a social disease. *Sex Transm Dis* 1985;12:25-32.
58. Aral SO, Holmes KK. Demographic and social correlates of sexually transmitted disease. In: Holmes KK, Mardh PA, Sparling PF, Wiesner PJ, editors. *Sexually transmitted diseases*. New York: McGraw-Hill, 1990:33.
59. Wallace R. A synergism of plaques: "planned shrinkage", contagious housing destruction, and AIDS in the Bronx. *Environ Res* 1988;47:1-33.
60. Adler M. Strategies for prevention and treatment of sexually transmitted infections. *Int J STD AIDS* 1998;9 Suppl 1:8-10.
61. Sexually transmitted diseases: policies and principles for prevention and care. UNAIDS/97.6.
62. Guidelines for the management of sexually transmitted infections. WHO/HIV\_AIDS/2001.01; WHO/RHR/01.10.
63. Guidelines for treatment of sexually transmitted diseases. Morbidity and mortality weekly report 1998;47:No. RR-1.
64. Editorial. Update of the CDC STD treatment guidelines: changes and policy. *Sex Transm Inf* 1998;2:98-91.

65. Dallabeta GA, Gerbase AC, Holmes KK. Problems, solutions, and challenges in syndromic management of sexually transmitted infections. *Sex Transm Inf* 1998;74 (Suppl 1):S1–S11.
66. Statistical Office of Estonia. Population 1999; 29,30,42,42,59. Tallinn 2000.
67. Mayfield D, McLeod G, Hall P. The CAGE questionnaire: Validation of a new alcoholism screening instrument. *American Journal of Psychiatry* 1974;131:1121–3.
68. Lauristin M, Vihalemm P. Return to the western world. Lauristin M, Vihalemm P, Rosengren E, Weibull, eds. Recent historical developments in Estonia: three stages of transition (1987–1997). Tartu University Press, Estonia 1997:79–83.
69. Statistical Office of Estonia. Regional Statistics. <http://www.stat.vil.ee/pks/indexli.html>
70. Kreiger JN. Trichomoniasis in men: old issues and new data. *Sex Transm Dis* 1995;2:83–95.
71. Wolner-Hanssen P, Krieger JN, Stevens CE, Kiviat NB, Koutsky L, Critchlow C, et al. Clinical manifestations of vaginal trichomoniasis. *JAMA* 1989;4:571–576.
72. Sutton MY, Sternberg M, Nsuami M, Behets F, Nelson AM, Sr Louis ME. Trichomoniasis in pregnant human immunodeficiency virus-infected and human immunodeficiency virus-uninfected congolese women: prevalence, risk factors, and association with low birth weight. *Am J Obstet Gynecol* 1999;3:656–65.
73. Cotch MF, Pastorek JG, Nugent RP, Hillier SL, Gibbs RS, Martin DH et al. *Trichomonas vaginalis* associated with low birth weight and preterm delivery. *Sex Transm Dis* 1997;6:353–60.
74. Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. *Lancet* 1998;Suppl III:5SIII–7SIII.
75. Draper D, Donohoe W, Mortimer L, Heine RP. Cysteine proteases of *Trichomonas vaginalis* degrade secretory leucocyte protease inhibitor. *J Inf Dis* 1998;3:815–9.
76. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. *Lancet* 1997;349:1868–73.
77. Hobbs MM, Kazembe P, Reed AW, Miller WC, Nkata E, Zimba D et al. *Trichomonas vaginalis* as a cause of urethritis in Malawian men. *Sex Transm Dis* 1999;7:388–9.
78. Laga M, Manoka A, Kivuvu M, Malele B, Tuliza M, Nzila N, et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: result from a cohort study. *AIDS* 1993;1:95–102.
79. Waugh MA. Task force for the urgent response to the epidemics of sexually transmitted diseases in eastern Europe and central Asia. *Int J STD AIDS* 1999;10:60–2.
80. Wallace R, Wallace D, Andrews H. AIDS, tuberculosis, violent crime, and low birthweight in eight US metropolitan areas: public policy, stochastic resonance, and regional diffusion of inner-city markers. *Environment and Planning* 1997;29:525–5.
81. Lapinskaite GS, Bingham JS. Sexually transmitted diseases in Lithuania: some epidemiological and social aspects. *Int J STD AIDS* 1999;10:673–6.
82. Miles TP, McBride D. World War I origins of the syphilis epidemic among 20th century black americans: a biohistorical analysis. *Soc Sci Med* 1997;45:61–9.
83. Ainsaar M. Transformation of society and migration: the case of Estonia. Estoniansocial science (online) 1999;1. <http://psych.ut.ee/esta>, 06.05.2001.
84. Krus DJ, Nelsen EA. Changes in crime rates and family related values in select east European countries. *Psychol Rep* 1997;81:747–51.
85. Kilmarx PH, Zaidi AA, Thomas JC, Nakashima AK, St.Louis E, Flock ML. Sociodemographic factors and the variation in syphilis rates among US counties, 1984 through 1993: and ecological analysis. *Am J Publ Health* 1997;87:1937–43.
86. CDC and Prevention. 1992 National Health Interview Survey. In: Healthy People 2000 Review. Washington, DC: US Dept of Health and Human Services; 1994.
87. Statistical office of Estonia 1995. Internal migration. In: Population of Estonia 1993, Tallinn.
88. Cook RL, Royce RA, Thomas JC, Hanusa BH. What's driving an epidemic? The spread of syphilis along an interstate highway in rural North Carolina. *Am J Pub Health* 1999;89:369–7.

89. Rothenberg RB, Sterk C, Toomey KE, Potterat JJ, Johnson D, Schrader M. Using social network and ethnographic tools to evaluate syphilis transmission. *Sex Transm Dis* 1998;25:154–60.
90. Woodhouse DE, Rothenberg RG, Potterat JJ, Darrow WW, Muth SQ, Klovdahl AS. Mapping a social network of heterosexuals at high risk for human immunodeficiency virus infection. *AIDS* 1994;8:1331–6.
91. Tichonova L, Borisenko K, Ward H, Meheus A, Gromyko A, Renton A. Epidemics of syphilis in the Russian Federation: trends, origins, and priorities for control. *Lancet* 1997;350:210–13.
92. Wallace R. Urban desertification, public health and public order: planned shrinkage, violent death, substance abuse and AIDS in the Bronx. *Soc Sci Med* 1990;31:801–31.
93. Kalikova N. The HIV epidemic in Estonia. Proceedings of the 3rd Congress of the Estonian Society of Sexually Transmitted Infections (EUSTI) 2001:14–5.
94. Kariis T, Malbe, R, Allaste AA, Ahven A, Jänes V, Paimre M. Summary Report on the National Drug Situation in Estonia. (Information For The EMCDDA's 2000 Annual Report). Estonian Foundation for Prevention of Drug Addiction. Tallinn 1999.
95. Kalikova, N. Intravenous drug users. An epidemiological overview. Unpublished report. AIDS Prevention Center, Tallinn, 2000.
96. Priimägi L, Kremerman I, Tefanova V, Tallo T, Osadtsaja G. Study on hepatitis C and hepatitis B infected intravenous drug users. *Eesti Arst* 1998;6:521–523.
97. Tefanova V, Krupskaja L, Kikos G, Tallo T, Priimägi L. Study on hepatitis B and hepatitis C epidemiology in Tallinn. *Eesti Arst* 1998;6:552–3.
98. Archive of HIV Reference Laboratory, HIV testing reports 1987 to 2000, HIV testing notification according to the decree no 54 (29.03.1994) and no 77 (13.12.2000) of Ministry of Social Affairs of Estonia.
99. Archive of Merimetsa Clinic of Infectious Diseases in Tallinn, 06/2001.a.
100. HIV infection in Estonia. <http://www.tervisekaitse.ee/jutud/aids> 29.01.2001.
101. 88. ESTONIAN HUMAN DEVELOPMENT REPORT 1999. Crime and crime control in Estonia. <http://www.undp.ee/nhdr99/en/contents.html>
102. CDC, National center for HIV, STD and TB prevention. Division of STDs. 1998 STD surveillance.
103. Borisenko KK, Tichonova LI, Renton AM. Syphilis and other sexually transmitted infections in the Russian Federation. *Int J STD AIDS* 1999;10:665–8.
104. Public Health Laboratory Service. Disease facts. Data on STIs in United Kingdom (1995 to 1999). <http://www.phls.co.uk/facts/STI/DataOnSTIsInEng9599.htm>. 25.07.01.
105. Infectious diseases in Finland 1995–1999. National Public Health Institution Publications KTL B 6 /2000.
106. Rubins A, Rubins S. Epidemiology of syphilis, gonorrhoea and AIDS in Latvia, Lithuania, Estonia in 1991–1998 and first months in 1999. Proceedings of 13th Meeting of the International society for STD research 1999:253.
107. Database of the Estonian Foundation for Prevention of Drug Addiction. <http://narko.sm.ee/Levik/2000/default.asp>.
108. Shiboski S, Padian NS. Population- and individualised approaches to desing and analysis of epidemiologic studies of sexually transmitted disease transmission. *JID* 1996;174 Suppl 2:S188–200.



## SUMMARY IN ESTONIAN

### Sugulisel teel levivad infektsioonid Eestis aastatel 1990–2000, epidemioloogiline uuring

Sugulisel teel levivad infektsioonid (suguhaigused) on juba aastaid tõsine probleem kogu maailmas. Inimese immuunpuudulikkuse viiruse (HIV) põhjustatud ja teistel sugulisel teel levivatel haigustel on olulised sotsiaalsed, demograafilised ja majanduslikud tagajärjed.

Sugulisel teel levib üle 30 nakkushaiguse, kuid üksikute jaoks on see levikuviis peamine. Suguhaigustest on kõige enam ohustatud seksuaalselt aktiivsed inimesed ja suguhaigusi põdevatelt emadelt sündivad lapsed, sest suguhaigused infitseerivad suguteed ja nende ülekande toimub sugulise vahekorra või sünnituse ajal. Suguhaigused on olulised just eelkõige (1) oma tüsistuste ja kaugtagajärgede tõttu. Näiteks on gonorröa või klamüdioosi esmasinfektsioon naistel sageli asümptomaatiline, kuid ravimata infektsioonile järgneb põletiku ülenemine suguteedes, põhjustades väikse vaagna põletikulist haigust, kroonilist valu-sündroomi, emakavälilist rasedust ning viljatust. (2) Ravimata põletikud suguteedes on seotud raseduse katkemise, madala sünnikaalu ning loote ja/või vastsündinu haigestumisega. (3) Suguhaigused soodustavad HIV-infektsiooni ülekannet, suurendades nii nakkuslikkust kui ka vastuvõtlikkust. Suguteede limaskestast põletik suurendab HIV-infektsiooniga nakatumisevõimeliste rakkude arvu piirkonnas ning rakkudel ekspresseeritud retseptorite arvu. HIV+uretriiti põdevad mehed eritavad oma spermaga oluliselt rohkem HI-viiruseid kui HIV+mehed, kel uretriiti ei ole. Olemasolev HIV tüsistab oluliselt teiste suguhaiguste kulgu organismis.

Suguhaigustesse haigestumise jälgimiseks on kaks peamist allikat: haigusjärelvalve riikliku andmehõive raames (uute haigusjuhtude registreerimine) ja epidemioloogilised uuringud. Eestis kuuluvad HIV-infektsioon, süüfilis, gonorröa, trihhomonoos, klamüdioos, suguelundite herpes ja kondüloomid kohustuslikus korras registreerimisele maakondade tervisekaitsetalitustes, vastavalt sotsiaalministri määrustele nr. 25 (12.06.1997) ja nr. 59 (07.01.1999.).

Haigusjärelvalvel juhtude kohustusliku registreerimise kaudu saadud informatsioon ei ole alati täielik ja usaldusväärne. See sõltub suguhaiguste ravi-asutuste olemasolust ja töö kvaliteedist (haiguste korrektne diagnoosimine ja haigusjuhtude registreerimine, uute haigusjuhtude — kontaktsete avastamine ja ravi), patsientide pöördumisest kontrollile ja ravile. Probleemi muudab keerukaks ka suguhaiguste säge asümptomaatiline kulg, mistõttu patsiendid ei pöördugi arsti poole. Kõige tõenäolisemalt alahindab registreerimisel baseeruv haiguste järelvalve süsteem oluliselt tegelikku suguhaigustesse nakatumist.

Võrdlevalt on esitatud haigestumus mõnedesse suguhaigustesse 1998. aastal Eestis, Vene Föderatsioonis, Inglismaal, Soomes ja Ameerika Ühendriikides tabelis 1.

Haigestumus süüfilisse ja gonorröasse on arenenud Euroopa riikides madal. Klamüdioos on neis riikides üks sagedasim suguhaigus. Põhja-Euroopa riikides on klamüdioosi haigestumine vähenenud seoses efektiivsete ennetusprogrammide rakendamisega. Trihhomonoos on kõige sagedam suguhaigus maailmas, sellele vaatamata andmed selle haiguse kohta sageli puuduvad; haigust on arenenud Euroopa riikides harva. Genitaalherpes-infektsioon on eluaegne, tema kulg krooniline, retsidiveeruv ja ettearvatu. HSV tüübispetsiifiliste testidega tehtud uuringud näitavad, et see infektsioon on sagedasem, kui varem arvati, et piirkonniti on infitseeritus erinev ning et HSV-2 seroprevalents paljudes arenenud riikides suureneb.

HIV-infektsiooni epideemia on ulatuslikum, kui oletati veel dekaad tagasi. MTO ja UNAIDSi andmeil elas aastal 2000 maailmas 36,1 miljonit HIV-ga infitseeritud inimest. Kõige rohkem on nakatunud Kesk-Aafrikas (haiguse levimusmäär täiskasvanute hulgas 8,8%), Kariibi mere saartel (levimusmäär 2,3%) ning Lõuna- ja Kagu-Aasias (levimusmäär 0,56%). Arvestades jätkuvalt kõrget haigestumust Ukrainas ja Vene Föderatsioonis, on MTO andmeil Ida-Euroopas ja Kesk-Aasias HIV-infektsiooni levimusmäär täiskasvanute seas aastal 2000 0,35% ning peamiseks nakkuse leviku viisiks parenteraalne nakkus süstivate narkomaanide seas.

Eestis sagenes haigestumine suguhaigustesse tuntavalt möödunud dekaadil; haigestumise tõus oli ilmne, vaatamata muutustele haigusjärelvalves ja puudulikule haiguste registreerimisele. Kuigi traditsioonilistesse suguhaigustesse (süüfilis, gonorröa, trihhomonoos, klamüdioos) nakatumine oluliselt sagenes jäi haigestumus HIV-nakkusesse Eestis peaaegu kümneks aastaks madalale tasemele. HIV-sse haigestumuse märkimisväärne tõus vallandus 2000. aastal seoses nakkuse levikuga süstivate narkomaanide seas.

Suguhaiguste epidemioloogia kirjeldab neisse haigestumist, haiguste levimust piirkonniti ja ajaliselt ning selle muutusi. Epidemioloogilised uuringud on näidanud, et haigestumus ja levimus on piirkonniti ja ajas erinev, mis peegeldab suguhaigustesse haigestumist määravate tegurite varieerumist. Tavaliselt on haigestumine kõrgem linnades, noorte ja vallaliste isikute seas. Suguhaigusi põevad naised nooremalt kui mehed.

Suguhaigustesse nakatumist määravaid tegureid saab käsitleda kahel — indiviidi (bioloogilised ja psühholoogilis-käitumuslikud tegurid) ja sotsiaalsel tasemel (geograafilised, tehnoloogilised, struktuuralsed, kultuurilised, majanduslikud faktorid). Indiviidi tasemel on suguhaigustesse nakatumisega seotud mitmesugused seksuaal- ja tervisekäitumise vormid ning erinevate ainete kuritarvitamine. Kõrgenenud riskiga on seotud varajane seksuaalne debüüt, seksuaalpartnerite suur arv kogu elu jooksul ja käesoleval ajal, valimatu seksuaalpartnerite valik ja teatud seksuaaltehnikad (anaalne seks, “kuiv” seks), seksuaalvahekordade sagedus ja ajastamine (nt haigustunnuste esinemise ajal),

seksuaalne kuritarvitatus lapseas. Erinevad tervisekäitumise mustrid mõjuvad kas nakatumisvõimalusi vähendavalt (pidev ja korrektne kondoomi kasutamine, ringlõikus meestel, arsti poole pöördumine ja ravi- ning režiiminõuete järgimine) või suurendavalt (kaitsmata seksuaalvahekorrad, tupeloputused). Ainete kuritarvitamine (k.a alkohol) on riskifaktoriks nakatumisel suguhaigustesse, sõltumata vanusest, vanusest seksuaalse debüüdi ajal ja seksuaalpartnerite arvust. Sageli esinevad individuaalsel tasemel mõjuvad riskifaktorid koos.

Suguhaiguste epidemioloogilised uuringud keskendusid varasematel aastatel indiviidi tasemel mõjuvate faktorite uuringuile, praegu kasvab huvi ühiskonna tasemel mõjurite vastu. Kirjeldatud on rida sotsiaalfüüsilisi faktoreid seoses suguhaigustesse haigestumisega: geograafilised (linnad, suurte maanteed lähedus), tehnoloogilised (vaktsiini või ravi ja raviastutuste ning arstide, haiguse ennetusprogrammide, süstalde vahetamisprogrammide, kondoomide kättesaadavus ja turustamine), sotsiaalkultuurilised (sugudevaheline subordinatsioon, rahvussuhted, kuritegevus, sündimus, hariduskulutused) ja majanduslikud (töötus, keskmine sissetulek).

Adekvaatne ja nõuetele vastav suguhaiguste ravi ja käsitlus on äärmiselt tähtis. Haigusjuhu käsitlusele kuuluvad anamneesi kogumine, läbivaatus, diagnoosi püstitamine, ravi ordineerimine, nõustamine, kondoomi kasutamise promotsioon, partnerite/kontaktsete selgitamine ja ravi, haigusjuhu registreerimine ja vajadusel järelkontroll. Suguhaiguste raviks on väljatöötatud standardiseeritud käsitlusprotokollid erinevatele arstiabi osutamise tasemeile. Lisaks haiguste efektiivsele ravile on nende protokollide järgimisel eelised: aitavad kaasa meditsiinitöötajate väljaõppele ja nende töö hindamisele, lükkavad edasi ravimiresistentsuse teket ning on vajalikud efektiivsete ravimitega varustamise planeerimiseks. Eestis on suguhaiguste ravis kasutusel etioloogilisel diagnoosil põhinev printsiip. Etioloogiline ravi on küll korrektne ja väldib üleravimist, kuid kallid (laboratoorsete uuringute, transpordi- jm kulud), mistõttu ravi alustamine viibib, lisaks on veel senini säilinud soovimatus, (vale)häbi suguhaiguste raviga tegelevasse asutusse pöörduda.

Arengumaade jaoks on MTO juhtimisel väljatöötatud nn. sündroomse ravi protokollid. Sündroomne ravi põhineb koosinevatel ja kergesti äratuntavatel sümptomidel (=sündroom) ning ravil, mis on efektiivne enamuse või kõigi nimetatud tunnuseid põhjustavate mikroorganismide likvideerimiseks (nt ureetriidi ravimisel tehakse korraga gonorröa ja klamüdioosi ravi).

## **Teesides esitatud uuringute eesmärgid**

Analüüsida Eestis sugulisel teel levivatesse infektsioonidesse haigestumist aastatel 1990–2000, et selgitada haigestumise kiire tõusu põhjusi.

1. Selgitada suguhaigustesse haigestumist aastatel 1990–2000: trendid, suguhaiguste etioloogia (artiklid I, III, IV, VI); kaasvalt selgitada, kas trihhomo-

noosi nakatumine on nii sage, et oleks põhjendatud metronidasooli lülitamine uretriidi sündroomse ravi protokollis (artikkel III).

2. Selgitada ja analüüsida indiviidi ja ühiskonna tasemel määravaid faktoreid suguhaigustesse nakatumisel (artiklid II, IV, V):

- välja tuua seksuaal- ja tervisekäitumise ning ainete kuritarvitamise iseärasused, selgitada seos haigestumisega suguhaigustesse (artiklid II, IV);
- uurida ja analüüsida ühiskonna tasemel määratavaid faktoreid seoses suguhaigustesse haigestumise tõusuga aastatel 1990–2000 Eestis (artikkel V).

## Materjalid ja meetodid

1. Suguhaigustesse haigestumise andmete kogumine.

Haigusjuhtude registreerimise andmed maakondade tervisekaitsetalitusest laekuvad tsentraalselt Tervisekaitseinspeksiooni. Kõik arstid peavad kohustuslikus korras registreerima HIV-nakkuse, süüfilise, gonorröa, klamüdioosi, trihhomoonosi, suguelundite herpese ja kondüloomid. Registreerimiskord ei ole uuringualuse aja jooksul muutunud.

2. Uuritavad ja uuringu ülesehitus.

Artikkel II. Juht-kontrolluuringu tegime Tartu Ülikooli naha- ja suguhaiguste kliiniku polikliinikus, 09.1996–06.1998. a. Juhud: 189 polikliiniku patsienti diagnoositud suguhaigusega (süüfilis, gonorröa, klamüdioos). Kontrollrühm: Eesti rahvastikuregistri Tartu linna ja maakonna elanike hulgast juhuvaliku teel teostatud valimisse kuulus 1100 isikut, kellele saatsime koju kutse osaleda uuringus — osales 112 isikut.

Uuringu protseduurid: (1) kõik osalejad täitsid küsimustiku, mis käsitles seksuaalkäitumist, tervisekäitumist, ainete kuritarvitamist ja teadmisi suguhaiguste vältimise võimalustest; (2) kõigil tehti uuringud suguhaiguste diagnoosimiseks; kõik uuritavad allkirjastasid informeeritud nõusoleku vormi.

Artikkel V. Ökoloogiline uuring, kus kasutasime postkommunistlike ülemineku-aastate perioodiseerimist vastavalt M. Lauristini (1998) pakutule: 1987–1991 vabadusliikumise ja poliitiline läbimurre; 1991–1994 sõltumatu riigi taastamine, radikaalsed poliitilised reformid; 1995. aastast alates stabiilse demokraatliku süsteemi kujunemine, majanduslik ja kultuuriline stabiliseerumine. Administratiivselt on Eesti Vabariik jagatud 15 maakonnaks. Analüüsiks kasutasime lisaks haigestumusele tuberkuloosi ja süüfilisse järgmisi maakondi iseloomustavaid andmeid Eesti Statistikaametilt: mitte-etniliste eestlaste ja linnaelanike osa rahvastikus, tapmiste määr 10 000 inimese kohta, töötusemäär, elussündide arv fertiilses eas naistel.

Artikkel VI. HSV-infektsiooni seroepidemioloogiline läbilõikeuuring, kasutades kliinilistel eesmärkidel kogutud seerumi ülejääke HSV-serotüübiliste testide tegemiseks. Kokku analüüsiti 2845 seerumit: 1016 lastelt, 794 rasedailt

ja 1036 doonoreilt. Kasutasime HSV-tüübispetsiifilist testi firmalt MRL Diagnostics, Cypress, USA.

