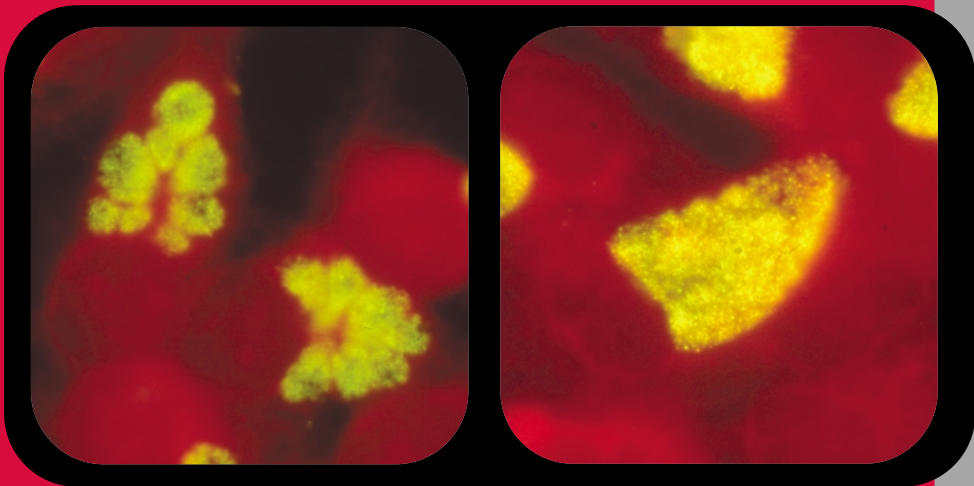


VU university medical center



Mini-symposium
17 December 2004
10:30 – 15:00

Chlamydia trachomatis infections



Venue:

Vrije Universiteit, Amsterdam
Building of the Faculty of Earth and Life Sciences,
De Boelelaan 1085, Room F123

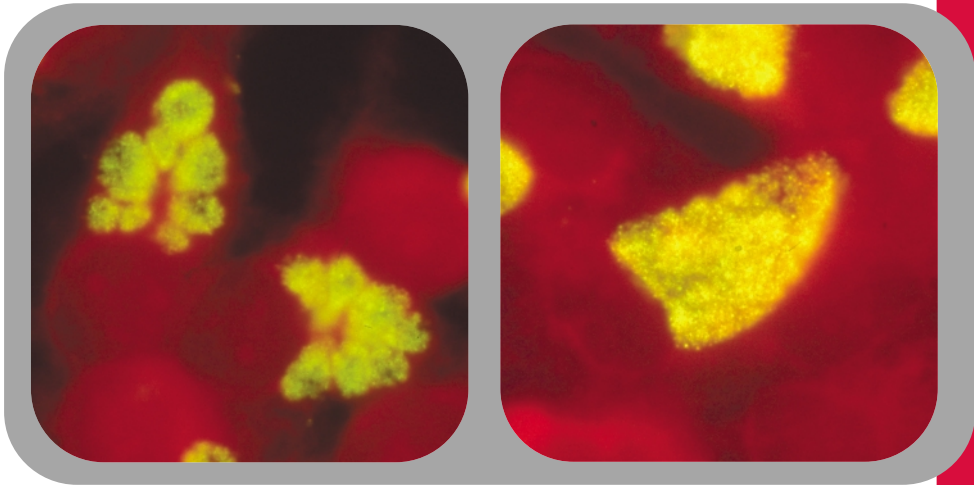
Cover photographs: Immunofluorescence staining of *Chlamydia trachomatis* within epithelial cells. HeLa cells were infected with a clinical isolate and stained with a monoclonal antibody specific for the major outer membrane protein (OmpA) of *C. trachomatis*. The left panel shows a non-fusogenic phenotype, while the right panel shows a fusogenic phenotype.

Images courtesy of Yvonne Pannekoek, Department of Medical Microbiology, Academic Medical Center, Amsterdam, The Netherlands.

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Mini-symposium

Chlamydia trachomatis infections



Organised by:

Prof. A. Salvador Peña and Dr. Servaas A. Morré
Laboratory of Immunogenetics

CME:

The Mini-symposium is accredited by
The Dutch Society of Medical Microbiology

Welcome

This mini-symposium entitled "*Chlamydia trachomatis* infections" has been organised by the Laboratory of Immunogenetics of the VU University medical centre (VUmc), Amsterdam with the aim of providing a platform for experts and PhD students alike to discuss their research on this widespread infection.

The Laboratory of Immunogenetics

Established by Prof. A.S. Peña in 1992, the Laboratory of Immunogenetics will become part of the Department of Pathology (Head Prof. Chris J.L.M. Meijer) starting 1 January 2005. The research conducted in the Laboratory primarily seeks to define the role of HLA-DQ and cytokine genes in chronic inflammatory bowel diseases and coeliac disease. In recent years, the Laboratory's research has expanded to include the study of the genetic background of patients with other chronic inflammatory, autoimmune and infectious diseases. The Laboratory links fundamental scientific research and clinical application (translational research). Research is divided into two interactive and productive lines: chronic inflammatory diseases (J.B.A. Crusius, PhD) and infectious diseases (S.A. Morré, PhD). Both lines interact using an experimental approach in order to obtain a better insight into disease pathogenesis.

The immunogenetics of infectious disease is in its infancy. It is a new exciting field with major developments in the last few years. Studies in twins and adopted children have shown that host genetic factors form an important element in the susceptibility to and the severity of infectious diseases in humans. Identification of these genes will give insight into the protective and pathogenic mechanisms of infectious diseases.

Chlamydia trachomatis

Bacterial, environmental and host genetic factors determine the clinical course of *C. trachomatis* infections. This infection is an excellent model for the