## Tulemused ja arutelu

Süüfilisse haigestumine tõusis 1990.–1998. aastal 23 korda: suurenedes vastavalt 3,3 haigusjuhult 75,7 haigusjuhule 1 000 000 kohta (joonised 1a ja 2). Pärast 8-aastast haigestumise tõusu langes 1999. a esmakordselt süüfilisse haigestumise tase 24%, moodustades 57,8 /100 000. Aastal 2000 see tendents jätkus. Gonorröasse haigestumus, mida Eestis iseloomustavad suured kõikumised eri aastakümnetel, on meil samas alati suhteliselt kõrge olnud, iseseisvusperioodi alguses see kahekordistus. Klamüdioosi haigestumus tõusis perioodi alguses oluliselt ning 1994. a oli esimene aasta, kui klamüdioosi haigestumus ületas gonorröasse haigestumuse. (Klamüdioosi haigestumise tõus perioodi algul kirjeldab eelkõige vastava diagnostika juurutamist Eestis neil aastatel.) Trihhomonoos on Eestis kõige sagedamini diagnoositav suguhaigus (joonis 2). Tartu Tervisekaitsetalitusse laekunud 1998. a registreeritud haigusjuhtude analüüsi tulemuste kohaselt oli trihhomonoos diagnoosimise sageduselt klamüdioosi järel teisel kohal, olles sagedasimaks uretriidi põhjustajaks meestel ning esines sageli kombinatsioonis teiste suguhaigustega (joonised 4 ja 5). Alates 1994. aastast võib Eestis täheldada mitmetesse suguhaigustesse haigestumise vähenemist (gonorröa, trihhomonoos, klamüdioos). Teadusajakirjanduses on arutletud suguhaigustesse haigestumise vähenemise põhjuste üle viimastel aastatel nii Eestis kui ka teistes hiljuti iseseisvunud riikides. Võimalike põhjustena tuuakse ära suguhaiguste puudulikku registreerimist arstide poolt, ühiskonna stabiliseerumist, aga ka asjakohaste ja efektiivsete raviskeemide rakendamist.

Seksuaal- ja tervisekäitumist ning ainete kuritarvitamist käsitletud uuringus leiti 112 kontroll rühma kuulunu hulgast 36-1 (32.,1%) vähemalt üks suguhaigus; 33-1 klamüdioos, kahel gonorröa ja ühel mõlemad haigused (süüfilist kontrollgrupi uuritavatel ei diagnoositud). Nimetatud uuringu oluliseks puuduseks on väike uuritute arv kontrollgrupis, mistõttu üldistavaid järeldusi on raske teha. Kuid ka olemasolevate tulemuste kohaselt esinesid nende käitumises statistiliselt tõepärased erinevused. Mõned kontrollrühma liikmetest võisid uuringus osaleda seoses eelneva kahtlusega, soovides uuringu raames läbida kontrolli suguhaiguste suhtes. Siiski tuleb arvestada, et klamüdioos kulgeb enamasti asümptomaatilisel, mistõttu meie tulemused on olulised, ilmestamaks suurt hulka haigeid inimeste seas ning ennetavate skriiningprogrammide vajalikkust nende väljaselgitamiseks ja raviks.

Traditsioonilistes suguhaigustesse nakatumise tõus on Eestis seotud kõrge riskiga seksuaalkäitumisega: mitmed seksuaalpartnerid, juhuslikud seksuaalsuhted (k.a juhuslikud seksuaalsuhted reisidel väljaspool Eestit), seksuaalvahekorrad alkoholijoobes. Mõlemas uuringugrupis (suguhaiged ja kontrollrühm) osalenute teadmised suguhaiguste levikuviisidest ja nende vältimis-

võimalustest olid puudulikud, mis seab inimesed suguhaigustesse nakatumise ohtu. Enamus osalejaist teadis, et kondoom kaitseb suguhaiguste eest, siiski uskus 65%, et kaitset pakub suguelundite pesemine, 19,5% uskus seda suukaudsetest rasestumisvastastest tablettidest. Alkoholi kuritarvitamine osalenute seas oli sage ning alkoholi kuritarvitajail oli rohkem seksuaalpartnereid, sh juhuslikke (Tabelid 2, 3).

Esimene HIV-nakkus registreeriti Eestis kümme aastat tagasi, 1988. aastal. 1988–1999 püsis haigestumine stabiilselt madalal tasemel, kõikudes 0,1/100.000 aastal 1988 kuni 0,6/100.000 aastal 1999. Kogu mainitud perioodi jooksul levis nakkus põhiliselt sugulisel teel, esimestel aastatel homoseksuaalselt, hiljem võrdselt homo- ja heteroseksuaalselt. Kaks esimest HIV-nakkuse juhtu veeni süstivatel narkomaanidel (VSN-del) diagnoositi 1997. ja 1998. a, sellele epideemilist levikut ei järgnenud.

HIV/AIDS-i suurenenud leviku ohule viitas juba 1995–1996 ilmnunud kõrgehaigestumine B- ja C-hepatiiti, kuna levikuteed on ühised: ohtlikud süstimistavad, ühiste süstalde kasutamine. 2000. a. mais–juunis diagnoositi esimesed viis HIV-nakkuse juhtu eeluurimisel viibivate kinnipeetavate VSN-de seas, nendest kolm oli Narvast. Augustis diagnoositi Narvas anonüümses VSN-del kabinetis kaheksa HIV-nakkuse juhtu.

VSN-de arvu plahvatuslik tõus algas 1994.–1995. a ja kestab tänaseni. Põhiline kontingent on heroiinitarbijad, valdavas enamuses vene keelt kõnelevad (ligi 90%), meessoost (85%), 15–25-aastased, oletatav arv kogu riigis 10 000–12 000.

Kokku registreeriti Eestis 2000. a jooksul 390 uut HIV-nakkuse juhtu (joonis 2), sellest ligi 90% moodustasid VSN-d. 304 juhtu registreeriti Narvas, 57 Kohtla-Järvel, 25 Tallinnas. 2001. aastal jätkus HIV-nakkuse epideemiline levik sama hoogsalt. Jaanuaris registreeriti 85, veebruaris 121, märtsis 170, aprillis 148 uut HIV-nakkuse juhtu. 2001. a levis nakkus Narvast teistesse Ida-Virumaa linnadesse ja Tallinnasse (vastavalt 180, 188 ja 124 juhtu). Epidemiooloogilised uuringud kinnitavad, et enim ohustatud on nooremad narkootikumide tarbijad, kes alles alustavad süstimist ja kasutavad ühte süstalt mitmekesi, jagades ühte uimastiannust mitmele.

Uuringus, mis käsitles süüfilise esinemist maakonniti seoses viis sotsiaal-majandusliku näitajaga, leidsime statistiliselt tõepärased positiivsed korrelatsioonid süüfilisse haigestumise ning maakonna mitte-etniliste eestlaste (Pearsons  $r=0,509$ ), linnaelanike osakaalu (Pearsons  $r=0,524$ ) ja tuberkuloosi haigestumuse (Pearsons  $r=0,444$ ) vahel (selgitab süüfilise haigestumuse varieeruvusest maakonniti vastavalt 25,9%, 27,5% ja 19,7%). Statistiliselt tõepärase negatiivse korrelatsiooni leidsime süüfilise haigestumise ja elussündide määra vahel (Pearsons  $p=-0,501$ ). Seost töötuse ja tapmiste määra ning süüfilise haigestumise vahel meie uuringus ei ilmnunud (joonis 6, Tabel 4). Nimetatud uuring käsitles unikaalset perioodi ühiskonna arengus, kus radikaalsed poliitilised ja majanduslikud muutused toimusid väga lühikese aja jooksul ning meil õnnestus ilmestada olulisi seoseid süüfilise haigestumise ja ühiskonna

taseme näitajate vahel. Tulemused toetavad arusaama suguhaigustest kui sotsiaalsetest haigustest.

### **Kokkuvõte**

Uuringu tulemused (suguhaigustesse nakatumist soodustavad kõrge riskiga seksuaalkäitumine ja puudulikud teadmised nende haiguste ennetamise võimaluste kohta uuritute hulgas) tähtsustavad tervise- ja seksuaalkasvatuse laiemat juurutamist oluliselt rahva tervise edendamises.

HIV-infektsioon levis Eestis plahvatuslikult alles pärast nakkuse levikut veeni süstivate narkomaanide seas. Protsessi pidurdamiseks on vaja oluliselt tõsta VSN-de teadlikkust ennetusmeetmetest (süstalde vahetus, asendusravi, kondoomide kasutamine, koolitus-/nõustamisprogrammid). Äärmiselt tähtis on ka efektiivne suguhaiguste ravi, vältimaks HIV-infektsiooni laialdast levikut heteroseksuaalse elanikkonna seas.

HIV/AIDS ja suguhaigused ei ole üksnes meditsiiniline, vaid ka riikliku tähtsusega sotsiaalne ja majanduslik riikliku tähtsusega probleem ning selle lahendamine on võimalik ainult juhul, kui võitlus AIDS-i, narkomaania ja suguhaigustega muutub riiklikuks prioriteediks, st liidetakse nii tervishoiu kui ka teised ühiskonna ressursid.





## **PUBLICATIONS**



Uusküla A, Silm H, Vessin T.  
Sexually transmitted diseases in Estonia: Past and present.  
International Journal of STD & AIDS 1997; 8, 1-5.

ORIGINAL ARTICLE

## Sexually transmitted diseases in Estonia: past and present

A Uusküla MD<sup>1</sup>, H Silm<sup>1</sup> and T Vessin MD<sup>2</sup>

<sup>1</sup>Department of Dermatology and Venereology, University of Tartu, Tartu, Estonia and

<sup>2</sup>Clinic of Dermatovenereology in Tallinn, Tallinn, Estonia

**Summary:** The present survey covers historical events in Estonia during the era of the USSR regime and the era after independence as regards incidence of sexually transmitted diseases (STDs). The diagnostic methods used as the reporting system are presented. Reasons for the increased incidence of traditional venereal diseases such as gonorrhoea and syphilis are discussed. The importance of migration of prostitutes from Russia is also considered.

**Keywords:** STD, Estonia, historical factors

### INTRODUCTION

Estonia, one of the Baltic states linked to the former USSR, regained its independence in 1991. The liberation was followed by rapid and dramatic changes, especially in the fields of economics and politics. This led to destabilization and social disintegration, with great changes in old moral norms and increased prostitution. In most developed countries the incidence of conventional STD such as gonorrhoea and syphilis has rapidly declined during the last 15 years<sup>1,2</sup>. The development in Estonia, as in the other Baltic countries and in Russia, has been completely different. During recent years the incidence of these STDs have increased rapidly.

Data as regards frequency and distribution of STDs are limited for several reasons. All STDs are not classified as reportable. Syphilis, gonorrhoea, *Chlamydia trachomatis* infections, trichomoniasis and genital herpes simplex virus (HSV) infections are reportable diseases in Estonia. Data about the annual incidence of gonorrhoea and syphilis are available from early 1930s. However, misdiagnosing and underdiagnosing are frequent and all new cases are not reported, especially if the diagnosis has been made by a gynaecologist or an urologist.

The population of Estonia is approximately 1.5 million and about one-third of the inhabitants live in the capital Tallinn, a seaport. The STD problem is especially concentrated to this area; in 1993 64% of new cases (240 cases) of syphilis and 50% of new cases (1783 cases) of gonorrhoea were reported from the Tallinn region<sup>3</sup>. In Estonia, like most western European countries, venereology is a

subspecialty of dermatology. Currently about 70 dermatologists are actively working in Estonia. The 4 special clinics are in the biggest cities, including Tallinn and Tartu. According to old traditions patients with syphilis have been hospitalized. This habit has slowly started to change after the introduction of long-acting penicillins. However, new modes of treatment are not sufficient for breaking down old traditions.

The diagnostics available and the procedure of use in Estonia are shortly presented in the following. During the USSR era the screening system for syphilis was entirely based on serological tests, mainly Wassermann complement-fixation (WR) test. All reported new cases with syphilis are and have been serologically verified. The tests available are as follows: the fluorescent treponemal antibody (FTA), the fluorescent treponemal antibody-absorption (FTA-Abs), the treponema pallidum haemagglutination (TPHA) and treponema pallidum immobilization (TPI) tests are used for verification and the WR and VDRL tests for screening purposes. The TPI test is performed only at the university clinic in Tartu. For diagnosing of bacterial STDs as gonorrhoea and chlamydia, microscopical and culture methods are used as routine tests. Different tests for antigen detection of *Chlamydia trachomatis* are available (IFA, ELISA). Culture diagnosis of chlamydia infections is carried out only in the central hospitals in Tartu and Tallinn. The diagnostic methods for viral STDs are restricted. Detection of HPV infections by use of PCR is carried out in cooperation between the University Clinic of Dermatovenereology and the Estonian Biocentre (mainly a basic science institution) in Tartu. The screening for HIV infection is carried out in the whole republic on a reliable level by the use of internationally accepted ELISA kits and verified by immunoblot.

Correspondence to: Dr A Uusküla, Department of Dermatology and Venereology, University of Tartu, Lõssi str. 21/23, Tartu EE 2400, Estonia

**THE CURABLE BACTERIAL SEXUALLY TRANSMITTED DISEASES**

Syphilis is a classical example of a STD which can be successfully controlled by public health measures<sup>1</sup>. After World War I and in the early 1930s the incidence of syphilis decreased in Estonia as in the other European countries, probably due to improved diagnostic tools, better treatment and control<sup>1</sup>.

In Estonia the incidence of syphilis decreased rapidly during this period, from 122/100,000 new cases to 43/100,000 in 1933 and remained on a stable level until World War II<sup>4</sup>. The decrease in the incidence of syphilis is comparable with data from other European countries. During the same time period the annual number of new cases/100,000 inhabitants in Sweden was lower than in Estonia, but a decline in incidence was observed<sup>5</sup>.

During and after World War II a dramatic increase in the incidence of syphilis occurred. The total number of new cases in 1949 was 1642 (149/100,000)<sup>4</sup>. After stabilization of the migration of ethnic groups and the economical situation in USSR and with the introduction of penicillin for treatment, the incidence of syphilis started to decrease. An improvement in disease control and partner notification system used became more effective during the same period. The annual incidence of new cases of syphilis remained stable (7/100,000) from 1959 to 1970 in Estonia<sup>4</sup>. A new increase of syphilis started and reached a peak in 1976 (42/100,000)<sup>4</sup>. If this was a marker for changed sexual behaviour (delayed sexual revolution) or a consequence of intense national policy of forced migration within USSR still remains unclear. The Soviet health care system reacted with rather repressive measures of partner notification and compulsory treatment and the incidence of syphilis decreased again to 8/100,000 in 1982<sup>4</sup>. All syphilis patients in Soviet Estonia were treated as in-patients.

From 1990 a constant increase of new cases has been recorded; 3/100,000 in 1990 and 56/100,000 in 1994 (Figure 1)<sup>4</sup>.

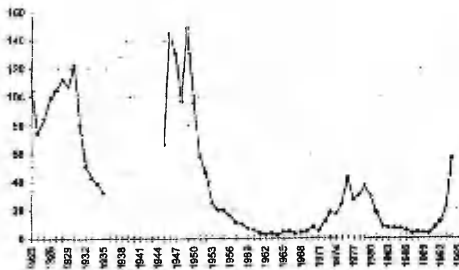


Figure 1. Incidence of reported syphilis cases per 100,000 inhabitants in Estonia, 1923-1994

The available data reporting the ratio of male to female new cases of syphilis during the last 25 years is very constant, never exceeding 2:1 (Figure 2).<sup>6</sup> One possible interpretation to that can be the mainly heterosexual transmission route of syphilis (also gonorrhoea) in Estonia. The Estonian data differ from available data from Sweden, where the same ratio has constantly been much higher than 2:1 during the same period<sup>1</sup>.

In Estonia syphilis is most prevalent in young adults. In 1994, 29% of women with verified syphilis were younger than 20 and 59% younger than 25. In 1992 the corresponding figures were even more intriguing: 35% of the infected women were younger than 20 and 67% younger than 25. In 1994, 44% of infected men were younger than 25 years and in 1992, 52% correspondingly<sup>3</sup>. The sexual activity of these young people probably started during the period of great changes in the community.

After many decades congenital syphilis was again diagnosed in 1993<sup>3</sup>.

Before World War II, from 1923 to 1935, the incidence of gonorrhoea varied on a level between 280-351/100,000 (Figure 3). In 1948 the incidence was 297/100,000 and thereafter a sharp decrease of annual reported cases took place. In 1951 the incidence was 92/100,000<sup>4</sup>. The decrease was probably related to the general stabilization after the war and



Figure 2. Male to female ratio of reported syphilis cases in Estonia, 1972-1994

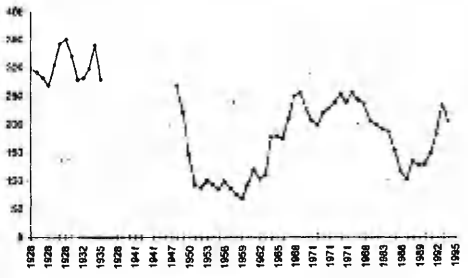


Figure 3. Incidence of reported cases of gonorrhoea per 100,000 inhabitants in Estonia, 1923-1994

to introduction of penicillin as well as a reform in notification of partners. The situation remained stable until 1961, whereafter a steady increase in new cases of gonorrhoea started and from 1968 to 1981 the annual incidence of new cases was steadily approximately 250/100,000 annually. Thereafter a steady decrease was recorded reaching a level of 100/100,000 in 1988<sup>4</sup>. It is of interest that a similar decrease started already in Sweden in 1972, in Finland in 1974 and in Norway in 1978. One reason for the prolonged high level of gonorrhoea was the routine use of penicillin or tetracyclines although gonococci rapidly developed resistance to these chemotherapeutics. One has to keep in mind that penicillin was used as an almost compulsory and only treatment in USSR. In a study carried out at the Department of Dermatovenereology, University of Tartu in 1994 it was found that 53% of isolated strains of *Neisseria gonorrhoeae* were  $\beta$ -lactamase producing, an incidence remarkably higher than in Sweden (7%) or USA (9%)<sup>7</sup>. It is highly probable, that the uniform treatment of gonorrhoea and the use of drugs without prescription in USSR resulted in a high incidence of antimicrobial non- $\beta$ -lactamase resistance.

During the last 15 years a sharp decrease of new cases of gonorrhoea has been observed in western Europe. In Sweden and Germany the current annual incidence of reported cases of gonorrhoea is approximately 10/100,000 and the majority of new gonorrhoea infections are imported to these countries<sup>2</sup>. The current epidemiological situation in these countries is partly a result of intervention programmes and partly due to changes in sexual behaviour as influenced by the existence of AIDS<sup>8</sup>. In Estonia the incidence of gonorrhoea is high and almost doubled from 128/100,000 in 1990 to 233/100,000 in 1993<sup>4</sup>. The marked increase again stresses how demographic, economic and political changes influence the pattern of STDs in a community. The decrease in incidence of new cases in 1994 and 1995 can partly be explained by the introduction of quinolones and cephalosporines in the treatment and probably related to stabilization in the community, but may also be related to incomplete case reporting. As in the case of syphilis the male to female ratio has remained stable as regards gonorrhoea, during the last 20 years (Figure 4)<sup>6</sup>. According to available statistical data the majority of affected individuals of both sexes were younger than 30 years of age from 1991 to 1994. The difference between the 2 sexes could be observed only in the age group under 20, in which approximately 40% more women than men were reported in both 1991 and 1992<sup>3</sup>.

*Chlamydia trachomatis* has been recognized as a genital pathogen during the last 25 years<sup>1</sup>. In Estonia, antigen detection methods for diagnosing chlamydial infections become available in 1990 and *C. trachomatis* culture a few years later. No data as regards the true incidence of genital chlamydia in Estonia are available. The diagnosis was primarily

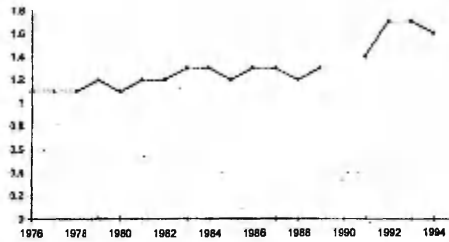


Figure 4. Male to female ratio of reported gonorrhoea cases in Estonia, 1976-1994

made by venereologists in symptomatic cases. Almost two-thirds of the reported cases were men in 1991 and 1992<sup>3</sup>. With increased screening of contacts and asymptomatic individuals the pattern has completely changed. In 1993 and 1994 over 80% of reported new cases were women<sup>3</sup>. In 1994, the total number of patients with genital chlamydial infection was approximately 4250 in Estonia and 1994 was the first year when chlamydial genital infections outnumbered the reported new cases of gonorrhoea<sup>4</sup>. It is still too early to draw any conclusions regarding the true incidence of chlamydial genital infections in Estonia.

#### Trichomoniasis

According to reported data *Trichomonas vaginalis* infections are the most prevalent STD in Estonia. The incidence has been high during the last 20 years and has especially increased during the last 5 to 6 years. The incidence in the whole population was 373/100,000 in 1994<sup>4</sup>. Approximately 75% of the reported patients were women and the most affected age group is between 20-24 years<sup>3</sup>.

In the Scandinavian countries trichomoniasis is not a reportable disease. But according to data obtained from visits to venereologists the incidence of this particular infection is low (approximately 1% of new patients).

#### SEXUALLY TRANSMITTED VIRAL INFECTIONS

Genital herpes has been a reportable disease in Estonia since 1991. The diagnosis is frequently made clinically by exclusion of other reasons for genital ulcers. Antigen detection is so far restricted to a few centres. The true incidence of genital herpes in Estonia is still unknown, although the disease is rather commonly detected at STD clinics.

Infections with HPV are not reportable in Estonia and no widely used screening system exist to detect this pathology (except Pap smears for women). In everyday practice this is not a rare

genital pathology among STD clinic patients, seen more commonly than genital herpes.

#### HIV infection

Until now HIV infections have rarely been diagnosed in Estonia, despite appropriate screening with reliable methods. Since March 1996, 59 seropositive cases have been reported. Presently, 44 HIV-positive individuals live in Estonia and 4 of these have developed AIDS. Previously 2 persons have died due to AIDS and one HIV-positive patient has committed suicide. According to available data, 21 of the HIV-positive individuals are homosexuals, 10 bisexuals and 18 heterosexuals. Four women have been found to be HIV positive. Fifteen of the HIV-positive patients have a history of a previous syphilis infection. One-fifth of the HIV-positive patients are sailors<sup>8,9</sup>.

#### DISCUSSION

An increased incidence of STD is a characteristic in countries, such as the Baltic area, which have recently regained independence. In such areas political and socioeconomical changes occur simultaneously and an increase in prostitution develops rapidly. In Estonia, the number of tourists has increased rapidly, however, mainly from Scandinavia, an area where the incidence of STD is low. The tourism from countries which belonged to the former USSR has decreased. One reason for the higher prevalence may therefore be the migration of prostitutes, especially from Russia. Other causes are probably connected with the dramatic changes within the society and a slowly responding medical service.

The lack in economic equilibrium and insecurity have deepened in the society, and on the other hand, the freedom to make decisions has increased without a simultaneous consciousness of responsibility. In the former communist countries the physicians were responsible. Currently the population of Estonia is not prepared to feel responsibility for their personal health. This is especially true for patients with STDs.

Estonia is gradually moving into a western-like society. However, one of the first steps has led to a rapid increase of prostitution and other forms of 'sex industry'. This type of problem is usually of economic origin. Young women without education have found an easy way to survive, but have no information on how to avoid catching an STD or avoid spreading STDs. This is an even more severe problem among migrating prostitutes and prostitutes belonging to foreign ethnic groups. As prostitution is closely connected with criminal groups, the problem is difficult to solve. A further problem is the high number of prostitutes not using condoms.

During the Soviet era contraceptives were equally unavailable. Abortion was the only method for family planning. Hence, the Estonian population still does not recognize the importance of using condoms, not even in the case of casual intercourse. The importance and necessity of using condoms are continuously advertised on television, in newspapers and magazines. However, major response has still not been notified.

In recently independent countries the economic situation is problematic with a high inflation rate. In Estonia, as in the other former communist countries, the economical distress has had a negative impact on the health care system in general and on the preventive services specifically. Medical services do not receive sufficient financial support. Although the AIDS problem has been recognized by the government of Estonia, the funds directed towards preventing the spread of HIV infections have entirely been allocated to the specialists of infectious diseases, leaving the venereologists without economical support. There are also no laws for infectious diseases, which causes problems regarding contact tracing in the field of STDs. A further problem is a lack of sufficient services for patients with STDs. Although the number of specialists is sufficient, most of them are working entirely as dermatologists. The centralized venereal service system created during the USSR era does not fit in with the changed conditions.

In conclusion, there was a 16 times increase in the incidence of new cases of syphilis during the period 1991 to 1994. This dramatic change does not compare with changes in other STDs. One possible cause may be that medical care does not sufficiently reach patients with syphilis; some are afraid of hospitalization and some may be incorrectly diagnosed and treated by gynaecologists or urologists. One reason is probably the high migration of prostitutes from Russia, especially from St Petersburg, an area with a very high prevalence of infectious syphilis. It is essential to carry out further investigations in order to sort out changes in epidemiology as well as tracing risk factors currently present in Estonia. This is of special importance as HIV transmission often occur among patients with genital ulcers.

Another question is, how reliable is the observation that the incidence of gonorrhoea has decreased during the last 2 years. This phenomenon may be explained by the increases in use of single dose quinolones and cephalosporines, which are also effective against B-lactamase producing gonococci. There may, however, be inaccurate data in the recording of new infectious cases.

Contact tracing is not on an appropriate level, as the working venereologists see too many patients daily and in practice there is not sufficient time to deal with this crucial matter. There is an urgent need for a new legislation and additional funding allocated to improve the system in order to

make it more effective and improve the availability for STD patients to receive correct and fast treatment.

It is also important to improve the cooperation between specialists in venereal diseases and specialists in infectious diseases. Problems with STD and HIV infections cannot be solved separately.

The major tool for dealing with viral STDs is prevention. The increased incidence of STDs is a marker of high-risk sexual behaviour, which creates a fertile soil for the spread of HIV infection. Further epidemiological studies regarding sexual/health behaviour as well as improved information as regards STD are currently needed in Estonia, in order to create a more effective preventive system.

*Acknowledgement:* Special thanks to Professor Allan Lassus from Institute of Derm/venereology Research, Helsinki Research Centre for help and useful advices.

## References

- 1 Adimora AA, et al. *Sexually Transmitted Diseases*, 2nd edn. New York: McGraw Hill, 1989:22,23,42
- 2 Kohl PK. Epidemiology of sexually transmitted diseases. *Sex Transm Dis* 1994;(suppl):81-3
- 3 Bureau of Estonian Medical Statistics. *Eesti tervishoiu statistika aastaraamat*. 1994:81-90
- 4 National Board of Health Protection. *Communicable Diseases Statistics in Estonia*, 1995:24,26,30,61
- 5 Danielson D. Gonorrhoea and syphilis in Sweden—past and present. *Scand J Inf Dis* 1990;69:69-76
- 6 Archive of Clinic of Dermatovenereology in Tallinn, Estonia.
- 7 Brilene T, Pöder A. Antibiotic susceptibility and B lactamase production of *Neisseria gonorrhoeae*. *IUVDT STD/AIDS World Congress*, 1995
- 8 Countine RA. Epidemiology of sexually transmitted diseases. *Sex Transm Dis* 1994;(suppl):51-2
- 9 *Anti-AIDS uudised*. Estonian Anti-AIDS News, 1995:12
- 10 Archive of Hospital of Infectious Diseases Merimetsa in Tallinn

(Accepted 25 November 1996)





Wilson TE, Uusküla A, Feldman J, Holman S, DeHovitz J.  
A case control study of beliefs and behaviors associated  
with STD occurrence in Estonia.  
Sexually Transmitted Diseases 2001; 28: 624–9.

# A CASE-CONTROL STUDY OF BELIEFS AND BEHAVIORS ASSOCIATED WITH STD OCCURRENCE IN ESTONIA

Tracey E. Wilson PhD<sup>1</sup>, Anneli Uusküla MD<sup>2</sup>, Joseph Feldman DrPh<sup>1</sup>,  
Susan Holman RN, MS<sup>1</sup>, and Jack DeHovitz, MD<sup>1</sup>

<sup>1</sup>State University of New York, Downstate Medical Center, Brooklyn, N.Y.,  
and <sup>2</sup>University of Tartu, Tartu, Estonia.

A case control study of patients at an STD clinic in Estonia found that individuals lacked adequate knowledge of disease transmission and that sexual behavior occurring during travel may contribute to disease rates.

## Abstract

**Background and Objectives.** Epidemiologic data document rapidly increasing rates of STD throughout Eastern Europe.

**Goal of this Study.** This case-control study was designed to delineate factors contributing to the STD epidemic in Estonia.

**Study Design.** One hundred eighty-nine cases and 112 controls completed a behavioral questionnaire and were tested for *Neisseria gonorrhoea*, *Chlamydia trachomatis*, and *Treponema pallidum*.

**Results.** STD prevalence among controls was 32%. Although participants believed that condoms prevent STDs, only 17% reported consistent use. Methods believed to prevent transmission included washing the genitals (65%), urinating (26%), douching (35%), and using oral contraceptives (19%). An interaction between sex and travel outside of Estonia (OR = 0.1, 95% CI = 0.0–0.7) reflects that males with STDs were more likely to report travel (46% cases, 45.5% controls with STD) than were those without STD (16.1% controls without STD).

**Conclusion.** STD rates are related to high-risk sexual behavior among males while traveling outside of Estonia. Intervention is needed to promote understanding of disease transmission dynamics in this area and to decrease sexual risk behavior, particularly in the context of travel.

Concomitant with the cessation of communist rule in 1991, the Baltic countries of Latvia, Estonia, and Lithuania have experienced a tenfold increase in rates of sexually transmitted disease (STD).<sup>1</sup> For example, in Estonia, incidence rates of syphilis have increased from 3 to 75.7 per 100,000 between 1990 and 1998 (Source: Estonian Ministry of Social Affairs, 10/2000). In addition, although there were relatively low rates of HIV infection in this country until last year, there has recently been a dramatic increase in the number of cases. At the end of 1999, the World Health Organization reported that there were only 50 known persons with HIV living in Estonia. However,

in 2000 an outbreak occurred in western Estonia, resulting in the report of over 300 cases to Estonia's mandatory State Health Protection Service.<sup>2</sup> Injection drug use (IDU) was posited to be a major contributing factor to this outbreak, as it has been throughout Eastern Europe.<sup>3-4</sup>

Several factors are likely to contribute to the increasing rates of STD/HIV infection in Estonia. First, the country borders the Russian Federation, where drug use, high rates of STD, economic instability, and low knowledge of disease transmission dynamics have been linked to a 100-fold increase in newly identified HIV infections between 1996 and 1998.<sup>5</sup> In this same time period, 3 to 175-fold increases in syphilis occurred in Eastern European and Central Asian countries,<sup>6-7</sup> with a prevalence rate among pregnant women of 710 per 100,000 in the Moscow region in 1997.<sup>8</sup> It has been posited that the increased mobility of populations across borders, in conjunction with a changing economic climate and shift toward a more western culture may make certain risk behaviors, such as trading sex for money and engaging in casual sexual relationships, more prevalent in Estonia and the other Baltic countries.<sup>9-10</sup>

Changes in the political and economic environment in Eastern Europe have also been associated with changes in the control of STDs. A highly developed system of surveillance for STDs was developed during the Second World War. At that time, there was active compulsory case finding and screening of certain occupational and clinical populations. The STD control system since the breakup of the Soviet Union has been characterized by serious shortfalls in funding, decentralization, and increased demand for confidentiality. Additionally, medications previously provided free must now be purchased.<sup>11</sup> These changes have been mirrored in former Soviet states such as Estonia,<sup>12</sup> and have clearly impacted the medical system's ability to track epidemics and to identify and treat patients with STD.

Although the prevalence of HIV in Estonia is still low overall, rising STD rates and drug use, coupled with increasing travel across borders to areas with higher HIV prevalence, could create the conditions for an HIV epidemic throughout the country. Irrespective of the changes occurring in the health system, little systematic research has been conducted to ascertain which risk behaviors are most closely associated with the evolving STD /HIV epidemic in these areas. In addition, there has not been adequate investigation into knowledge regarding disease transmission within this population. The current study seeks to identify predictors of STD acquisition in Estonia and to provide further insight into the factors that may be responsible for the increase in their incidence.

## Materials and Methods

Respondents. Study activities took place at the Tartu University Clinic of Dermatovenerology. The medical school is the only one in Estonia, and the STD clinic is the second largest in the country. A case control methodology was used. Between 9/96 and 6/98, 301 men and women over the age of 18 were recruited for study participation. Cases were composed of all participants who presented for care to the clinic of Dermatovenerology with a diagnosis of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Treponema pallidum*. Of the 229 clinic registrants approached for study participation, 189 were enrolled as cases.

Controls were selected at random from the regional population registry. Each participant selected was sent a letter describing the study and requesting them to contact study representatives at Tartu University. The letter included information that the study would involve an STD examination. A total of 1,100 letters were sent from the registry, and 112 persons responded and were enrolled as controls. Controls were further divided as a function of their STD status at the time enrollment. Demographic information derived from the registry revealed no statistically significant differences between those recruited and those declining participation as a function of their documented sex, marital status, or education.

**Procedures.** All patients who engaged in the study were asked to complete a self-administered questionnaire, after providing informed consent for their participation. Items included in the questionnaire were developed in English with the input of STD health care providers in Estonia, translated into Estonian and Russian, and piloted on a sample of 10 clinic patients. All study procedures were approved by the Institutional Review Board at SUNY Downstate Medical Center and by the Ethics Board at Tartu University.

Participants were asked to report on their lifetime history of STD diagnosis prior to study entry, drug use, and of paying for sexual activity. The prevalence of alcohol-related problems was determined via the four-item CAGE questionnaire.<sup>13</sup> Respondents also answered a series of questions on behavior in the last 3 months, including whether they had been sexually active, had greater than three sexual partners, used condoms consistently (always or almost always), engaged in sexual activity while drunk, offered money to someone in exchange for sex, had a casual sexual partner, engaged in anal sex, and whether they had used illicit drugs. Additional questions focused on whether respondents believed that their current sexual partners had other sexual partners in the last 3 months and whether they had traveled outside of Estonia in the past year. Finally, ratings were conducted on beliefs regarding STD prevention. The perceived efficacy of different activities in preventing the transmission of STD was assessed on three-point scales (ineffective, effective, don't know). Items included washing the genital area after having sex, urinating after sex, condom use, douching after sex, and using birth control pills.

All participants received an exam in which cervical or urethral cultures were obtained for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Specimens for gonorrhea were plated on Thayer-Martin medium (Nouva Aptaca srl, Italy). Cultures for chlamydia were performed using McCoy cell monolayers (European Collection of Cell Cultures, Salisbury, UK). In addition, syphilis serologic status was determined using the rapid plasma reagin test with *Treponema pallidum* with FTA for confirmation.

**Statistical analysis.** Demographic and behavioral variables were compared across groups (i.e., cases, controls with STD, controls without STD) using the Fisher exact test for dichotomous variables and t-tests for continuous variables. Beliefs about STD transmission were compared across groups using likelihood ratio chi-square tests. Odds of having an STD associated with engaging in a series of sexual risk behaviors were estimated among those who reported sexual activity in the last 3 months via logistic regression models, with group and sex included as main effects and a product term included to assess moderator effects. Demographic and behavioral factors that differentiated group membership based on these analyses were selected for inclusion in a multinomial logistic regression model.

## Results

**Participant characteristics.** Of the total study participants, 225 (74.7%) tested positive for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Treponema pallidum*. Among the 189 cases, 71% were positive for chlamydia, 24.1% for gonorrhea, and 25% for syphilis. Among cases, 15 were positive for gonorrhea and chlamydia, 11 for syphilis and chlamydia, 1 for syphilis and gonorrhea, and 1 for all STDs. Among the 112 controls, 36 (32.1%) were positive for at least 1 STD; 33 for chlamydia, 2 for gonorrhea, and 1 for gonorrhea and chlamydia. No controls were positive for syphilis. Controls with STD were more likely to test positive for chlamydia than were cases (94.4% versus 71.0%,  $p < .05$ ), and less likely to test positive for gonorrhea (8.6% versus 24.1%,  $p < .05$ ).

Respondents ranged in age from 18 to 57 (Mean = 26.5, SD = 6.4). A small majority of respondents were female (56.7% versus 43.3% male). Cases tended to be younger than controls; 67.5% of these fell below the median age of 25, as opposed to 50.0% of controls who presented with an STD and 36.6% of controls who were not positive for an STD ( $p < .05$ ). Approximately half (54.0%) of the participants included in the study were either married or living with a sexual partner. Sixty-two percent of the sample was employed, and 29.2% reported that they were currently going to school. Most of the population (80.7%) reported that they were Estonian, and 15.9% reported a Russian background. A history of drug use was reported by 15.1% of the entire sample, with 6.6% reporting drug use in the past 3 months. The drugs reported by those who had used in the past 3 months included marijuana ( $n = 6$ ), cocaine ( $n = 4$ ), and amphetamines ( $n = 6$ ). Injection heroin use was reported by 1 respondent, who also reported using ketamine. The prevalence of a clinically significant CAGE score was 35.2% across the entire sample. There were no statistically significant differences between cases, controls with STDs, or controls without STDs in terms of sex, marital status, employment rates, drug use history, or CAGE scores.

**Beliefs about STD prevention.** Both cases and controls held misperceptions about methods for preventing the transmission of STDs, although there were no statistically significant group differences in terms of level of knowledge. Across the entire sample, 65.2% believed that washing the genital area after sex is an effective means for preventing STD (6.3% reported that they did not know), 25.7% believed that urinating afterwards is effective (35.8% did not know), 35.5% believed that douching is effective (43.8% did not know), and 19.5% believed that using birth control pills is effective (22.2% did not know). Most of the participants believed that condoms are effective for STD prevention (94.5%); 3.1% claimed that they were unsure about their efficacy.

**Univariate behavioral associations with group membership.** Across all groups, respondents reported that they had recently engaged in a series of sexual behaviors (Table 1). In logistic regression models, there was a main effect of group membership after controlling for sex across several behaviors, including the proportion who reported (1) having a previous STD diagnosis (58.1% cases; 26.5% controls with STD; 40% controls w/o an STD), (2) having three or more sexual partners in the last 3 months (21.0% cases; 5.7% controls with an STD; 8.5% controls without an STD,  $p < .05$ ), (3) having a casual sexual partner in the last 3 months (43.0% cases; 20.6% controls with an STD; 20.3% controls without an STD,  $p < .05$ ), and (4) engaging in sexual activity while intoxicated from alcohol (67.4% cases; 48.5% controls with an STD; 43.1% controls without an STD,  $p < .05$ ). In turn, respondents who reported engaging in sexual

activities while intoxicated were more likely to report that in the last 3 months they had been inconsistent condom users (86.3% versus 76.4%,  $p = .055$ ), to have had three or more sexual partners (25.9% versus 6.4%,  $p < .05$ ), to report a casual sexual relationship (52.6% versus 19.6%,  $p < .05$ ), and to have solicited sexual activity (7.8% versus 1.1%,  $p < .05$ ). There were no group differences detected in the proportion reporting lifetime drug use, a high CAGE score, travel outside the country in the last year, abstinence in the last 3 months, a belief that the respondent's sexual partners had concurrent sexual relationships in the last 3 months, paying for sexual activity in the last 3 months, and always or almost always using condoms in the last 3 months.

There were main effects of sex after adjusting for group membership for (a) lifetime drug use (22.7% males; 9.5% females,  $p < .05$ ), (b) CAGE scores denoting alcohol problems (56.9% males; 18.8% females,  $p < .05$ ), (c) three or more sex partners in the last 3 months (30.2% males; 5.4% females,  $p < .05$ ), (d) prevalence of a casual sex partners in the last 3 months (50.8% males; 22.3% females,  $p < .05$ ), (e) being intoxicated during sexual activity (69.4% males; 51.6% females,  $p < .05$ ), and (f) paying for sex in the last 3 months (10.5% males, 0% females,  $p < .05$ ).

Product terms were computed between sex and group membership for each behavior. The interaction predicting travel outside of Estonia in the last year approached statistical significance ( $p = .07$ ), such that males with STDs were more likely to report travel in the past year (46% cases, 45.5% controls with STD) than were those without STD (16.1% travel for controls without STD). These differences were not seen among women (32% cases, 36% controls with STD, 31.8% controls without STD). Sexual relationships with new partners while traveling in the last year were reported by 16.1% of male cases, while none of the controls reported this behavior.

Multivariate behavioral associations with group membership. A multinomial logit model was conducted to assess for group differences as a function of age, STD history, travel, casual sexual partners, having three or more sexual partners, sexual activity while intoxicated, and sex (Table 2). A product term representing the interaction of sex and travel significantly increased the fit of the model, and was also included ( $\chi^2$  difference = 6.9,  $df = 2$ ,  $p < .05$ ). The resulting equation was statistically significant ( $\chi^2 = 53.1$  (16),  $p < .05$ ), with age, lifetime history of an STD, sexual intercourse while intoxicated, and the product term of sex and travel differentiating the groups. In terms of age, those less than the median age of 25 were significantly more likely to have an STD than were controls without an STD (OR = 3.3, 95% CI = 1.7 – 10.0), and controls with an STD (OR = 3.3, 95% CI = 1.5 – 10.0). Individuals who reported an STD diagnosis prior to study entry were over four times more likely to be cases than to be controls with an STD (OR = 4.2, 95% CI = 1.6 – 11.2). The only sexual behavior that differentiated group membership after controlling for other factors in the model was whether the respondent had engaged in sexual intercourse while intoxicated. Those engaging in this behavior were three and a half times more likely to be cases than to be controls without an STD (OR = 3.5, 95% CI = 1.6 – 7.6). Finally, after controlling for all other variables in the multivariate model, there was a statistically significant interaction detected between having traveled outside of Estonia by sex of the respondent for the comparison of cases versus controls without STD (OR = 0.1, 95% CI = 0.0 – 0.7), and a trend toward statistical significance for the comparison of controls with STD versus controls without STD (OR = 0.1, 95% CI = 0.0 – 1.0). These interactions reflect the greater odds of STD among males who traveled (OR = 4.4, 95% CI = 1.5 – 16.0).

## Conclusions

Increased rates of STD in Estonia are associated with patterns of sexual risk behaviors typical of STD epidemics in countries with similarly shifting political and social climates. Foremost, travel outside of Estonia among men was associated with risk for STD. Travel was also a marker for engaging in casual sexual relationships, in sex in exchange for money, and for sexual activity with a new partner while traveling. This suggests that sexual risk taking outside of the country may increase the likelihood of exposure to disease and subsequently increase the pool of infected persons within the region. Further investigation into the sexual health of travelers may yield important insights into STD transmission in this population.

Cases and controls exhibited similarly high levels of misconceptions regarding methods for preventing disease transmission. Although this population was generally aware that condom use is an effective prevention tool, over 65% believed that washing the genital area is effective, and between a fifth and a third of the population believed that using birth control pills, douching after intercourse, or urinating after intercourse are also effective. Incorrect knowledge regarding these issues may place individuals at increased risk for HIV/STD if they rely on these behaviors for disease prevention; education regarding the efficacy of different modes of disease transmission and prevention is important in this population.

Those who reported recent alcohol intoxication during sexual intercourse were more likely to be cases than to be controls testing negative for STD. Individuals reporting this behavior were also more likely to have multiple and casual sexual partners, to have engaged in sex exchange behavior, and were less likely to report using condoms consistently. It may be the case that a variable such as reporting engaging in sexual activity while intoxicated may be a marker for a behavioral style that is more risky overall (as opposed to this behavior playing more of a causal role in STD transmission). However, these findings, when coupled with the fact that over a third of the population had a CAGE score that indicating alcohol-related problems, suggest that identification and treatment of alcohol addiction may be an important component of disease control in this population. Further study is needed to ascertain the precise relationships between these variables.

Low rates of drug use may help explain why there has been a low impact of HIV in this area. Fewer than 7% of respondents reported any recent drug use, and only 1 reported injection drug use. In the neighboring Russian Federation, however, the UNAIDS has estimated that the proportion of HIV infections has nearly doubled from the end of 1997 to the end of 1999, and that nearly all of these infections were attributable to injection drug use.<sup>14</sup> Given increased travel between these regions, drug use prevention may be an important tool in preventing an epidemic of HIV infection in Estonia.

Although other sexual risk behaviors did not differentiate between cases and controls with and without an STD, there are several findings that warrant further attention. First, despite the fact that almost all respondents were aware that condom use protects against STD, less than one-fifth reported always or almost always using condoms. Second, the 32% STD prevalence rate among those recruited into the study as controls indicates that improved disease identification and treatment is warranted. Those individuals with STD in the control group were more likely to have chlamydia, and less likely to have had gonorrhea or syphilis. Given that symptoms of chlamydia are often



less noticeable than these other diseases, it may be that many of these individuals were probably unaware of their disease, rather than avoiding treatment for a suspected condition. These findings suggest that this population may benefit from efforts aimed at greater outreach and screening, coupled with sexual risk reduction counseling.

Several limitations to the data exist. First, given the low rate of response from the mail recruitment of controls, coupled with the extremely high rate of STD among this group, it is likely that some bias exists in this group. For instance, our letter of invitation explicitly stated that an STD examination would be provided as part of study activities. Thus, controls who responded to this letter may have done so because they were explicitly seeking STD care for an extant symptomatic condition. For these reasons, the STD prevalence rate among controls is likely to over-represent the true rate of infection in this group. Similarly, differences reported in risk behavior and cognitions may be attributable to sample selection, such that those with suspected conditions were more likely to differ than those without. These methodological concerns are often inherent in a case-control study such as this one. Given that there were still statistically significant behavioral differences between the cases and controls, however, this supports rather than detracts from the contention that these two groups are fundamentally different. A second issue relates to the relatively low sample size in the study. The smaller number of participants may have resulted in a decreased power to detect differences of interest, particularly as they relate to moderating relationships. Clearly, further research with a larger and more representative sample would help support the validity of the cognitive and behavioral differences found between cases and controls in this study.

The epidemic nature of STDs currently documented in Estonia and the other Baltic countries is consistent with our findings demonstrating high rates of sexual risk behavior and inadequate knowledge regarding prevention of disease transmission. It is important to note that the rise in STDs in the region, although quite dramatic, is also very recent. These factors signify that basic health education and promotion efforts implemented across the entire population should be a public health priority, particularly now while rates of HIV within this area are still low.

### **Footnotes**

Correspondence regarding this manuscript should be directed to Tracey E. Wilson, Ph.D., Department of Preventive Medicine and Community Health, State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Box 1240, Brooklyn, N.Y., 11203. This research was supported by Fogarty International Central/Eastern European HIV Research Program, #3 D43 TW00233-05S3. The Institutional Review Board of the participating institutions approved all study procedures, and informed consent was obtained from all study participants. The authors would like to acknowledge the contributions of Drs. Helgi Silm, Heli Raudsepp, and Airi Poder at the Tartu University Clinic of Dermatovenereology, Estonia, and Dr. Jonathan Zenilman at Johns Hopkins University, Maryland, US.

**Table 1.** Univariate logistic regressions predicting behavior as a function of group and sex.

	Cases (%) (N = 189)			Controls w/o STD (%) (N = 76)			Controls w/ STD (%) (N = 36)		
	M	F	Total	M	F	Total	M	F	Total
Lifetime history of STD *	55.2	60.6	58.1	29.0	47.7	40.0	27.3	26.1	26.5
Lifetime history of drug use †	24.4	12.0	17.7	19.4	6.8	12.0	18.2	4.0	8.3
CAGE score indicative of alcohol problems †	56.8	19.8	37.0	64.5	18.2	37.3	36.4	16.0	22.2
Travel outside Estonia in the last year ‡	46.0	32.0	38.5	16.1	31.8	25.3	45.5	36.0	38.9
Abstinent last 3 months	9.3	9.0	9.1	20.7	16.7	18.3	27.3	12.5	17.1
Three or more sexual partners last 3 months * †	34.9	9.0	21.0	20.7	0.0	8.5	18.2	0.0	5.7
Sexual relationship with a casual partner last 3 months * †	56.3	31.3	43.0	40.0	6.8	20.3	36.4	13.0	20.6
Sexual activity while intoxicated on alcohol last 3 months * †	77.4	58.5	67.4	50.0	38.5	43.1	54.5	45.5	48.5
Believes partner(s) had other sexual relationships last 3 months	17.7	20.2	19.2	9.5	15.8	13.6	0.0	21.1	15.4
Paid for sexual intercourse last 3 months †	13.1	0.0	6.0	3.4	0.0	1.4	9.1	0.0	3.0
Always used condoms last 3 months	18.8	21.3	20.1	4.2	18.4	12.9	0.0	15.0	10.7

\*  $p < .05$  main effect of group membership

†  $p < .05$  main effect of sex

‡  $p = .07$  interaction of sex \* group

**Table 2.** Multinomial logit model regressing group membership onto sexual risk behaviors.

	Chi-square (all df= 2)	Cases vs Controls w/o STD		Cases vs Controls w/ STD		Controls w/ STD vs controls w/o STD	
		OR	95% CI	OR	95% CI	OR	95% CI
Male	0.3	1.2	0.6 – 2.6	1.2	0.5 – 3.2	1.0	0.3 – 2.7
Age greater than 25	15.5 *	0.3	0.1 – 0.6	0.3	0.1 – 0.7	1.0	0.4 – 2.6
Travel outside Estonia in last year	1.4	1.5	0.7 – 3.2	0.8	0.3 – 2.0	1.8	0.6 – 5.1
Three or more sexual partners; 3 months	0.7	0.6	0.1 – 2.5	1.4	0.2 – 9.0	0.4	0.0 – 3.9
Sexual activity while intoxicated; 3 months	10.1 *	3.5	1.6 – 7.6	1.5	0.6 – 3.8	2.3	0.8 – 6.5
Sexual relationship with casual partner; 3 months	3.0	2.1	0.7 – 6.4	2.1	0.6 – 7.2	1.0	0.2 – 4.4
Ever been diagnosed with an STD	9.8 *	1.6	0.7 – 3.3	4.2	1.6 – 11.2	0.4	0.1 – 1.1
Travel * Male sex	6.9 *	0.1	0.0 – 0.7	1.1	0.2 – 6.8	0.1	0.0 – 1.0

\*  $p < .05$  for the overall parameter estimate.

## References

1. Lazdane G Bukovskis M. Epidemiology of sexually transmitted diseases in the Baltic countries. *Acta Obstetricia et Gynecologica Scandinavica — Supplement* 1995; 164: 1997; 128–31.
2. Stephenson J. HIV/AIDS surging in Eastern Europe. *JAMA* 2000; 284: 3113–3114.
3. Rhodes T Ball A Stimson G Kobyschcha Y Fitch C et al. HIV infection associated with drug injecting in the Newly Independent States, Eastern Europe: The social and economic contexts of epidemics. *Addiction* 1999; 94: 1323–1336.
4. Dehne K Khodakevich L Hamers F Schwartlander B. The HIV/AIDS epidemic in Eastern Europe: recent patterns and trends and their implications for policy-making. *AIDS* 1999; 13: 741–9.
5. Kalichman S Kelly J Sikkema K Koslov A Shaboltas A et al. The emerging AIDS crisis in Russia: Review of enabling factors and prevention needs. *Intl J STD & AIDS* 2000; 11: 71–75.
6. Dehne K Pokrovskiy V Kobyschcha Y Schwartlander B. Update on the epidemics of HIV and other sexually transmitted infections in the newly independent states of the former Soviet Union. *AIDS* 2000; 14(suppl 3): S75–S84.
7. Linglof T. Rapid increase of syphilis and gonorrhoea in parts of the former USSR. *Sexually Transmitted Diseases* 1995; 22: 160–1.
8. Borisenko K Tichonova L Renton A. Syphilis and other sexually transmitted diseases in the Russian Federation. *Intl J STD & AIDS* 1999; 10: 665–668.
9. Uuskula A Silm H Vessin T. Sexually transmitted diseases in Estonia: past and present. *Intl J STD & AIDS* 1997; 8: 446–50.
10. Mardh P. The changing face of prostitution in the Baltic Sea area. *Acta Obstetricia et Gynecologica Scandinavica — Supplement* 1997; 164: 132–3.
11. Bingham J. Waugh M. Sexually transmitted infections in the Russian Federation, the Baltics, and Poland. *Intl J STD & AIDS*. 10: 657–658, 1999.
12. Poder A Bingham J. Sexually transmitted infections in Estonia. *Intl J STD & AIDS* 1999; 10: 669–72.
13. Mayfield D McLeod G Hall P. The CAGE questionnaire: Validation of a new alcoholism screening instrument. *American Journal of Psychiatry* 1974; 131: 1121–3.
14. Anonymous. *AIDS Epidemiological Update*. Geneva, Switzerland: WHO, 2000.



Uusküla A, Plank T, Lassus A, Bingham JS.  
Sexually Transmitted Infections in Estonia —  
syndromic management of urethritis in a European country?  
International Journal of STD & AIDS 2001; 12: 493–49.

ORIGINAL ARTICLE

## Sexually transmitted infections in Estonia — syndromic management of urethritis in a European country?

Anneli Uusküla MD<sup>1</sup>, Toomas Plank MSc<sup>2</sup>, Allan Lassus MD PhD<sup>3</sup>  
and James S Bingham MB FRCP FRCOG<sup>4</sup>

<sup>1</sup>Clinic of Dermatovenereology, <sup>2</sup>Institute of Experimental Physics and Technology, University of Tartu, Estonia, <sup>3</sup>University of Helsinki, Helsinki, Finland and <sup>4</sup>Guy's & St Thomas' Hospital, London, UK

**Summary:** Sexually transmitted infections (STIs) are considered a major public health problem, globally. In particular, increasing STI rates have been documented throughout eastern Europe and central Asia. The Russian Federation and adjacent countries have, traditionally, managed STIs on an aetiological basis. This approach is expensive in terms of laboratory costs and it may lead to delayed diagnosis and treatment. To overcome the limitations of the aetiological management of STIs, the World Health Organization (WHO) has placed an increased emphasis on integrated care using syndromic management at the primary care level, especially in developing countries. This article reviews the current aetiology of STIs in Estonia, an eastern European country bordering the Baltic Sea and formerly a part of the Soviet Union, with the aim of defining whether infection with *Trichomonas vaginalis* is common enough to include its management in a syndromic management protocol. The use of syndromic management, in general, is also discussed.

**Keywords:** Sexually transmitted infections, syndromic management, trichomoniasis, Estonia

### INTRODUCTION

Sexually transmitted infections are considered a major public health problem, globally. HIV and STI epidemics have had remarkable social, demographic and economic consequences in Africa and Asia. Since the 1990s, there has been a dramatic increase in the reported incidence of STIs in eastern Europe and central Asia<sup>1</sup>. Despite under-reporting of cases and a decline in mass screening, an epidemic has been documented<sup>2,5</sup>.

The Russian Federation and its adjacent countries have, traditionally, managed STIs on an aetiological basis, i.e. the diagnosis is made first before treatment is given. This approach is expensive because of physician, laboratory and consumable costs, it may also lead to delay in diagnosis and treatment and might carry the risk of stigma if the clinic is designated as an STI clinic<sup>3</sup>. Economic difficulties, market reforms and political restructuring have had a detrimental impact on the healthcare system. Medical services have not received sufficient financial support<sup>4,5</sup> and limited resources have led to a situation where specialist STI services are

available to a minority only, i.e. those who can pay (in some regions) or urban residents near centres with laboratory support<sup>1</sup>. To overcome the limitations and the expense of aetiological management of STIs, the WHO emphasizes an integrated primary care approach using syndromic management. The advantages of this might be prompt care and cost saving, with increased patient satisfaction. However, the syndromic approach is of limited use in those with poor treatment-seeking behaviour and is only applicable to patients with symptomatic infection<sup>6</sup>. Further, while it may be useful in the management of urethritis and genital ulceration, its value is less well proven for the management of vaginal discharge. In addition, the epidemiology of STIs may vary from country to country, even within the same region<sup>7</sup>. These differences may reflect a variety of social, cultural and socioeconomic factors including access to appropriate treatment<sup>8</sup>. In order to maximize the value of the syndromic approach the prevalence of the various STIs and their susceptibility to antibiotic treatment needs to be known<sup>6,9</sup>.

This article reviews the current epidemiology of STIs in Estonia, an eastern European country bordering the Baltic Sea and formerly a part of the Soviet Union. The aim is to define whether infection with *T. vaginalis* in men is common

Correspondence to: Anneli Uusküla, Clinic of Dermatovenereology, University of Tartu, Lossi st. 21/23, Tartu 51003, Estonia  
E-mail: annskla@ut.ee

enough to include its treatment in a syndromic management protocol. The use of syndromic management, in general, for the management of STIs is also discussed.

**INCIDENCE AND TRENDS OF STIs IN ESTONIA, 1988-1999**

Epidemiological information about STIs in Estonia is derived from notification of cases and epidemiological studies. Syphilis, gonorrhoea, trichomoniasis, chlamydial infection, genital herpes and anogenital wart virus infections, as well as HIV infection are all notifiable to the Health Protection Inspectorate and this is a mandatory obligation on physicians. However, all STI surveillance systems underestimate the prevalent caseload since not all infections are reportable and many patients with STIs are asymptomatic and, therefore, do not seek care. Because of the continuing public perception of social stigma associated with the acquisition of an STI, many patients do not seek care at all and, even if they do, as elsewhere in the world, misdiagnosis may occur and infections may not be reported because of this. Despite these well known problems, and a decline in the mass screening which used to take place during the Soviet era, the incidence of reported STIs increased during the early 1990s (Figure 1), the most dramatic rise being in new cases of syphilis where the prevalence increased between 1990 and 1998 from 3.3 to 75.7 per 100,000<sup>10</sup>. The prevalence of gonorrhoea almost doubled between 1990 and 1993 (the first years of independence in Estonia) from 128 to 233 per 100,000<sup>10</sup>. Antigen detection methods for diagnosing genital infection as *Chlamydia trachomatis* became available in 1990 with culture coming on line a few years later. The reported number of new cases of chlamydial infection exceeded that of gonorrhoea for the first time in 1994. In 1995, the prevalence of chlamydial infections was 364 per 100,000 population<sup>10</sup>.

Infection with *T. vaginalis* is the most prevalent non-viral STI in Estonia. The incidence has been

high over the last 20 years and showed an increase in the beginning of 1990s. In 1996, the reported incidence was 400 per 100,000 population, being the leading STI for men (Figure 2), and frequent cause of male urethritis (Figure 3). In recent years, however, the reported number of infections has declined<sup>10</sup>. Genital herpes has been reportable since 1991. The diagnosis is frequently made on clinical grounds and antigen detection is, so far, restricted to only a few centres. The incidence of neonatal herpes infection is estimated to be approximately one per 4000 deliveries<sup>11</sup>. A seroprevalence study, conducted in the years 1996-1997 showed that 12.7% of pregnant women had herpes simplex virus (HSV-2) antibodies and 36.1% had antibodies to human papillomavirus (HPV-16)<sup>12</sup>.

The incidence of HIV infection in Estonia has remained low. Since 1988, 334 cases have been identified with a male to female ratio of 274/60<sup>14</sup>. The available data on those tested for HIV infection indicate that the high-risk groups in Estonia are injecting drug users, patients with other STIs and sailors<sup>13-15</sup>.

**DIAGNOSIS OF STIs IN ESTONIA**

Syphilis is diagnosed both clinically and in the case of a primary chancre by dark ground examination of secretions from the lesion for identification of *Treponema pallidum*. All cases, whether associated with clinical infection or not, are confirmed using serological tests. Blood is screened using either the rapid plasma reagin (RPR) test or the Venereal Diseases Reference Laboratory (VDRL) test. Confirmation is with the *Treponema pallidum* haemagglutination assay (TPHA) and/or the fluorescent treponemal antibody-absorbed (FTA-Abs) test. Detection of chlamydial infection is by one of the antigen detection methods such as enzyme immunoassay (EIA) or indirect fluorescent antibody (IFA) test and, where available, deoxyribonucleic acid (DNA) amplification tests such as the ligase chain reaction (LCR) or polymerase chain reaction (PCR). These latter tests are not widely available

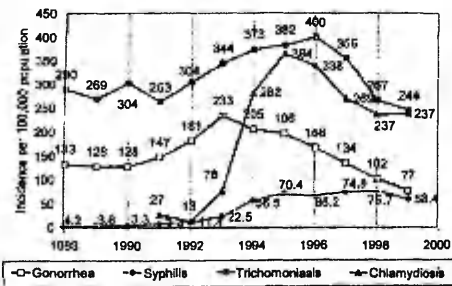


Figure 1. Reported incidence of sexually transmitted infections in Estonia 1988-1999

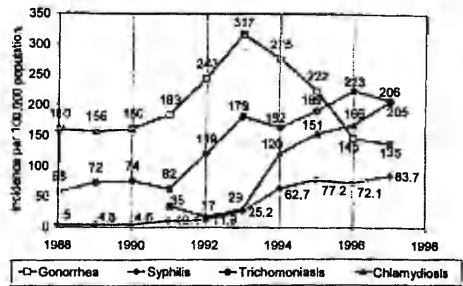


Figure 2. Reported incidence of sexually transmitted infections in men in Estonia 1988-1997



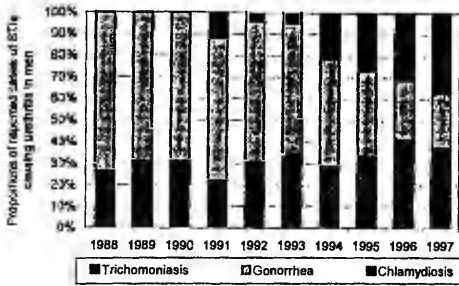


Figure 3. Proportions of reported cases of sexually transmitted infections causing urethritis in men in Estonia 1988-1997

due to their high cost. Gonorrhoea is diagnosed on microscopy of a Gram-stained smear of genital secretion and by culture on a selective medium. Trichomoniasis is identified on microscopy of a wet preparation and by culture (using Trichomonas Medium No. 2, Oxoid Ltd, UK), taken from the urethra. Genital herpes has been a reportable disease in Estonia since 1991. The diagnosis is frequently made clinically by exclusion of other reasons for genital ulcers. Antigen detection is restricted, so far, to a few centres and identification by culture method is not available in Estonia. The true incidence of genital herpes in Estonia is still unknown, although the disease is rather commonly detected at STI clinics.

Detection of HIV antibodies in Estonia is through the use of internationally accepted enzyme-linked immunosorbent assay (ELISA) kits and positive results are verified by immunoblot.

**ANALYSIS OF STI DATA REPORTED TO THE HEALTH PROTECTION SERVICE IN THE TARTU DISTRICT**

Tartu is the second largest city in Estonia with a population of approximately 100,000. The population of Tartu District (including Tartu city) is 150,000. Tartu University has the only medical school in the country. Each district in Estonia has a Health Protection Service, which collects data about notified cases of STIs from all medical facilities in its locality. Until 1998 the data included a patient's personal identification number. We used this to find out people with several concomitant infections and/or persons with frequently diagnosed STIs. In 1998, in Tartu city and its district, 1558 cases of STIs were reported from 19 different medical facilities. The male to female ratio was 41:59. There were 61 cases of syphilis, 92 cases of gonorrhoea, 386 cases of trichomoniasis, 673 cases of chlamydia infection, 90 cases of genital herpes and 256 cases of anogenital wart infection. Of these 1558, 1387 cases (1219 individuals) were eligible for further analysis of concomitant infections. In other

cases (171), some digits of patient's personal identification number, needed for identifying people, were missing.

In 1998, 46 females (5.8%) and 74 males (17.6%) were reported to have co-infection with at least 2 different STIs during the same clinical episode. The most frequent combination was, in women, co-infection with *C. trachomatis* and *T. vaginalis* (36%). In women with more than one infection, *T. vaginalis* was found in 56% of cases (Figure 4). In men, trichomonal infection was accompanied by chlamydia infection in 28% of cases and by genital wart virus infection in 16% of cases. In men with more than one infection, *T. vaginalis* was found in 59% of cases (Figure 4).

Co-infection with *C. trachomatis* and *Neisseria gonorrhoeae* was found in only 9 patients (0.7% of all patients) and the detection of more than 2 STIs, simultaneously, was very rare (13 patients, 1.1% of all persons with STIs). Of those with more than 2 infections 85% were men. Two point nine per cent of patients with proven STIs had repeated episodes within the same year.

Finally, all medical facilities are supposed to report their data to the Health Protection Service. In spite of that, in Tartu city and its district, 98% of cases of syphilis, 90% of gonorrhoea cases and 97% of those notified with genital wart virus infection were reported from the University STI Clinic. Furthermore, 96% of cases of trichomoniasis in

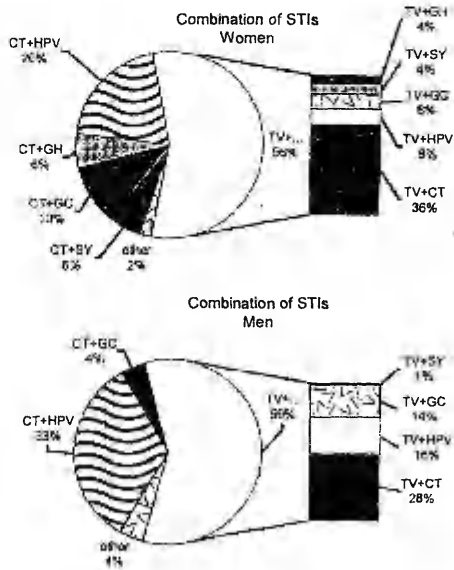


Figure 4. Combination of sexually transmitted infections. CT=chlamydiae, TV=trichomoniasis, HPV=anogenital HPV infection, GC=gonorrhoea, GH=genital herpes, SY=syphilis

men and 97% of cases of chlamydiosis in men were reported from the University STI Clinic.

## DISCUSSION

Sexually transmitted infections have significant complications and social stigma associated with them. Pelvic inflammatory disease, ectopic pregnancy and tubal infertility are well recognized complications of chlamydial and gonococcal infections but some STIs may influence the risk of still birth, preterm labour and can affect the neonate<sup>3</sup>. In Estonia, the ectopic pregnancy rate is high and has increased from 11 to 16 per 1000 pregnancies between 1990 and 1996<sup>16</sup>. Local studies, in Estonia, suggest a high rate of secondary infertility and signs of tubal damage were detected at laparoscopy in 63–80% of infertile female patients<sup>17</sup>. After an absence of many decades, 17 cases of congenital syphilis have been reported since 1993<sup>10</sup>.

The WHO syndromic management guidelines opine that, apart from gonococcal and chlamydial infections, it is not necessary to treat other causes of urethral discharge such as *Ureaplasma urealyticum* or *T. vaginalis*. This is because neither are supposed to be common and they do not lead to complications<sup>18</sup>. Nevertheless, high rates of trichomonal infection have been found in developing countries<sup>19,27</sup> and in industrialized countries<sup>20,28</sup>. Recently published findings suggest that, even in industrialized countries, diagnostic evaluation and empirical treatment of older men with non-gonococcal urethritis<sup>25</sup>, and partner management in both sexes should include treatment for *T. vaginalis*<sup>25,26</sup>. In Estonia, trichomoniasis and chlamydial infection are the most prevalent non-viral STIs and, according to published data, this is also the situation in the Russian Federation<sup>29</sup> and in Mongolia<sup>20</sup>. Unfortunately there is scant data from other countries in eastern Europe and central Asia, partly because trichomoniasis is not a reportable disease in some countries (Latvia and Lithuania). In a study of prostitutes in Riga, Latvia, of 107 enrolled prostitutes studied, in none was evidence of HIV infection detected but the prevalences of trichomoniasis, syphilis and gonorrhoea among these women were 35.5, 15.7 and 10.2%, respectively<sup>31</sup>.

In men, trichomoniasis has been associated with prostatitis, epididymitis and infertility with the strongest association being with non-gonococcal urethritis. Balanitis and posthitis have been described with trichomoniasis and, in severe cases penile ulceration too<sup>32</sup>. In women, vaginitis and vulvitis are the main clinical conditions<sup>33</sup>. Recent studies have shown an association between trichomoniasis and low birth rate babies (independent of HIV infection and other risk factors associated with low birth rate)<sup>21,34</sup> and preterm labour<sup>34</sup>. Classic STIs may facilitate HIV transmission both ways—increasing the infectiousness of and susceptibility to HIV infection<sup>35</sup>. Degradation of secretory leucocyte protease inhibitors (SLPI) is associated

with trichomonal infection. SLPI is believed to limit the transmission of HIV infection by inhibiting virus entry into monocytes (*in vitro*)<sup>36</sup>. Urethral infection with gonorrhoea and trichomoniasis has been found to have a significant effect on HIV-1 RNA excretion<sup>35,37,38</sup>. Data from Laga and her colleagues show an association between trichomoniasis and acquisition of HIV infection in women, with estimated relative risks ranging from 1.8–3.0<sup>22</sup>.

Trichomoniasis is the most common non-viral STI worldwide<sup>39</sup> and, although often asymptomatic in men, it may be more common than is generally believed and may persist in the genital tract over a long period of time. Although there is information that trichomoniasis may play a role in increasing HIV transmission, further studies to clarify this will be needed.

Algorithms for the management of urethral discharge in men have been evaluated and have been proven to be valid and sensitive<sup>9</sup> but, with a caveat: that the chosen antimicrobial regimens should cover the major pathogens responsible for the syndromes in a specific region<sup>7</sup>. By ignoring trichomoniasis as a cause of urethritis in men in a setting where trichomonal prevalence is high, basic syndromic management targets might be missed: firstly, effective treatment of the genital tract at the first visit and patient satisfaction<sup>6,9</sup>. The first visit may be the only opportunity to treat and counsel, as follow-up rates in men can be low<sup>6</sup>. The role of metronidazole as a first-line medication in the syndromic management of STIs has been discussed by other authors<sup>23,40</sup>. Researchers in southern Thailand have agreed that, in their region, *T. vaginalis* was not common enough to include it in a first-line syndromic management protocol for male urethritis (prevalence 1.6%)<sup>23</sup>. However, in Estonia, trichomoniasis accounts for 35% of cases of male urethritis<sup>10</sup> and is found in 59% of men with mixed STIs (in a situation where co-infection with *C. trachomatis* and *N. gonorrhoeae* is detected in less than 1% of patients with STIs). Thus it might be reasonable to include metronidazole among the first-line treatments for the urethral discharge syndrome in men.

To control the incidence of STIs it is important that services are accessible, acceptable and that the treatment prescribed is effective. Because of economic difficulties in Estonia, the management of STIs and control efforts are limited and a specialist service using full laboratory facilities is expensive and is really only accessible to urban residents near centres with laboratory support or to the minority who can afford to pay for the services. Under the Soviet era, the healthcare system was centralized, with STI care being mostly provided through dermatovenereology clinics which used a laboratory-based system of diagnosis. After independence in Estonia, while the centralization of services is less, it may be appropriate, outside the main centres, to provide care for STIs within the primary healthcare system<sup>1</sup>. Certainly, in Estonia, it

is perfectly legal to provide STI care at that level but doctors practising in that situation often do not have adequate training nor access to appropriate laboratory facilities and, therefore, accurate diagnosis may not always be made—a situation described by other authors<sup>41</sup>. In Tartu, almost all gonorrhoea and syphilis cases are reported from the University Clinic but, bearing in mind that many infections are asymptomatic, and the lack of expertise among other doctors (family doctors, gynaecologists and urologists), the opportunity is probably being lost to treat symptomatic patients or, the diagnosis may be completely overlooked. We feel that, in the primary care setting there would be considerable advantage to the use of syndromic STI management protocols and, in Estonia, the inclusion of metronidazole amongst the medications used for the urethral discharge syndrome would be appropriate.

**Acknowledgement:** Parts of the information provided herein were presented at the XIII Meeting of the International Society for Sexually Transmitted Diseases Research, Denver, Colorado, July 1999.

## References

- 1 Waugh MA. Task force for the urgent response to the epidemics of sexually transmitted diseases in eastern Europe and central Asia. *Int J STD AIDS* 1999;10:60–2
- 2 Tichonova L, Borisenko K, Ward H, Meheus A, Gromyko A, Renton A. Epidemics of syphilis in the Russian Federation: trends, origins, and priorities for control. *Lancet* 1997;350:210–13
- 3 Adler M. Strategies for prevention and treatment of sexually transmitted infections. *Int J STD AIDS* 1998;9(suppl. 1):8–10
- 4 Uusküla A, Silm H, Vessin T. Sexually transmitted diseases in Estonia: past and present. *Int J STD AIDS* 1997;8:446–50
- 5 Bingham JS, Waugh MA. Sexually transmitted infections in the Russian Federation, the Baltic States and Poland. *Int J STD AIDS* 1999;10:657–8
- 6 Dallabeta GA, Gerbase AC, Holmes KK. Problems, solutions, and challenges in syndromic management of sexually transmitted infections. *Sex Transm Inf* 1998;74(suppl. 1):S1–S11
- 7 Gerbase AC, Rowley JT, Mertens TE. Global epidemiology of sexually transmitted diseases. *Lancet* 1998;351(suppl. III):2–4
- 8 Wasserheit J. The significance and scope of reproductive tract infections among Third World women. *Int J Gynecol Obstet* 1989;3(suppl.):145–68
- 9 *Sexually Transmitted Diseases: Policies and Principles for Prevention and Care*. UNAIDS/97.6
- 10 National Board of Health Protection. *Communicable Diseases Statistics in Estonia* 1998;24,26,30,61
- 11 Szirko F. Prevention of a neonatal infection. *Proceedings of the 2nd Conference of the Estonian Union Against Sexually Transmitted Infections*, 9–10 June 2000, Otepää, Estonia
- 12 Kibur M, Koskela P, Dillner J, et al. Seropositivity to multiple STIs is not common. *Sex Transm Dis* 2000;27:425–30
- 13 Tammi L, Ustina V, Raukas M. Ülevaade eestis registreeritud HIV-nakkustest aastatel 1988–1997. *Eesti Arst* 1998;suppl. 1:547–50
- 14 Archive of Estonian Health Protection Inspectorate and HIV/AIDS reference laboratory, Hospital Merimetsa in Tallinn, 27 December 2000
- 15 Dehne KL, Khodakevich L, Hamers FF, Schwartlander B. The HIV/AIDS epidemic in eastern Europe: recent patterns and trends and their implications for policy-making. *AIDS* 1999;13:741–9
- 16 Szirko F. Emakaväline rasedus suguhaiguste esinemissageduse indikaatorina. *Proceedings of the 1st Conference of Estonian Union Against Sexually Transmitted Infections*, 11–12 June 1999, Roosta, Estonia.
- 17 Saarma I. *Chlamydia trachomatis* ja naise fertiilsus. *Proceedings of the 2nd Conference of the Estonian Union Against Sexually Transmitted Infections*, 9–10 June 2000, Otepää, Estonia.
- 18 *STD Case Management*. WHO/GPA/TCO/PMT/95.18 B
- 19 Wawer MJ, McNairn D, Wabwire-Mangen F, Paxton L, Gray RH, Kiwanuka N. Self-administered vaginal swabs for population-based assessment of *Trichomonas vaginalis* prevalence. *Lancet* 1995;345:130–1
- 20 Sorvillo F, Kovacs A, Kerndt P, Stek A, Munderspach L, Sanchez-Keeland L. Risk factors for trichomoniasis among women with human immunodeficiency virus (HIV) at a public clinic in Los Angeles County, California: implications for HIV prevention. *Am J Trop Med Hyg* 1998;4:495–500
- 21 Sutton MY, Sternberg M, Nsuami M, Behets F, Nelson AM, Sr Louis ME. Trichomoniasis in pregnant human immunodeficiency virus-infected and human immunodeficiency virus-uninfected congolese women: prevalence, risk factors, and association with low birth weight. *Am J Obstet Gynecol* 1999;3:656–65
- 22 Laga M, Manoka A, Kivuvu M, et al. Non-ulcerative sexually transmitted diseases as risk factors for HIV-1 transmission in women: result from a cohort study. *AIDS* 1993;1:95–102
- 23 Chandeying V, Skov S, Tabrizi SN, Kemapunmanus M, Garland S. Can a two-glass urine test or leucocyte esterase test of first-void urine improve syndromic management of male urethritis in southern Thailand? *Int J STD AIDS* 2000;11:235–40
- 24 Sorvillo F, Kerndt P. *Trichomonas vaginalis* and amplification of HIV-1 transmission. *Lancet* 1998;351:213–14
- 25 Joyner JL, Douglas JM Jr, Ragsdale S, Foster M, Judson FN. Comparative prevalence of infection with *Trichomonas vaginalis* among men attending a sexually transmitted diseases clinic. *Sex Transm Dis* 2000;27:236–40
- 26 Niccolai LM, Kopicko JJ, Kassie A, Petros H, Clark RA, Kissinger P. Incidence and predictors of reinfection with *Trichomonas vaginalis* in HIV-infected women. *Sex Transm Dis* 2000;27:284–8
- 27 Passey M, Mgone CS, Lupiwa S, et al. Community based study of sexually transmitted diseases in rural women in the highlands of Papua New Guinea: prevalence and risk factors. *Sex Transm Dis* 1998;2:120–7
- 28 Shuter J, Bell D, Graham D, Holbrook KA, Bellin EY. Rates of and risk factors for trichomoniasis among pregnant inmates in New York City. *Sex Transm Dis* 1998;6:303–7
- 29 Borisenko KK, Tichonova LI, Renton AM. Syphilis and other sexually transmitted infections in the Russian Federation. *Int J STD AIDS* 1990;1:665–8
- 30 Purevdawa E, Moon TD, Baigalmaa C, Davaajav K, Smith ML, Vermund SH. Rise in sexually transmitted diseases during democratization and economic crisis in Mongolia. *Int J STD AIDS* 1997;8:398–401
- 31 Kurova T, Shoubnikova M, Malceva A, Mardh PA. Prostitution in Riga, Latvia—a socio-medical matter of concern. *Acta Obstet Gynecol Scand* 1998;1:83–6
- 32 Kreiger JN. Trichomoniasis in men: old issues and new data. *Sex Transm Dis* 1995;2:83–95
- 33 Wolner-Hanssen P, Krieger JN, Stevens CE, et al. Clinical manifestations of vaginal trichomoniasis. *JAMA* 1989;4:571–6

- 34 Cotch MF, Pastorek JG, Nugent RP, *et al.* *Trichomonas vaginalis* associated with low birth weight and preterm delivery. *Sex Transm Dis* 1997;6:353-60
- 35 Cohen MS. Sexually transmitted diseases enhance HIV transmission: no longer a hypothesis. *Lancet* 1998;suppl. III:5SIII-7SIII
- 36 Draper D, Donohoe W, Mortimer L, Heine RP. Cysteine proteases of *Trichomonas vaginalis* degrade secretory leucocyte protease inhibitor. *J Infect Dis* 1998;3:815-19
- 37 Cohen MS, Hoffman IF, Royce RA, *et al.* Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. *Lancet* 1997;349:1868-73
- 38 Hobbs MM, Kazembe P, Reed AW, *et al.* *Trichomonas vaginalis* as a cause of urethritis in Malawian men. *Sex Transm Dis* 1999;7:388-9
- 39 WHO/Global Programme on AIDS. *Global Prevalence and Incidence of Selected Curable Sexually Transmitted Diseases: Overview and Estimates.* WHO/GPA/STD/95
- 40 Jackson DJ, Rakwar JP, Bwayo JJ, Kreiss JK, Moses S. Urethral *Trichomonas vaginalis* infection and HIV-1 transmission. *Lancet* 1997;350:1076
- 41 Iskandar MB, Patte JH, Qomariyah SN, Vickers C, Molyneux SI. Detecting cervical infection among family planning clients: difficulties at the primary health-care level in Indonesia. *Int J STD AIDS* 2000;11:180-6

(Accepted 25 February 2001)



Uusküla A, Kalikova N, Zilmer K, Tammi L, DeHovitz J.  
The role of injecting drug use in the emergence of HIV in Estonia.  
International Journal of Infectious Diseases 2002; 6: (accepted for publication)

# THE ROLE OF INJECTING DRUG USE IN THE EMERGENCE OF HIV IN ESTONIA

*Anneli Uusküla<sup>1</sup>, Nelli Kalikova<sup>2</sup>, Kai Zilmer<sup>3</sup>, Lea Tammat<sup>3</sup>, Jack DeHovitz<sup>4</sup>*

<sup>1</sup>Clinic of Dermatovenerology, University of Tartu, Estonia

<sup>2</sup>AIDS Prevention Center, Tallinn, Estonia

<sup>3</sup>Hospital Merimetsa, Tallinn, Estonia

<sup>4</sup>State University of New York, Downstate Medical Center, Brooklyn, New York, USA

Human immunodeficiency virus (HIV) and sexually transmitted disease (STD) epidemics have had remarkable social, demographic and economic consequences in Africa and Asia. More recently there has been a dramatic increase in the reported STD incidence in East-Europe and Central Asia<sup>1</sup>. Despite the underreporting of cases and a decline in mass screening, an epidemic has been documented<sup>2,3</sup>. Besides a rise in the STD incidence, increasing rates of HIV/AIDS, especially in the Russian Federation, have been reported<sup>2</sup>.

Injecting drug use is only one of several risks promoting the spread of HIV in Europe. Indeed, several countries in West-Europe have reported declining HIV incidences among the drug users during the last decade<sup>4</sup>. In contrast, the dramatic increase in HIV incidence in the countries in East-Europe and in the Russian Federation can be attributed primarily to injection drug use<sup>5,6</sup>.

In the countries in East-Europe, economic distress, market reforms and political restructuring has had a radical impact on everyday life, as well as a negative impact on the health care system<sup>3,7</sup>. These conditions make the communities in those countries particularly vulnerable to out-breaks of STDs and HIV<sup>8,9</sup>.

This article reviews the marked increase in HIV infection among injecting drug users (IDU) in Estonia, a former Soviet Union republic bordering the Baltic Sea.

## Background and methods

Estonia is a country in East Europe on the shores of the Baltic Sea, which was a Soviet republic until it regained its independent statehood in 1991. Estonia is the smallest of the three Baltic Republics, covering an area of approximately 45,215 square kilometers with a population of approximately 1.4 million people, of whom more than two thirds live in urban areas. Administratively, Estonia is divided into 15 counties, the smallest with the population of approximately 12,000 and the largest of 535,000. The 2<sup>nd</sup> largest, Ida-Virumaa county (population 193,610 as of 01.01.2000) is located at the North-Eastern border with the Russian Federation; the county's administrative center Narva (population 73,831) is a cross-border town.

During the first ten years of independence, a decrease in agricultural and industrial production occurred, and the economy became more oriented towards provision of services. The role of industrial production declined from 39% to 31% in 1991–1995, and then it became stabilized. Approximately 6% of Gross Domestic Product (GDP) is spent on health care<sup>10</sup>. The two main sources of finance for health care provision in

Estonia are the health insurance system and the state budget. The public health insurance embraces about 90% of the Estonian population; it is based on residency, not citizenship.

Basic general statistical data show that the health of Estonians has been deteriorating since 1990; the death rates due to cardiovascular diseases, accidents and poisonings have all risen. In 1994 life expectancy was lowest, being for men 61.1 years and for women 73.1, the former having declined from 66.5 and the latter from 74.9 in 1988<sup>11</sup>. However some signs of improvement have been noted in recent years. The infant mortality rate that was 15.8 per 1000 live births in 1993 (having been as low as 12.4 in 1990) has fallen to an all time low of 9.5 in 1999<sup>11</sup>.

HIV testing was introduced in Estonia in 1987; by now over 2 million HIV tests have been performed. In the early years of HIV testing in Estonia, the categories of population to be HIV tested were: blood donors (765,442 tests) and pregnant women (318,330 tests), and the so-called category of "prophylactic HIV testing" subjects (600,370 tests). These included hospital in-patients, and staff in certain occupations (food providers, kindergarten staff, etc) as well testing on persons request. The total number of HIV tests also include the tests made for medical indications (119,118 tests). The tests for medical indications and the tests made for above mentioned transmission categories (blood donors, pregnant women, patient request, prophylactic testing) constitute 90% of all the tests performed. The remaining ten per cent of tests made on the subjects grouped under other transmission categories (Table 1)<sup>12</sup>. A total number of tests performed per year was the highest in 1990 (269,749 tests). The number fell to about 80,000 tests per year by 1997, because of changes in the screening policy. Today HIV testing is obligatory only for blood donors; pregnant women and prison inmates are routinely checked for HIV infection as well. For HIV testing ELISA kits (*Abbott*, USA; *Ortho Clinical Diagnostics*, USA; *BioRad*, France) are uniformly used and the results verified by the immuno-blot method (*Ortho Clinical Diagnostics*, USA; *BioRad*, France; *Innogenetics*, Belgium).

In Estonia, surveillance of HIV infection and STDs is based on the mandatory universal notification of newly identified cases to the State Health Protection Service (with the same reporting principles in use throughout the last decades).

By legal regulations every sample sent for HIV testing has to be coded (on the testing form) to identify the transmission category it belongs to.

## Results

The incidence of syphilis and gonorrhea increased substantially during the early 1990s and then it began to decline (Figure 1)<sup>3,13</sup>. In contrast, there has been an increase in the rate of hepatitis B (17,5/100.000 in 1996 and 34,1/100.000 in 1998) and hepatitis C (6,2/100.000 in 1996 and 25,3/100.000 in 1998) in recent years<sup>13</sup> (Figure 1).

To date since 1987, 1305 cases of HIV have reported in Estonia (male/female ratio of 914 /255)<sup>14,15</sup>. The incidence of HIV infections remained very low until recently, even when a considerable rise occurred in the incidence of sexually transmitted diseases, especially syphilis. Through 1999, only 96 cases of HIV had been reported nationally. Since then however, a dramatic increase has occurred: 357 new HIV positive



cases were reported during the last 4 months of the year 2000, and an additional 819 cases during the first 6 months of 2001 (Figure 1). The available data on the transmission categories of HIV testing identified groups at risk, including STD patients, sailors, and the sexual contacts of HIV-positive persons<sup>12,16</sup>. Now, according to the data of 2000, injecting drug users (IDU) have emerged as group at risk (Table 1)<sup>12,14,15,17</sup>.

As stipulated by legal regulations, every sample sent for HIV testing has to be coded (on the testing form) to identify the transmission category of the sample<sup>12</sup>. Before 1999, only one out of 96 HIV+ cases was categorized as an illegal drug user. According to data from testing forms in 2000, 265 (68%) out of 390 HIV + tested persons were identified as illegal drug users<sup>12</sup>. More than one transmission category code can be indicated. The illegal drug use category was mostly combined with the “prisoners” or “anonymous testing” transmission categories<sup>12</sup> (Table 1). The cumulative data, including the information recorded on HIV testing forms<sup>12</sup> and clinical records<sup>15,17</sup> suggest that IDU was a factor in nearly 90% of the new HIV cases reported in year 2000.

Of now, the majority of new HIV+ cases (797 (74%)/1037) in the years of 2000 and 2001 are residents in the North-East of Estonia<sup>12,14,15,17</sup>.

## Discussion

HIV infection associated with injecting drug use has been reported worldwide, and is established as the major cause of rapidly increased rates of HIV infection in several countries throughout East-Europe<sup>5,6,18</sup>. In the newly independent states of the former Soviet Union Republics large-scale HIV epidemics have been observed from 1995 onward, after IDU communities became infected<sup>19</sup>.

In Estonia a substantial increase of IDU began in 1994, and it is still on the increase. According to the Estonian Health Statistics the number of patients admitted for care for psychiatric and behavioral disorders caused by the use of illegal drugs has more than tripled during the late 1990s (24.5 / 100000 in 1995, 82.2 / 100 000 in 1998)<sup>31</sup>. Only ten years ago, procurement of illegal narcotic substances in Estonia was difficult if not impossible. Older people, whose substance abuse pattern has already been established based on consumption of alcohol, do not usually reorient themselves to new substances. In 1999, Estonia carried out the European School Survey Project on Alcohol and Other Drugs (ESPAD). According to these results, the share of students who have experimented with drugs is almost equal in Tallinn and the towns of Ida-Virumaa county. Nevertheless, in Tallinn, narcotic substance use tends to remain within the limits of recreational consumption and club life (rave drugs, amphetamines), but in Ida-Virumaa county the most popular drugs are opiates. In Estonia there are no great ethnic differences related to alcoholism. Even so, among the drug addicts admitted for treatment in 2000 there were 83.2% Russians and 11.3% Estonians<sup>31</sup>. According to the data from the same database (drug addicts treatment database) IDU was reported by 83.4% of drug addicts, and 84% were living either in Tallinn or in Ida-Virumaa county<sup>20</sup>. Unfortunately, no verified data on the extent of drug abuse are available, but the number of IDUs in Estonia is estimated to be 10,000–12,000; the majority are Russian-speaking (90%) males, aged 15–25 (85%) heroin addicts<sup>15,20,21</sup>. The marked increase in HIV incidence in Estonia was preceded with an increase in the numbers of registered cases of hepatitis B and hepatitis C<sup>13</sup>, likely related to the spread of injecting

drug use in Estonia<sup>15,22,23</sup>. The increase may also have been caused by a change in the pattern of drug use<sup>15</sup>, from smoking to injecting drugs. The affected patients are young: in the 1994 to 1997 period there has been an almost five-fold increase in the absolute numbers of the registered new cases of hepatitis B and C in the age group 15–19; 50% of hepatitis B and 52% of hepatitis C cases were diagnosed in this age group in year 1997<sup>24</sup>.

A study from Estonia by Priimägi and co-workers showed that of the 57 IDUs under study, serological markers of hepatitis B were detected in 79% and of hepatitis C in 83% of the cases<sup>22</sup>. The incidence of reported new cases of hepatitis B and C is the highest in the North-East of Estonia and in Tallinn (the capital city)<sup>25</sup>. While in the year 2000 the incidence of hepatitis B was 30.1 and hepatitis C was 20.1 per 100,000 for the whole Estonia, in the Ida Virumaa county in the North East it was 122.8 and 76.4, and in Tallinn 41.7 and 40.7 accordingly<sup>13</sup>. These two regions are also known to have the worst illegal drug problems in Estonia.

Social and economic factors are important in the development of risk environments conducive to HIV and epidemic spread<sup>8</sup>. An growing admission of the role of social and economic factors in STD and HIV spread is subject of the STDs prevention strategies which place a great emphasis on the social and structural interventions that require joint efforts from the health sector and other community resources<sup>26</sup>. Economic distress is known to be accompanied by an increase of poverty and unemployment. The employment in Estonia decreased by 23% in 1989–1998, according to labor market studies. As segmentary territorial labor division was the rule during the Soviet period in Estonia's history, social problems are different in different parts of Estonia. Unemployment is a great problem in the Ida-Virumaa county because of the high concentration of the former centrally controlled Soviet enterprises in that county<sup>27</sup>. The inhabitants in the Ida-Virumaa county (bordering on Russia) mostly work in those branches of economy (e.g. machine-building and metalworking), which have reduced their production following the restoration of Estonia's independence, since they cannot use the same capacities of raw material or marketing opportunities they had been offered in the Soviet Union. The so-called "underground" economies, including those associated with crime, and drugs have grown as they can draw their labor force from among the unemployed and poor. As shown by the official statistical data, crime was highest in Narva and its vicinity crime was also high in Tallinn, the capital of the Republic of Estonia<sup>28</sup>. Free migration and mixing of people is probably one of the key factors in HIV infection outbreaks. Major motorways may serve as conduits for illegal drug trafficking. Drugs are known to have a potential of altering sexual mixing patterns<sup>29</sup>. Narva is located on the route of transport from Russia to Estonia not far from St Petersburg. Importantly, Russian Federation also has reported a hundred-fold increase in the number of new HIV cases over 1996–1998, with most cases diagnosed in the large urban centers of Moscow and St Petersburg<sup>7</sup>. While in the year 1998, the incidence of syphilis for the whole territory of Estonia was 75.7 per 100 000 of population, the syphilis incidence (258.8 per 100 000 population) in Narva was much of the same magnitude as the syphilis incidence in the Russian Federation in 1998 (234 per 100 000 population)<sup>13,30</sup>.

One of the interesting observations from the last decade of the 20<sup>th</sup> century in Estonia is that the number of HIV infection cases initially remained relatively low, despite to the rapidly and substantially increasing STD rates (syphilis in particular)

(Figure 1). HIV epidemic began to develop only after it was introduced to the drug injecting community

HIV infection appeared in Estonia much later than in many other parts of the world, so the experience from other countries that have confronted with the challenges of HIV could be of great help and importance for Estonia. The IDU related HIV infection epidemic in Estonia emphasizes an urgent need for preventive measures for IDUs as the target group. These measures may include syringe needle exchange and distribution programs, substitution pharmacotherapy, condom distribution, outreach to IDUs, peer education programs. Failure to act now will result in an even more dramatic and widespread HIV epidemic in Estonia.

## References

1. Waugh MA. Task force for the urgent response to the epidemics of sexually transmitted diseases in Eastern Europe and central Asia. *Int J STD AIDS* 1999; 10: 60–2.
2. Tichonova L, Borisenko K, Ward H, Meheus A, Gromyko A, Renton A. Epidemics of syphilis in the Russian Federation: trends, origins, and priorities for control. *Lancet* 1997; 350: 210–13.
3. Uusküla A, Silm H, Vessin T. Sexually transmitted diseases in Estonia: past and present. *Int J STD and AIDS* 1997; 8: 446–50.
4. Hamers FF, Batter V, Downs AM, Alix J, Cazein F, Brunet JB. The HIV epidemic associated with injecting drug use in Europe: geographic and time trends. *AIDS* 1997; 11: 1365–74.
5. Stephenson J. HIV/AIDS Surging in Eastern Europe. *JAMA* 2000; 284: 3113.
6. Dehne KL, Khodakevich L, Hamers FF, Schwartlander B. The HIV/AIDS epidemic in Eastern Europe: recent patterns and trends and their implications for policy-making. *AIDS* 1999; 13: 741–9.
7. Bingham JS, Waugh MA. Sexually transmitted infections in the Russian Federation, the Baltic States and Poland. *Int J STD AIDS* 1999; 10: 657–58.
8. Rhodes T, Ball A, Stimson GV, Kobysheva Y, Fitch C, Pokrovsky V. HIV infection associated with drug injecting in the newly independent states, eastern Europe: the social and economic context of epidemics. *Addiction*. 1999; 94: 1323–36.
9. Thomas JC, Clark M, Robinson J, Monnett M, Kilmarx PH, Peterman TA. The social ecology of syphilis. *Soc Sci Med* 1999; 48: 1081–94.
10. ESTONIAN HUMAN DEVELOPMENT REPORT 2000. Suggested required tables. <http://www.undp.ee>, 03.07.2001
11. Statistical Office of Estonia. *In Population* 1999: 29, 30, 42, 42, 59. Tallinn 2000.
12. Archive of HIV Reference Laboratory, HIV testing reports 1987 to 2000, HIV testing notification according to the decree no 54 (29.03.1994) and no 77 (13.12.2000) of Ministry of Social Affairs of Estonia.
13. Health Protection Inspectorate. Communicable Diseases Statistics in Estonia, 2000.
14. HIV infection in Estonia. <http://www.tervisekaitse.ee/teatedjastat> 10.08.2001.
15. Kalikova N. The HIV epidemic in Estonia. Proceedings of the 3rd Congress of the Estonian Society of Sexually Transmitted Infections (EUSTI) 2001: 14–5.
16. Tammi L, Ustina V, Raukas M. HIV infection in Estonia in 1988–1997, an overview. *Eesti Arst* 1998; Suppl 1: 547–550
17. Archive of Merimetsa Clinic of Infectious Diseases in Tallinn, 06/2001. a.
18. Kalichman SC, Kelly JA, Sikkema KJ, Koslov AP, Shaboltas A, Granskaya J. The emerging AIDS crisis in Russia: review of enabling factors and prevention needs. *Int J STD AIDS* 2000; 11: 71–5.

19. Dehne KL, Pokrovskiy V, Kobysheva Y, Schwartländer B. Update on epidemics of HIV and other sexually transmitted infections in the newly independent states of the former Soviet Union. *AIDS* 2000; 14 (suppl 3): S75–84.
20. Kariis T, Malbe R, Allaste AA, Ahven A, Jänes V, Paimre M. Summary Report on the National Drug Situation in Estonia. (Information For The EMCDDA's 2000 Annual Report). Estonian Foundation for Prevention of Drug Addiction. Tallinn 1999.
21. Kalikova, N. Intravenous drug users. An epidemiological overview. Unpublished report. AIDS Prevention Center, Tallinn, 2000.
22. Priimägi L, Kremerman I, Tefanova V, Tallo T, Osadtsaja G. Study on hepatitis C and hepatitis B infected intravenous drug users. *Eesti Arst* 1998; 6: 521–523
23. Tefanova V, Krupskaja L, Kikos G, Tallo T, Priimägi L. Study on hepatitis B and hepatitis C epidemiology in Tallinn. *Eesti Arst* 1998; 6: 552–3.
24. Health care statistics report. <http://www.sm.ee/stat.html> 10.08.2000.
25. Health Protection Inspectorate. Reported infectious diseases in Estonia, 1999. *Eesti Arst* 2000; 4: 222–5.
26. Wasserheit JN. Syphilis, a barometer of community of community health. *Sex Transm Dis* 2000; 27: 311–2.
27. Statistical Office of Estonia. Labor Force 1998, Tallinn, 1999.
28. Statistical Office of Estonia. Justice statistics. <http://www.stat.vil.ee/pks/kuritegevus/crime/sisu.htm>. 29.01.2001.
29. Cook RL, Royce RA, Thomas JC, Hanusa BH. What's driving an epidemic? The spread of syphilis along an interstate highway in rural North Carolina. *Am J Pub Health* 1999; 89: 369–7.
30. Borisenko KK, Tichonova LI, Renton AM. Syphilis and other sexually transmitted infections in the Russian Federation. *Int J STD AIDS* 1999; 10: 665–9.
31. Database of the Estonian Foundation for Prevention of Drug Addiction. <http://narko.sm.ee/Levik/2000/default.asp>.

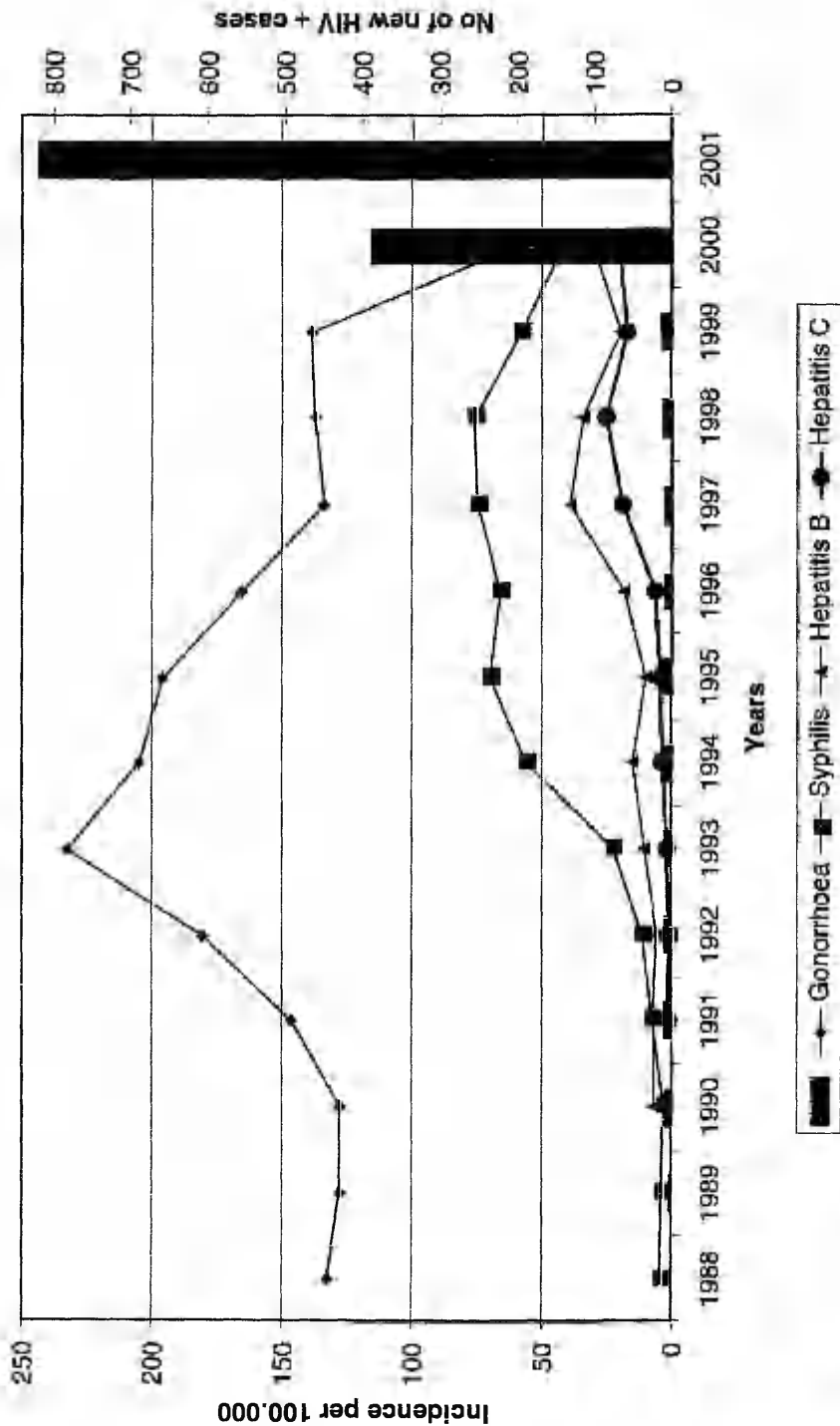


Figure 1. Incidence of reported STDs and absolute number of HIV positive cases in Estonia, 1988-2001.

Table 1. HIV testing in Estonia 1987-2000

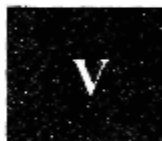
Transmission category xxi	1987-1999		2000		Total	
	HIV +	% of tested *	HIV +	% of tested *	HIV +	% of all HIV+
	Number		Number		Number	
sexual contacts of HIV +	9	6.52	0	0	9	1.9
drug addicts	1	0.07	53***	7.83	54	11.1
STD patients	15	0.03	22	1.18	37	7.6
immigration permit applicants	1	0.02	6	0.7	7	1.4
women undergoing abortion	2	0.02	0	0	2	0.4
blood donors	6	0	1	0	7	1.4
pregnant women	1	0	6	0.05	7	1.4
prisoners	0	0	80	7.44	80	16.5
on clinical indications	9	0.01	55	1.17	64	13.2
anonymous testing	13	0.06	160	4.13	173	35.6
prophylactic testing	14	0	7	0.06	21	4.3
sailors	17	0.05	0	0	17	3.5
non estonian citizens	8	0.18	0	0	8	1.6
other**	0	0	0	0	0	0
Total	96	0	390	0.46	486	100

\* % of tested in this transmission category

xxi identification code of the transmission category of a studied sample has to be marked on every test sent for HIV testing

\*\* blood products recipient, army recruits, medical personnel

\*\*\* more than 1 transmission categories code could be marked on the HIV test form. drug use reported altogether for 265 HIV + persons in 2000 (12)



Uusküla A, Nygård JF, Kibur M.  
Syphilis as a social disease:  
experience from post-communist transition period in Estonia.  
(submitted).



# **SYPHILIS AS A SOCIAL DISEASE: AN EXPERIENCE FROM POST-COMMUNIST TRANSITION PERIOD IN ESTONIA**

*Anneli Uusküla<sup>1</sup>, Jan F. Nygård<sup>2,3</sup>, Mari Kibur<sup>4,5</sup>*

<sup>1</sup>Clinic of Dermatovenerology, University of Tartu, Estonia

<sup>2</sup>Institute of population-based cancer research. The Cancer registry of Norway

<sup>3</sup>Institute of Behaviour Science in Medicine, University of Oslo, Norway

<sup>4</sup>Department of Epidemiology and Biostatistics, Institute of Experimental and Clinical Medicine, Tallinn, Estonia

<sup>5</sup>Department of Infectious Disease Epidemiology, National Public Health Institute, Helsinki, Finland

## **Abstract**

**Introduction:** Since the 1990s, the countries in Eastern Europe and the former republics of the Soviet Union have experienced major changes in their political, economic and legal systems during the post-communist transformation period. Following the collapse of the Soviet regime, there has been a dramatic increase in the reported incidence of sexually transmitted diseases (STD). The models of social ecology describe the interrelationship between individuals and environment. The factors of sociophysical environment associated with the STD community rates are geographic, structural, technological and sociocultural.

**Aim:** to study the community-level associations and the incidence rate of syphilis in Estonia during the post-communist transition period.

**Methods:** We selected the years 1991, 1994 and 1999 to represent the post-communist transition period, and studied five sociodemographic characteristics (the percentage of non-ethnic Estonians in the population, the percentage of urban population, the rate of homicides, the unemployment rate, the number of live births per 1000 females) and the tuberculosis incidence rate. The correlation and regression coefficients, and the explained variance values were estimated by the ordinary least square regression method.

**Results:** Statistically significant relationships were discovered between the syphilis incidence rate and the percentage of non-ethnic Estonians in the population (Pearson's  $r = 0.509$ ), the percentage of urban population (Pearson's  $r = 0.524$ ), the tuberculosis incidence (Pearson's  $r = 0.444$ ) and the birth rate (Pearson's  $r = -0.501$ ). Statistically significant associations between the syphilis incidence rate and the homicides rate (Pearson's  $r = -0.308$ ), and unemployment rate (Pearson's  $r = -0.022$ ) were not identified. This ecological analysis of the unique situation characterized by the radical changes in the community in a very limited time period is a clear illustration of the importance of environmental ties for community syphilis (an example of a sexually transmitted disease). Our findings emphasize the importance of considering the close relationships between health care sector and other community resources in the process of developing strategies to prevent sexually transmitted infections.

**Key words:** syphilis, Estonia, socioeconomic factors, birth rate, urban

## Introduction

Since the 1990s, the countries in Eastern Europe and the former republics of the Soviet Union have experienced major changes in their political, economic and legal systems during the post-communist transformation period. Following the collapse of the Soviet regime, there has been a dramatic increase in the reported incidence of sexually transmitted diseases (STD) in Eastern Europe and Central Asia. Although a number of cases have escaped reporting, and the mass screening is on the decline, an STD epidemic has been documented<sup>1,2,3</sup>.

Estonia, a country in Eastern Europe, and one of the three Baltic States, was a part of the Soviet Union until it regained its independent statehood in 1991. In Estonia, STD surveillance is conducted by the physicians who notify the Health Protection Inspectorate of the new cases diagnosed. The reporting principles of STDs have remained unchanged for the decades.

During and after World War II, a dramatic increase in the incidence of syphilis occurred. The total number of new cases in 1949 was 1642 (149/100.000)<sup>5</sup>. Since then the incidence of syphilis started to decrease after the migration and the economical situation in the USSR had stabilized, and penicillin was introduced for treatment. The disease control and partner notification system became more effective in the same period. In Estonia, the annual incidence of new cases of syphilis remained stable (< 7/100.000) from 1959 to 1970<sup>2,5</sup>. A new increase of syphilis occurred and reached the highest levels in 1976 (42/100.000)<sup>5</sup>. Whether it was a marker of changed sexual behavior (delayed "sexual revolution") or a consequence of intense national policy of forced migration within the USSR, remains unclear. The Soviet health care system reacted to the increase with relatively repressive measures of partner notification combined with compulsory treatment, and as a result, the incidence of syphilis decreased again to 8/100.000 in 1982<sup>5</sup>. The available data on the last 30 years indicate that the ratio of male to female new cases of syphilis has been very constant, never exceeding 2:1<sup>2,5</sup>.

The incidence of STDs (syphilis, gonorrhea, chlamydiosis, trichomoniasis) increased rapidly and substantially during the first years of independence from the Soviet Union and started to decline after 1994<sup>2,4,5</sup>; so the syphilis incidence rate per 100,000 of population was 7.4, 75.7 and 41.6 in 1991, 1998 and 2000 respectively. Similar decline in the STD incidence has been observed not only in Estonia, but also in the neighboring countries<sup>6</sup>.

The health factors on the individual level are biological and psychological-behavioral. The focus in this study was on the latter and their association with the syphilis incidence rates. The factors of sociophysical environment associated with the STD community rates are geographic (urban areas, proximity to major motorways), structural and technological (availability of treatment services and provision of treatment, number of physicians, disease prevention programs, STD outreach programs), sociocultural and economic (nationality/race relations, mean income, rate of violent crime, unemployment rate, birth rate), and prevalence of disease in the population<sup>8,9,10</sup>. The awareness of the importance of secondary factors beside individual level ones and the impact of those factors on the morbidity rate in communities is growing. This notion provides new opportunities for STD prevention by conditioning a more fruitful co-operation between the health care sector and the other community resources<sup>11,12</sup>. The models of social ecology describe the interrelationship between individuals and environment.

The origins of public health and public order overlap to a great extent and they are embedded in the security and stability of personal, domestic and community networks and other institutions. Disruption of such networks will lead to the increase of violence, sexuality, substance abuse and general criminality<sup>13,27</sup>. Socially disruptive situation is a critical and unique environmental condition that may trigger syphilis epidemic<sup>15</sup>. In addition to STDs, social disintegration has demonstrated to exacerbate epidemics of several other infectious diseases including tuberculosis<sup>29</sup>. Population downturn (including decrease in birth rates) is an additional phenomenon to coincide with radical changes in political, economic and social conditions<sup>18</sup>.

## **Aim**

This study focused on analyzing the community-level associations and the incidence rate of syphilis in Estonia during the post-communist transition period.

## **Material and Methods**

### **Periods of post-Communist transition**

The post-communist transition in Estonia has been divided into the following periods.

- I. 1987–1991 — Liberation movements and political breakthrough.
- II. 1991–1994 — Restoration of the independent statehood involving radical political reforms.
- III. 1995 – present — Emergence of a stable democratic system, economic and cultural stabilization.

For the samples of the statistical analysis, the data of the years 1991 (the final year of period I), 1994 (the final year of period II), and 1999 (the last reported year of period III) were selected.

## **Syphilis**

The data on syphilis incidence were taken from the national syphilis case surveillance register; syphilis cases are reported to the County Health Protection Bureaus, which send monthly reports to the Health Protection Inspectorate. The county syphilis rates were calculated with the Statistical Office of Estonia population count estimates (1991–1999) as the population denominator for the percentages and rates.

### **Sociodemography of counties**

The data used in the analysis were provided by the Statistical Office of Estonia. Administratively, Estonia is divided into 15 counties, the smallest has the population of approximately 12,000 and the largest of 535,000. The available sociodemographic

characteristics of the counties were reviewed, and possible markers of socially disruptive situation; unemployment as a new phenomenon in post-communist countries; two basic demographic variables, and the tuberculosis incidence rate per 100,000 were selected for more detailed analysis. These characteristics were:

- (1) percentage of the non-ethnic Estonians in the population
- (2) percentage of urban population
- (3) rate of homicides per 100,000
- (4) unemployment rate per 100
- (5) number of live births per 1000 females at age 15–49

## **Methods**

The regression coefficients and the explained variance values were estimated by the ordinary least square regression. A five per cent significance level was chosen for the p-value of the regression coefficient. Pearson's correlation coefficients were calculated.

## **Results**

### **Changes in syphilis occurrence and sociodemographic characteristics**

(Table 1, Figure 2, a-c)

Syphilis incidence increased from 7.4 per 100,000 in the first period (1990) to 58.4 per 100,000 in the third period (Table 1). Syphilis is focally distributed in Estonia; there are striking local differences in the STD incidence rates. The counties of Põlvamaa and Hiiumaa report low syphilis incident rates (5.6/100,000 and 8.4/100,000 respectively), but this can partly be attributed to poor syphilis registration in these counties, as there are no STD physicians in Põlvamaa and Hiiumaa. The two counties of the highest STD rates are: Tallinn, the capital of the Republic of Estonia and Narva, the 3rd largest city situated in the North–East of Estonia, near Estonia's border with the Russian Federation (Figure 1, Figure 2a).

The ethnic composition of the population of Estonia has been stable in the past decade. Ethnic Estonians comprise about two thirds of the total population. There are two regions where the proportion of the non-ethnic Estonians in the population is considerably higher than in other places in Estonia: in Tallinn, the capital of the Republic of Estonia, non-ethnic Estonians make up nearly 50 per cent and in the Ida-Virumaa County (in the North East of Estonia) 72 per cent of the population. During the 1990s, the proportion of urban (~70%) and rural (~30%) population in Estonia was stable (Figure 2c).

The number of live births continuously decreased in Estonia during the period under observation. The decrease was more rapid in the first half of the 1990s. The decline in fertility slowed down in 1993, and a rise in the birth rate began in 1999.

A clear trend can be observed when studying the data on homicides in Estonia in the 1990s. The number of homicides began to grow at the beginning of the decade. In first period, the homicide rate was more than 8.7 per 100,000. The worst year was 1994,

with 365 homicides, a rate of 24.4. In the third period, the rate of homicide was less than 14 per 100,000. The areas of the highest crime levels were Tallinn, Narva and Ida-Virumaa county.

Unemployment was virtually non-existent during the years of socialism. After the collapse of the Soviet Union, unemployment rose during the first and the second period, and increased further due to the impact of the Russian economic crisis in the third period, to 12.8% (Table 1, Figure 2b).

The incidence of tuberculosis rose from 21.5 per 100,000 in the first period to 42.3 per 100,000 in the third period. The majority of the infected were men (approximately 70%), and the age group 35-55 was the most affected (Figure 2a).

### **Association of syphilis with sociodemographic characteristics**

Statistically significant positive correlation was found between syphilis incidence rate and percentage of non-Estonian population (Pearson's  $r= 0.509$ ), urban population (Pearson's  $r= 0.524$ ), and tuberculosis incidence (Pearson's  $r= 0.444$ ), which explains 25.9 %, 27.5 %, and 19.7 % of the variation in the syphilis incidence rates across the counties and the three time periods, respectively (Table 2). A statistically significant negative correlation was also found for syphilis incidence rate and the birth rate (Pearson's  $r= -0.501$ ), which explains 25% of the variance.

No associations between the syphilis incidence rate, homicides rate, and unemployment rate were found (Figure 3, a-f).

### **Discussion**

Social disintegration has proven to exacerbate epidemics of infectious diseases, including AIDS, and tuberculosis, and such behavioral pathologies as substance abuse and violence<sup>13</sup>. Especially in case of STDs, societal factors tend to influence risk behavior, and consequently the probability of being infected. First, society provides the context in which behaviors are shaped and conducted. We observed the reported syphilis incidence rate in Estonia during the period of great changes in the society — a shift from being a Soviet socialist republic to an independent country with a new developing market economy.

On the basis of the character and scope of societal changes (Lauristin *et al.*<sup>14</sup>), the transitional process in Estonia can be divided into three following stages. Stage I: 1987–1991; 'The breakthrough'. Strong political mobilization and the rebirth of civil society, the beginning of a rapid economic decline and hyperinflation characterize this period of liberation movements and political breakthrough. Stage II: 1991–1994; 'Change takes hold'. This period after the restitution of the independent statehood was characterized by radical political (the constitutional reform, the institutionalization of the multi-party system) reforms. In the field of economy "shock therapy" was applied in line with the currency reform, privatization, the rebirth of the independent banking system, decreasing inflation, first bankruptcies, rapidly growing consumption. That was a period of rapid social differentiation: poor-rich opposition became significant, regional differences in the standard of living increased, unemployment slowly grew but was not

yet a big issue. Stage III: from 1995 onwards; 'Emergence of a stable democratic system'. Economy and banking system stabilized and inflation. Estonia's policymakers aimed at integration with the European Union and the North Atlantic Treaty Organization. Syphilis is a classical example of a STD. Remarkably, syphilis is apparently the most consistently reported STD in Estonia<sup>1,6</sup>. During the 1990s, we observed eight-fold increase, from 7,4 to 56,6 per 100,000, in syphilis rate between I and II stages. The difference between II and III period was 1.1 fold only, from 56,6 to 58,4 per 100,000. The incidence of other reported bacterial STD (gonorrhea, chlamydiosis) started to decline already in 1994-1995<sup>2,4,5</sup>, the trend toward stabilization and decline in the incidence of syphilis is apparent from 1999<sup>4,5</sup>. Decline in STDs incidences have been attributed to a variety of different factors. It has been interpreted to reflect that the peak values have been achieved among those socially disadvantaged and at risk. The decline is also associated with the changes in care seeking patterns, incomplete case reporting due to prescribing symptomatic treatment without the verification of the causative agent, and the thorough alterations in the health care system as such<sup>1,2,7</sup>. This reversal of the trend may also be explained by the introduction of new and potent medicines, (e.g. quinolones and cephalosporines in the treatment of gonorrhea), treatment schedules (WHO treatment guidelines and syndromic management principles), but also a socio-financial stabilization in the community could be considered<sup>2</sup>. In Estonia, the period of economical and cultural stabilization and slow growth in living standard began in 1995<sup>14</sup>. Any type of relational placement in society greatly affects how the environment, the individual and the behavioral options are experienced by the individual: i.e. individuals who live in poverty perceive the same society and behavioral options differently from those with high income. In addition, individuals who have means to make decisions experience their society more positively and their behavioral options are less dependent on the opinion of others. In our study we constantly identified the highest syphilis incidence rates in Ida-Virumaa (Figure 1), region with a high percentage of non-ethnic Estonian population and unemployment rate. Syphilis rate was positively associated with proportion of non-Estonians (Pearson's  $r=0.509$ ), but we found almost no association with unemployment rate. The ethnic origin is not considered a biological risk factor for syphilis; ethnicity is probably a marker of interrelationships of ethnicity with other socioeconomic and demographic factors. Due to the language-based labor division during the Soviet period, changes in society influenced Estonians and non-ethnic Estonians in different ways. The Russian-speaking population is largely working in those branches of the economy, which have deteriorated after the restoration of Estonia's independence deepening the problem of unemployment, furthermore, it is complicated for the non-Estonians residing in Ida-Virumaa county (Northeast Estonia) to seek work outside their home county because of language barriers<sup>16</sup>.

The theories on STD transmission have drawn the readers' attention to the importance of current prevalence of infection in population<sup>32</sup>, and to social networks<sup>25,26</sup>. Major motorways may serve as conduits for illegal drug trafficking. Drugs are known to have a potential of altering sexual mixing patterns<sup>22</sup>. Sexual behavior on travel might contribute to STD rates according to a recent Estonian case-control study on sexual beliefs and behaviors determining the STD occurrence patterns<sup>23</sup>. The capital city of Ida-Virumaa county, Narva, is located on a cross-border motorway between Estonia and the Russian Federation, connecting Tallinn with St Petersburg. This area has extremely high STD rates (especially syphilis). For example, in 1998, the incidence of syphilis in

Estonia was 75.7 per 100,000 population on average, but in Narva, it was 258.8 per 100,000 population<sup>4,5</sup> which is comparable to the syphilis incidence rate in the Russian Federation (234 per 100,000 population)<sup>24</sup>.

Large population downturn subsequent to radical socioeconomic changes during the transition period is also noted in the context of other Eastern European countries<sup>17</sup>. The rate of live birth is considered to be a marker of social integration; in our study birth rate was inversely associated with county syphilis rate (Pearson's  $r = -0.501$ ). The Estonians have higher total fertility rate than non-Estonians, but the declining trend and the slight increase in 1999 was similar in both groups. The share of legitimate birth is continuously falling, and the mean age of women at child birth and the mean age of women at the birth of the first child were steadily increasing during the 1990s<sup>19</sup>.

The high incidence rate of syphilis was observed in Tallinn, the capital of Estonia. Urban residence has proven to be associated with high syphilis rates<sup>20</sup>, although there may also be a surveillance artifact, with better access to medical care in urban areas<sup>21</sup> resulting in higher rates of appropriate diagnosis and reporting syphilis cases. In this study, the proportion of urban population in the county was strongly associated with the county's syphilis rate (Pearson's  $r = 0.524$ ). Age specific migration rates revealed that the growth of internal migration had mostly taken place on account of the decrease of non-registered changes of the place of residence of 15–34 year old males and 15–29 year-old females<sup>19</sup> — the age groups most vulnerable to STD related problems.

In our study, the homicide rate was not associated with the syphilis rate. The high crime rate is primarily observed in Estonia's urban areas which are characterized by heterogeneous populations, the highest crime rate was recorded in Tallinn, Narva and Ida-Virumaa county. These are also the regions with the highest syphilis rates. The homicide rate and the syphilis incidence rate in Estonia have manifested similar trends for the last decade. According to the 1994 statistics concerning intentional homicides, Estonia occupied the seventh place, two places higher than Russian Federation<sup>28</sup>.

We found that syphilis rate was positively associated with the tuberculosis incidence rate, which further supports the notion of similar risk factors for these infections, e.g. social disintegration. In Estonia the tuberculosis incidence increased during 1990s<sup>30</sup>. This increase, although not so distinctly, coincided with the syphilis incidence increase during in the 1990s. Similarly, a stabilization or even a decrease in the tuberculosis incidence rates has been evident from the late 1990s onward. Compared with syphilis incidence, the tuberculosis incidence has manifested less substantial regional differences, with the rates being highest in some rural regions of Estonia (Viljandi, Lääne-Virumaa, Tartumaa counties). Tuberculosis has been noted as a marker disease of extreme poverty<sup>29</sup>. Alarming, the population most affected by tuberculosis in Estonia is prison inmates, with the estimated tuberculosis incidence rate in prisons as high as 764 per 100,000<sup>30</sup>. Tuberculosis infection rate is even more problematic because of the fact that multi-resistant *Mycobacterium tuberculosis* strains — from 9 to 20% of newly diagnosed tuberculosis cases are being isolated by diagnosis<sup>31</sup>.

Our study on associations between community level determinants and syphilis incidence rate is limited in several ways: we used only available county-level data. There is an absence of reliable national level data on sexual behavior and alcohol/substance abuse. However, this ecological analysis utilized the unique social and political situation with radical changes in community in a very limited period, and signified the central associations between community-level indicators and the rate of syphilis incidence. The results support the theory of syphilis as a social disease. The

incidence of syphilis showed considerable variation across space and time, asserting the social pattern of the disease. Several sociodemographic characteristics were significantly associated with the syphilis incidence rate: the percentage of non-ethnic Estonian population, the percentage of urban population, the tuberculosis incidence rate, and the birth rate. These results underline the magnitude of the socioeconomic and demographic factors, and the complex social dimensions of public health problems. Our findings emphasize the importance of establishing close ties between the health care sector and the other community resources to prevent sexually transmitted infections. The importance of effective measures in STD control is further accentuated in the light of the advent of HIV/AIDS epidemic in Estonia.

## References

1. Waugh MA. Task force for the urgent response to the epidemics of sexually transmitted diseases in eastern Europe and central Asia. *Int J STD AIDS* 1999; 10: 60–2.
2. Uusküla A, Silm H, Vessin T. Sexually transmitted diseases in Estonia: past and Present. *Int J STD AIDS* 1997; 8: 446–50.
3. Gomberg MA, Akovbian VA. Resurgence of sexually transmitted diseases in Russia and eastern Europe. *Dermatol Clin* 1998; 16: 659–62.
4. Health Protection Inspectorate. Reported infectious diseases in Estonia, 1999. *Eesti Arst* 2000; 4: 222–5.
5. National Board of Health Protection. Communicable Diseases Statistics in Estonia, 1998: 24, 26, 30, 61.
6. Lapinskaite GS, Bingham JS. Sexually transmitted diseases in Lithuania: some epidemiological and social aspects. *Int J STD AIDS* 1999; 10: 673–6.
7. Dehne KL, Pokrovskiy V, Kobysheva Y, Schwartländer B. Update on epidemics of HIV and other sexually transmitted infections in the newly independent states of the former Soviet Union. *AIDS* 2000; 14 (suppl 3): S75–84.
8. Stokols D. Establishing and maintaining healthy environments: toward a social ecology of health promotion. *Am psychologist* 1992; 42: 6–22.
9. Thomas JC, Clark M, Robinson J, Monnett M, Kilmarx PH, Peterman TA. The social ecology of syphilis. *Soc Sci Med* 1999; 48: 1081–94.
10. Aral SO, Holmes KK. Demographic and social correlates of sexually transmitted disease. In: Holmes KK, Mardh PA, Sparling PF, Wiesner PJ, editors. *Sexually transmitted diseases*. New York: McGraw-Hill, 1990: 33
11. Aral SO, Holmes KK, Padian NS, Cates W. Individual and population approaches to the epidemiology and prevention of sexually transmitted infections and human immunodeficiency virus. *J Inf Dis* 1996; 174 Suppl 2: S127–33.
12. Wasserheit J. In: Syphilis as a barometer of community health. *Sex Transm Dis* 2000; 27: 311–2.
13. Wallace R, Wallace D, Andrews H. AIDS, tuberculosis, violent crime, and low birthweight in eight US metropolitan areas: public policy, stochastic resonance, and regional diffusion of inner-city markers. *Environment and Planning* 1997; 29: 525–5.
14. Lauristin M, Vihalemm P. Return to the western world. Lauristin M, Vihalemm P, Rosengren E, Weibull, eds. *Recent historical developments in Estonia: three stages of transition (1987-1997)*. Tartu University Press, Estonia 1997: 79–83.
15. Miles TP, McBride D. World War I origins of the syphilis epidemic among 20th century black americans: a biohistorical analysis. *Soc Sci Med* 1997; 45: 61–9.
16. Statistical office of Estonia. Labour force survey. *Estonian statistics* 2000: 7.



17. 32. Krus DJ, Nelsen EA. Changes in crime rates and family related values in selected east European countries. *Psychol Rep* 1997; 81: 747–51.
18. Ainsaar M. Transformation of society and migration: the case of Estonia. *Estonian social science (online)* 1999;1. <http://psych.ut.ee/esta>, 06.05.2001.
19. Statistical office of Estonia 1995. Internal migration. In: *Population of Estonia 1993*, Tallinn.
20. Kilmarx PH, Zaidi AA, Thomas JC, Nakashima AK, St.Louis E, Flock ML. Sociodemographic factors and the variation in syphilis rates among US counties, 1984 through 1993: and ecological analysis. *Am J Publ Health* 1997; 87: 1937–43.
21. CDC and Prevention. 1992 National Health Interview Survey. In: *Healthy People 2000 Review*. Washington, DC: US Dept of Health and Human Services; 1994.
22. Cook RL, Royce RA, Thomas JC, Hanusa BH. What's driving an epidemic? The spread of syphilis along an interstate highway in rural North Carolina. *Am J Pub Health* 1999; 89: 369–7.
23. Wilson T, Uusküla A, Feldman J, Holman S, DeHovitz J. A case control study of beliefs and behaviors associated with STD occurrence in Estonia. *Sex Transm Dis* 2001 /accepted for publication/.
24. Tichonova L, Borisenko K, Ward H, Meheus A, Gromyko A, Renton A. Epidemics of syphilis in the Russian Federation: trends, origins, and priorities for control. *Lancet* 1997; 350: 210–13.
25. Rothenberg RB, Sterk C, Toomey KE, Potterat JJ, Johnson D, Schrader M. Using social network and ethnographic tools to evaluate syphilis transmission. *Sex Transm Dis* 1998; 25: 154–60.
26. Woodhouse DE, Rothenberg RG, Potterat JJ, Darrow WW, Muth SQ, Klovdahl AS. Mapping a social network of heterosexuals at high risk for human immunodeficiency virus infection. *AIDS* 1994; 8: 1331–6.
27. Wallace R. Urban desertification, public health and public order: planned shrinkage, violent death, substance abuse and AIDS in the Bronx. *Soc Sci Med* 1990; 31: 801–31.
28. ESTONIAN HUMAN DEVELOPMENT REPORT 1999. Crime and crime control in Estonia. <http://www.undp.ee/nhdr99/en/contents.html>
29. Wallace R. A synergism of plaques: “planned shrinkage”, contagious housing destruction, and AIDS in the Bronx. *Environ Res* 1988; 47: 1–33.
30. Archive of Tuberculosis registry, Hospital of Kivimäe, Tallinn 2001.
31. Kruuner A, Sillastu H, Danilovich M, Levina K, Svenson SB; Källenius G. Drug resistant tuberculosis in Estonia. *Int J Tuberc Lung Dis* 1998; 2: 130–133.
32. Shiboski S, Padian NS. Population- and individualised approaches to desing and analysis of epidemiologic studies of sexually transmitted disease transmission. *JID* 1996; 174 Suppl 2: S188–200.

### **Acknowledgements**

The authors thank Marika Kivilaid and Aime Lauk from the Statistical Office of Estonia for their assistance in data collection, and Avo Trumm from the Department of Sociology, Faculty of Social Sciences, University of Tartu, for his advice and comments helpful in revision.

**Table 1.** Explained variance, correlation and regression coefficient for the association between syphilis rate and six sociodemographic characteristics

	Explained variance	Regression coefficient	p-value of regression coefficient	Correlation coefficient
Non-Estonian population(percentage)	0.2587	0.738	0.000	0.509
Urban population (percentage)	0.2745	0.841	0.000	0.524
Homicides Rate (per 100,000)	0.0948	-0.632	0.118	-0.308
Unemployment rate (percentage)	0.0005	-0.002	0.909	-0.022
Live births (per 1000 females at age 15-49)	0.2513	-0.012	0.000	-0.501
Tuberculosis incidence rate (per 100,000)	0.1974	0.009	0.002	0.444

Table 2. Syphilis incidence rate (per 100,000) and six socio-demographic characteristics by time periods in Estonia.

Period	Syphilis incidence	non-Estonian population (percentage)	Urban population (percentage)	Homicides Rate (per 100 000)	Unemployment rate (percentage)	TBC* incidence rate	Live births (per 1000 females at age 15-49)
I	7,4	38%	71%	8,7	1,5	21,5	51,0
II	56,5	36%	70%	24,2	7,9	34,6	38,6
III	58,4	35%	69%	13,8	12,8	42,3	34,5

\* TBC — tuberculosis

**Figure 1.** Syphilis incidence per 100 000 in countries and selected towns of Estonia, 1991, 1994, 1999

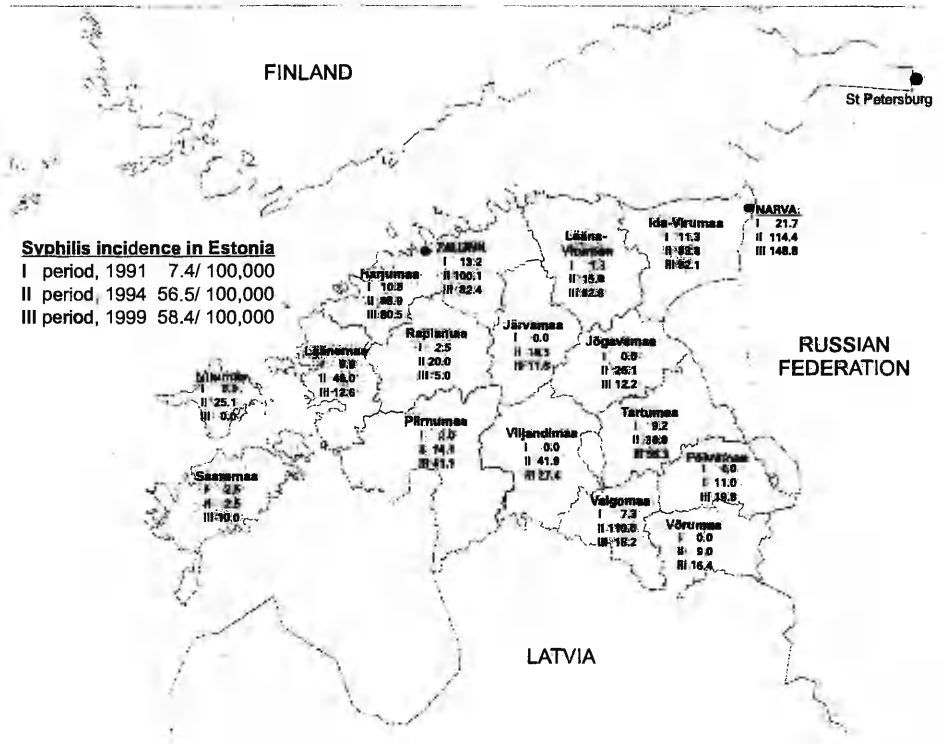


Figure 2. Selected sociodemographic factors, 1991–2000.

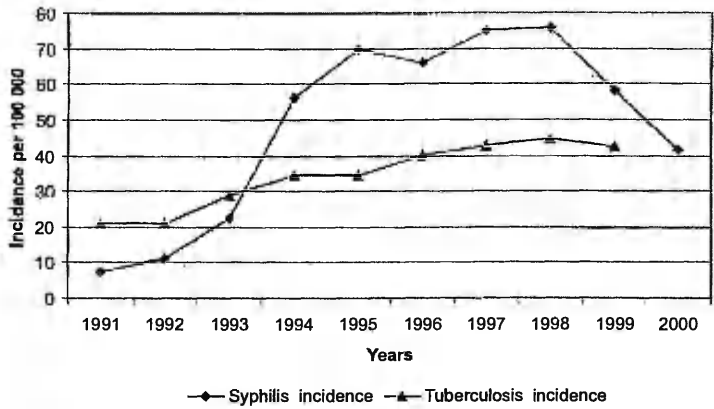


Figure 2a. Incidence of syphilis and tuberculosis in Estonia.



Figure 2b. Homicide, unemployment and birth rate in Estonia.

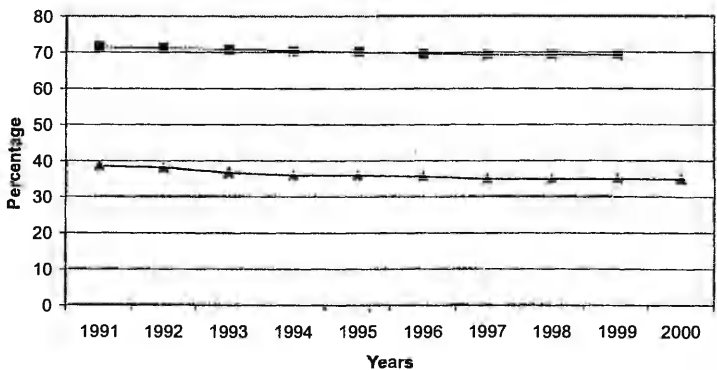
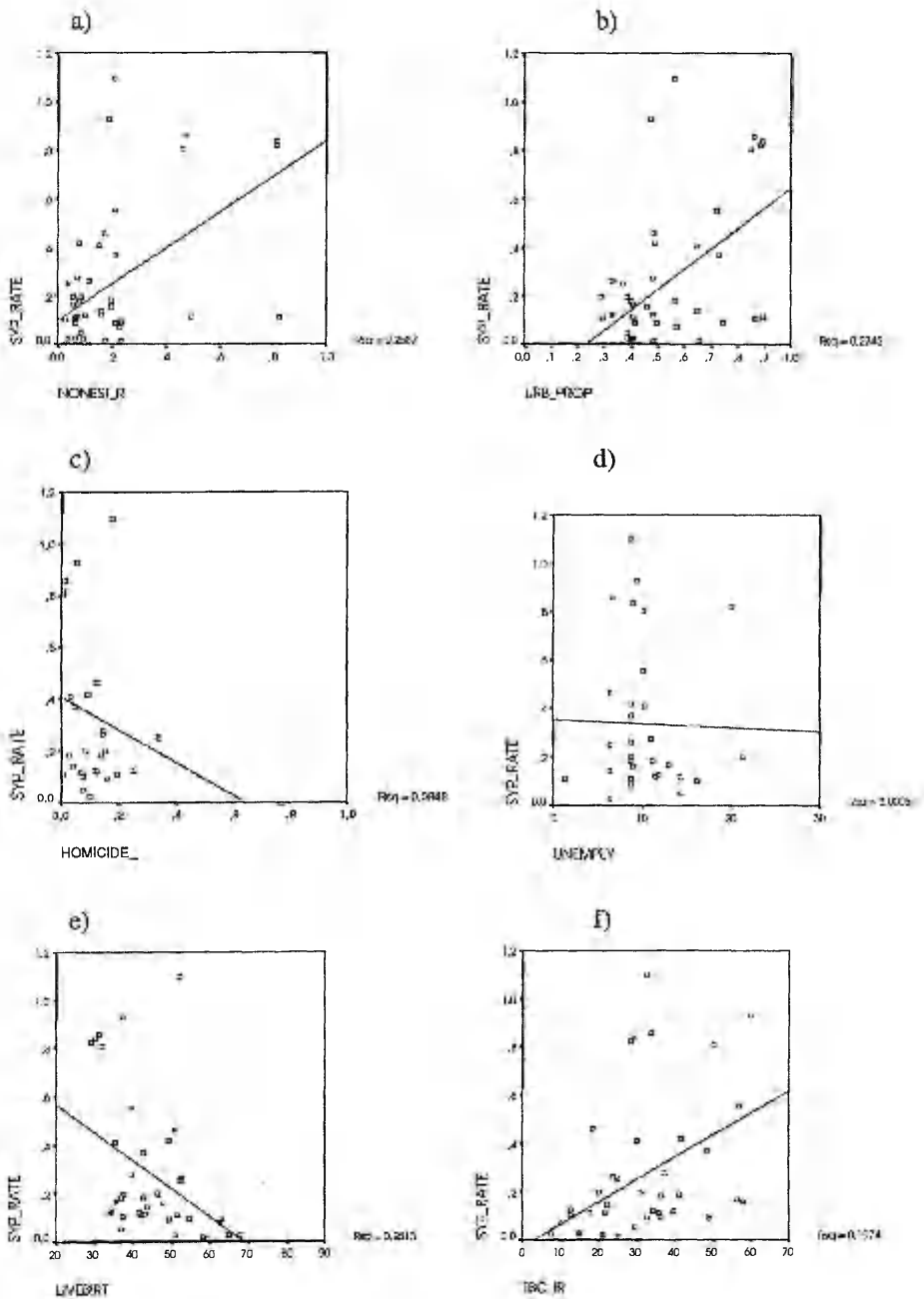


Figure 2c. Percentage of non-ethnic Estonian and urban population in Estonia.

**Figure 3.** Association of syphilis incidence rate with a) proportion of non-Estonian b) urban proportion c) homicides rate d) unemployment rate e) live birth rate f) incidence of tuberculosis



(abbreviations: SYF RATE — syphilis incidence rate, NONEST\_R — proportion of non-Estonian, URB\_PROP — urban proportion, HOMICIDE\_ — homicides rate, UNEMPLY — unemployment rate, LIVBIRT — live birth rate, TBC\_IR — incidence of tuberculosis).



Uusküla A, Kibur M, Tamm A, Robinson NJ.  
HSV Seroepidemiology Multi-Centre Study Group.  
HSV-1 and HSV-2 seroprevalence study in Estonia.  
International Journal of STD & AIDS 2001;12 Suppl 2: 152 (abstract).



and 6% (1/18) for vehicle ( $P=0.039$ ). The median estimate of recurrences in observation was 1.0 for resiquimod versus 5.5 for vehicle ( $P=0.018$ ).

**Conclusions:** Topical resiquimod 0.01% was well tolerated. Treatment of genital herpes lesions with resiquimod delayed subsequent recurrences in this study.

**HSV-1 and HSV-2 seroprevalence study in Estonia**

Uusküla A<sup>1</sup>, Kibur M<sup>2</sup>, Robinson N J<sup>3</sup>, Tamm A<sup>4</sup>, HSV Seroepidemiology Multi-Centre Study Group

<sup>1</sup>Department of Dermatovenereology, University of Tartu, Estonia, <sup>2</sup>Department of Epidemiology and Biostatistics, Institute of Experimental and Clinical Medicine, Tallinn, Estonia, <sup>3</sup>Worldwide Epidemiology Department, GlaxoSmithKline, <sup>4</sup>United Laboratories, Tartu University Clinics, Estonia

**Introduction:** The knowledge of the prevalence of Herpes simplex virus type 1 (HSV-1) and 2 (HSV-2) is limited in Estonia.

**Objectives:** To estimate seroprevalence of HSV-1 and HSV-2 by age and gender in different non-high risk target groups from Southern Estonia.

**Methods:** We obtained consecutive serum samples from 1016 children (aged 1–12), 794 1st trimester antenatal women (aged 15–44) and 1036 blood donors (462 male, 574 female, aged 18–66). All sera had been submitted to Tartu University Clinics' central laboratory for serological analyses unrelated to HSV disease. Sera were tested using FDA-approved type specific ELISA assays (MRL).

**Results:** Overall, seroprevalence of HSV-1 among children, pregnant women and (non-paid) blood donors was 44%, 88% and 85% respectively. In children, HSV-1 prevalence increased from 17.8% in 1 year olds to 62.9% in 9–12 year olds. By age 20–24, pregnant women and blood donors had an HSV-1 prevalence of 86.6% and 79% respectively. HSV-2 seroprevalence was 23% in pregnant women; 11% in male and 21% in female blood donors. Increase in HSV-2 seroprevalence by age was found among blood donors and pregnant women.

**Conclusions:** HSV-1 seroprevalence was high in adults. HSV-2 seroprevalence was higher among women than men and increased substantially with age. In comparison with published data from other European countries, HSV-2 prevalence in these non-high risk populations was relatively high.

## **CURRICULUM VITAE**

### **Anneli Uusküla, M.D.**

Riia str. 7-3, Tartu, 51010, Estonia

Telephone (work): 3727.375319

E-Mail: annskla@ut.ee

### **Education**

- 2001 present State University of New York, University at Albany, School of Public Health, degree program studies in epidemiology
- 1993,1997-2001 Tartu University Medical Doctorancy in Dermatovenereology
- 1994-1997 Tartu University Clinic of Dermatovenereology, Medical Residency in Dermatovenereology
- 1991-1993 Tartu University Medical Internship
- 1985-1991 Tartu University Medical Faculty

### **Position**

- 2000 – since Foundation of Tartu University Clinics, Clinic of Dermatology, specialist-dermatovenereologist

### **Publications**

- Uusküla A, Kohl PK. *Genital mycoplasmas, including Mycoplasma genitalium as sexually transmitted infections.* International Journal of STD & AIDS 2001, accepted for publication, 2001.
- Uusküla A, Kalikova N, Zilmer K, Tammai L, DeHovitz J. *The role of injecting drug use in the emergence of HIV in Estonia.* International Journal of Infectious Diseases, accepted for publication, 2001.
- Wilson TE, Uusküla A, Feldman J, Holman S, DeHovitz J. *A case control study of beliefs and behaviors associated with STD occurrence in Estonia.* Sexually Transmitted Diseases, 2001, 2001; 28: 624-9.
- Uusküla A, Plank T, Lassus A, Bingham JS. *Sexually Transmitted Infections in Estonia - syndromic management of urethritis in a European country?* International Journal of STD & AIDS 2001;12: 493-49.
- Uusküla A, Silm H, Vessin T. *Sexually transmitted diseases in Estonia: Past and present.* International Journal of STD & AIDS 1997; 8: 1-5.
- Silm H, Majass M, Uusküla A. *Epidemiology of STDs in Estonia.* Forum for Nordic dermatovenereology 1998; 3: 7-9.

- Uusküla A, Kivi H, Pöder A, Vaher R, Silm H. *Trial of single-dose spectinomycin in treatment of uncomplicated gonorrhea in Estonia*. Eesti Arst, 1996; 4: 300–302.
- Pöder A, Uusküla A. *Treatment of uncomplicated gonorrhea with Ceftriaxone and Fleroxacin*. Eesti Tervishoiu Ajakiri 1996; 6: 20–22.
- Silm H, Kaur S, Uusküla A, Vaher R, Karelson M, Rajangu H. *Locally used fibrolan solution and ointment in the treatment of ulcers*. Eesti Arst 1996; 2; 124–127.
- Silm H, Karelson M, Kaur S, Rajangu H, Rannala-Lille T, Vahlberg A, Pärna E, Uusküla A. *Fucicort in dermatology*. Eesti Arst 1996; 3: 223–226.
- Kaur S, Uusküla A, Vindirevskih G, Silm H. *The need and possibilities of early diagnosis of syphilis in Estonia*. Eesti Arst 1995; 5: 396–399.
- Silm H, Elberg E, Kaur S, Rajangu H, Uusküla A. *Topical Vitamin D derivatives in treatment of psoriasis vulgaris*. Eesti Arst 1994; 4: 297–299.

### Research Activities:

1996–1998.

Principal Investigator, “Behavioral and Epidemiologic Factors related to Sexually Transmitted Disease Transmission in Estonia”. Funded by Fogarty International /Eastern European HIV Research Program, #3 D43 TW00233-05S3, National Institutes of Health.

1999–2001.

Principal Investigator, “HSV Seroepidemiology study”. Funded by GlaxoWellcome R&D, Valtex IPDT ( International Product Development Team).

### Presentations:

- Uusküla A. Genital mycoplasmas as sexually transmitted infections. 9<sup>th</sup> Congress of the European Academy of Dermatology and Venerology, Geneva, Switzerland, 2000.
- Uusküla A, Silm H, Pöder A. Current situation with sexually transmitted diseases in Estonia — favorable ground for spread of HIV infection in community. 3<sup>rd</sup> Nordic-Baltic Congress on Infectious Diseases, Lithuania, Vilnius, 1998.
- Uusküla A, Silm H. Warning signs of HIV infection risk factors in Estonia. Presented at the 5<sup>th</sup> Congress of the European Academy of Dermatology and Venereology, Portugal, Lisbon, 1996.
- Uusküla A, Kivi H, Pöder A, Vaher R, Silm H. Trial of single-dose spectinomycin in treatment of uncomplicated gonorrhea in Estonia. Presented at the

- 4<sup>th</sup> Congress of the European Academy of Dermatology and Venereology, Brussels, Belgium, 1995.
- Uusküla A, Kangur A, Silm H, Majass M, Elberg E, Kaur S, Rajangu H. Topical Vitamin D derivate in treatment of psoriasis vulgaris. Presented at the 4<sup>th</sup> Congress of the European Academy of Dermatology and Venereology, Brussels, Belgium, 1995.
- Silm H, Kaur S, Uusküla A, Vaheer R, Karelson M, Rajangu H. Locally used fibrolan solution and ointment in the treatment of ulcers. Presented at the 4<sup>th</sup> Congress of the European Academy of Dermatology and Venereology, Brussels, Belgium, 1995.
- Uusküla A, Kivi H, Pöder A, Vaheer R, Silm H. Trial of single-dose spectinomycin versus ofloxacin in treatment of uncomplicated gonorrhea. Presented at the International Meeting of Recent Achievements in the Diagnosis, Pathogenesis, and Treatment of Skin and Sexually Transmitted Diseases, Riga, Latvia, 1995.
- Uusküla A. Scerning for syphilis. European School of Transfusion Medicine. Proceedings of the ESTM residential course, 1998, 49–54.
- Uusküla A, Silm H. Etiological structure of sexually transmitted infections in Estonia. 13th Meeting of the International Society for Sexually Transmitted Diseases Research, July 11–14, 1999, Denver, USA.
- Wilson T, DeHovitz J, Holman S, Uusküla A, Feldman J. Beliefs and behaviors associated with STD prevalence in Estonia. 13th Meeting of the International Society for Sexually Transmitted Diseases Research, July 11–14, 1999, Denver, USA.
- DeHovitz J, Holman S, Uusküla A, Feldman J, Raudsepp H, Wilson T Silm H. Risk factors for STDs in Estonia and possible implications for other eastern European countries. 13th Meeting of the International Society for Sexually Transmitted Diseases Research, July 11–14, 1999, Denver, USA.

# CURRICULUM VITAE

## Anneli Uusküla

Riia tn. 7–3, Tartu, 51010, Eesti Vabariik

Telefon: 3727.375319

E-post: annskla@ut.ee

### Haridustee

- 1985–1991 TÜ arstiteaduskond ravi eriala  
1991–1993 üldinternatuur TÜ kliinikute baasil  
1994–1997 residentuur dermatoveneroloogia erialal  
1993, 1997–2001 doktorantuur Tartu Ülikoolis  
2001 alates kraadiõpe epidemioloogia alal (*MS degree program in Epidemiology*), State University of New York, School of Public Health)

### Teenistuskäik

- 10.1993–10.2000 TÜ naha- ja suguhaiguste õppetooli vanemlaborant  
01.01.2000 SA TÜK, Nahahaiguste Kliinik, arst-õppejõud

### Publikatsioonid

- Uusküla A, Kohl PK. *Genital mycoplasmas, including Mycoplasma genitalium as sexually transmitted infections*. International Journal of STD & AIDS 2001, vastuvõetud avaldamiseks, 2001.
- Uusküla A, Kalikova N, Zilmer K, Tammai L, DeHovitz J. *The role of injecting drug use in the emergence of HIV in Estonia*. International Journal of Infectious Diseases, vastuvõetud avaldamiseks 2001.
- Wilson TE, Uusküla A, Feldman J, Holman S, DeHovitz J. *A case control study of beliefs and behaviors associated with STD occurrence in Estonia*. Sexually Transmitted Diseases, 2001, 28: 624–9.
- Uusküla A, Plank T, Lassus A, Bingham JS. *Sexually Transmitted Infections in Estonia - syndromic management of urethritis in a European country?* International Journal of STD & AIDS 2001;12: 493–49.
- Uusküla A, Silm H, Vessin T. *Sexually transmitted diseases in Estonia: Past and present*. International Journal of STD & AIDS 1997; 8: 1–5.
- Silm H, Majass M, Uusküla A. *Epidemiology of STDs in Estonia*. Forum for Nordic dermatovenerology 1998; 3: 7–9.
- Uusküla A, Kivi H, Pöder A, Vaher R, Silm H. *Komplitseerumata gonorröa ravi ühekordse spektrinomiitsiini annusega*. Eesti Arst, 1996; 4: 300–302.

- Pöder A, Uusküla A. *Komplitseerumata gonorröa ravi tseftriaksooni ja fleroksatsiiniga*. Eesti Tervishoiu Ajakiri 1996; **6**: 20–22.
- Silm H, Kaur S, Uusküla A, Vaher R, Karelson M, Rajangu H. *Fibrolaansalv ja -lahus haavandite lokaalses ravis*. Eesti Arst 1996; **2**: 124–127.
- Silm H, Karelson M, Kaur S, Rajangu H, Rannala-Lille T, Vahlberg A, Pärna E, Uusküla A. *Fucicort dermatoloogias*. Eesti Arst 1996; **3**: 223–226.
- Kaur S, Uusküla A, Vindirevskih G, Silm H. *Vajadus ja võimalused süüfilise diagnostikaks Eestis*. Eesti Arst 1995; **5**: 396–399.
- Silm H, Elberg E, Kaur S, Rajangu H, Uusküla A. *Lokaalselt kasutatavad vitamiin D derivaadid psoriaasi ravis*. Eesti Arst 1994; **4**: 297–299.

### **Teadustöö põhisuunad**

- 1996–1998, peamine uuringu läbiviija projektis “Behavioral and Epidemiologic Factors Related to Sexually Transmitted Disease Transmission in Estonia”, finantseerija *Fogarty International Center, National Institutes of Health*.
- Alates 1999, kohalik uuringujuht projektis “HSV seroepidemiology multicentre study”, finantseerija *GlaxoWellcome R&D, Valtex IPDT (International Product Development Team)*.
- Sugulisel teel levivate infektsioonide epidemioloogia Eestis.

### **Ettekanded**

- Uusküla A. *Genital mycoplasmas as sexually transmitted infections*. 9<sup>th</sup> Congress of the European Academy of Dermatology and Venerology, Geneva, Switzerland, 2000.
- Uusküla A, Silm H, Pöder A. *Current situation with sexually transmitted diseases in Estonia — favorable ground for spread of HIV infection in community*. 3<sup>rd</sup> Nordic-Baltic Congress on Infectious Diseases, Lithuania, Vilnius, 1998.
- Uusküla A, Silm H. *Warning signs of HIV infection risk factors in Estonia*. Presented at the 5<sup>th</sup> Congress of the European Academy of Dermatology and Venereology. Portugal, Lisbon, 1996.
- Uusküla A, Kivi H, Pöder A, Vaher R, Silm H. *Trial of single-dose spectinomycin in treatment of uncomplicated gonorrhoea in Estonia*. Presented at the 4<sup>th</sup> Congress of the European Academy of Dermatology and Venereology, Brussels, Belgium, 1995.
- Uusküla A, Kangur A, Silm H, Majass M, Elberg E, Kaur S, Rajangu H. *Topical Vitamin D derivate in treatment of psoriasis vulgaris*. Presented at the 4<sup>th</sup> Congress of the European Academy of Dermatology and Venereology. Brussels, Belgium, 1995.
- Silm H, Kaur S, Uusküla A, Vaher R, Karelson M, Rajangu H. *Locally used fibrolan solution and ointment in the treatment of ulcers*. Presented at the

- 4<sup>th</sup> Congress of the European Academy of Dermatology and Venereology, Brussels, Belgium, 1995.
- Uusküla A, Kivi H, Põder A, Vaher R, Silm H. Trial of single-dose spectinomycin versus ofloxacin in treatment of uncomplicated gonorrhea. Presented at the International Meeting of Recent Achievements in the Diagnosis, Pathogenesis, and Treatment of Skin and Sexually Transmitted Diseases, Riga, Latvia, 1995.
- Uusküla A. Scerning for syphilis. European School of Transfusion Medicine. Proceedings of the ESTM residential course, 1998, 49–54.
- Uusküla A, Silm H. Etiological structure of sexually transmitted infections in Estonia. 13th Meeting of the International Society for Sexually Transmitted Diseases Research, July 11–14, 1999, Denver, USA.
- Wilson T, DeHovitz J, Holman S, Uusküla A, Feldman J. Beliefs and behaviors associated with STD prevalence in Estonia. 13th Meeting of the International Society for Sexually Transmitted Diseases Research, July 11–14, 1999, Denver, USA.
- DeHovitz J, Holman S, Uusküla A, Feldman J, Raudsepp H, Wilson T Silm H. Risk factors for STDs in Estonia and possible implications for other eastern European countries. 13th Meeting of the International Society for Sexually Transmitted Diseases Research, July 11–14, 1999, Denver, USA.

## DISSERTATIONES MEDICINAE UNIVERSITATIS TARTUENSIS

1. **Heidi-Ingrid Maaroo**s. The natural course of gastric ulcer in connection with chronic gastritis and *Helicobacter pylori*. Tartu, 1991.
2. **Mihkel Zilmer**. Na-pump in normal and tumorous brain tissues: Structural functional a. tumorigenesis aspects. Tartu, 1991.
3. **Eero Vasar**. Role of cholecystokinin receptors in the regulation of behaviour and in the action of haloperidol and diazepam. Tartu, 1992.
4. **Tiina Talvik**. Hypoxic-ischaemic brain damage in neonates (clinical, biochemical and brain computed tomographical investigation) Tartu, 1992.
5. **Ants Peetsalu**. Vagotomy in duodenal ulcer disease: A study of gastric acidity, serum pepsinogen I, gastric mucosal histology and *Helicobacter pylori*. Tartu, 1992.
6. **Marika Mikelsaar**. Evaluation of the gastrointestinal microbial ecosystem in health and disease. Tartu, 1992.
7. **Hele Everaus**. Immuno-hormonal interactions in chronic lymphocytic leukaemia and multiple myeloma. Tartu, 1993.
8. **Ruth Mikelsaar**. Etiological factors of diseases in genetically consulted children and newborn screening: dissertation for the commencement of the degree of doctor of medical sciences. Tartu, 1993.
9. **Agu Tamm**. On metabolic action of intestinal microflora: clinical aspects. Tartu, 1993.
10. **Katrin Gross**. Multiple sclerosis in South-Estonia (epidemiological and computed tomographical investigations). Tartu, 1993.
11. **Oivi Uibo**. Childhood coeliac disease in Estonia: occurrence, screening, diagnosis and clinical characterization. Tartu, 1994.
12. **Viiu Tuulik**. The functional disorders of central nervous system of chemistry workers. Tartu, 1994.
13. **Margus Viigimaa**. Primary haemostasis, antiaggregative and anticoagulant treatment of acute myocardial infarction. Tartu, 1994.
14. **Rein Kolk**. Atrial versus ventricular pacing in patients with sick sinus syndrome. Tartu, 1994.
15. **Toomas Podar**. Incidence of childhood onset type 1 diabetes mellitus in Estonia. Tartu, 1994.
16. **Kiira Subi**. The laboratory surveillance of the acute respiratory viral infections in Estonia. Tartu, 1995.
17. **Irja Lutsar**. Infections of the central nervous system in children (epidemiologic, diagnostic and therapeutic aspects, long term outcome). Tartu, 1995.
18. **Aavo Lang**. The role of dopamine, 5-hydroxytryptamine, sigma and NMDA receptors in the action of antipsychotic drugs. Tartu, 1995.
19. **Andrus Arak**. Factors influencing the survival of patients after radical surgery for gastric cancer. Tartu, 1996.



20. **Tõnis Karki.** Quantitative composition of the human lactoflora and method for its examination. Tartu, 1996.
21. **Reet Mändar.** Vaginal microflora during pregnancy and its transmission to newborn. Tartu 1996.
22. **Triin Remmel.** Primary biliary cirrhosis in Estonia: epidemiology, clinical characterization and prognostication of the course of the disease. Tartu 1996.
23. **Toomas Kivastik.** Mechanisms of drug addiction: focus on positive reinforcing properties of morphine. Tartu, 1996.
24. **Paavo Pokk.** Stress due to sleep deprivation: focus on GABA<sub>A</sub> receptor-chloride ionophore complex. Tartu, 1996.
25. **Kristina Allikmets.** Renin system activity in essential hypertension. Associations with atherothrombogenic cardiovascular risk factors and with the efficacy of calcium antagonist treatment. Tartu, 1996.
26. **Triin Parik.** Oxidative stress in essential hypertension: Associations with metabolic disturbances and the effects of calcium antagonist treatment. Tartu, 1996.
27. **Svetlana Päi.** Factors promoting heterogeneity of the course of rheumatoid arthritis. Tartu, 1997.
28. **Maarike Sallo.** Studies on habitual physical activity and aerobic fitness in 4 to 10 years old children. Tartu, 1997.
29. **Paul Naaber.** *Clostridium difficile* infection and intestinal microbial ecology. Tartu, 1997.
30. **Rein Pähkla.** Studies in pinoline pharmacology. Tartu, 1997.
31. **Andrus Juhan Voitk.** Outpatient laparoscopic cholecystectomy. Tartu, 1997.
32. **Joel Starkopf.** Oxidative stress and ischaemia-reperfusion of the heart. Tartu, 1997.
33. **Janika Kõrv.** Incidence, case-fatality and outcome of stroke. Tartu, 1998.
34. **Ülla Linnamägi.** Changes in local cerebral blood flow and lipid peroxidation following lead exposure in experiment. Tartu, 1998.
35. **Ave Minajeva.** Sarcoplasmic reticulum function: comparison of atrial and ventricular myocardium. Tartu, 1998.
36. **Oleg Milenin.** Reconstruction of cervical part of esophagus by revascularised ileal autografts in dogs. A new complex multistage method. Tartu, 1998.
37. **Sergei Pakriev.** Prevalence of depression, harmful use of alcohol and alcohol dependence among rural population in udmurtia. Tartu, 1998.
38. **Allen Kaasik.** Thyroid hormone control over  $\beta$ -adrenergic signalling system in rat atria. Tartu, 1998.
39. **Vallo Matto.** Pharmacological studies on anxiogenic and antiaggressive properties of antidepressants. Tartu, 1998.
40. **Maire Vasar.** Allergic diseases and bronchial hyperreactivity in Estonian children in relation to environmental influences. Tartu, 1998.

41. **Kaja Julge.** Humoral immune responses to allergens in early childhood. Tartu, 1998.
42. **Heli Grünberg.** The cardiovascular risk of Estonian schoolchildren. A cross-sectional study of 9-, 12- and 15-year-old children. Tartu, 1998.
43. **Epp Sepp.** Formation of intestinal microbial ecosystem in children. Tartu, 1998.
44. **Mai Ots.** Characteristics of the progression of human and experimental glomerulopathies. Tartu, 1998.
45. **Tiina Ristimäe.** Heart rate variability in patients with coronary artery disease. Tartu, 1998.
46. **Leho Kõiv.** Reaction of the sympatho-adrenal and hypothalamo-pituitary-adrenocortical system in the acute stage of head injury. Tartu, 1998.
47. **Bela Adojaan.** Immune and genetic factors of childhood onset IDDM in Estonia. An epidemiological study. Tartu, 1999.
48. **Jakov Shlik.** Psychophysiological effects of cholecystokinin in humans. Tartu, 1999.
49. **Kai Kisand.** Autoantibodies against dehydrogenases of  $\alpha$ -ketoacids. Tartu, 1999.
50. **Toomas Marandi.** Drug treatment of depression in Estonia. Tartu, 1999.
51. **Ants Kask.** Behavioural studies on neuropeptide Y. Tartu, 1999.
52. **Ello-Rahel Karelson.** Modulation of adenylate cyclase activity in the rat hippocampus by neuropeptide galanin and its chimeric analogs. Tartu, 1999.
53. **Tanel Laisaar.** Treatment of pleural empyema — special reference to intrapleural therapy with streptokinase and surgical treatment modalities. Tartu, 1999.
54. **Eve Pihl.** Cardiovascular risk factors in middle-aged former athletes. Tartu, 1999.
55. **Katrin Õunap.** Phenylketonuria in Estonia: incidence, newborn screening, diagnosis, clinical characterization and genotype/phenotype correlation. Tartu, 1999.
56. **Siiri Kõljalg.** *Acinetobacter* — an important nosocomial pathogen. Tartu, 1999.
57. **Helle Karro.** Reproductive health and pregnancy outcome in Estonia: association with different factors. Tartu, 1999.
58. **Heili Varendi.** Behavioral effects observed in human newborns during exposure to naturally occurring odors. Tartu, 1999.
59. **Anneli Beilmann.** Epidemiology of epilepsy in children and adolescents in Estonia. Prevalence, incidence, and clinical characteristics. Tartu, 1999.
60. **Vallo Volke.** Pharmacological and biochemical studies on nitric oxide in the regulation of behaviour. Tartu, 1999.
61. **Pilvi Ilves.** Hypoxic-ischaemic encephalopathy in asphyxiated term infants. A prospective clinical, biochemical, ultrasonographical study. Tartu, 1999.

62. **Anti Kalda.** Oxygen-glucose deprivation-induced neuronal death and its pharmacological prevention in cerebellar granule cells. Tartu, 1999.
63. **Eve-Irene Lepist.** Oral peptide prodrugs — studies on stability and absorption. Tartu, 2000.
64. **Jana Kivastik.** Lung function in estonian schoolchildren: relationship with anthropometric indices and respiratory symptoms, reference values for dynamic spirometry. Tartu, 2000.
65. **Karin Kull.** Inflammatory bowel disease: an immunogenetic study. Tartu, 2000.
66. **Kaire Innos.** Epidemiological resources in Estonia: data sources, their quality and feasibility of cohort studies. Tartu, 2000.
67. **Tamara Vorobjova.** Immune response to *Helicobacter pylori* and its association with dynamics of chronic gastritis and epithelial cell turnover in antrum and corpus. Tartu, 2001.
68. **Ruth Kalda.** Structure and outcome of family practice quality in the changing health care system of Estonia. Tartu, 2001.
69. **Annika Krüüner.** *Mycobacterium tuberculosis* — spread and drug resistance in Estonia. Tartu, 2001.
70. **Marlit Veidi.** Obstructive Sleep Apnoea: Computerized Endopharyngeal Myotonometry of the Soft Palate and Lingual Musculature. Tartu, 2001.



ISSN 1024-395X  
ISBN 9985-56-611-4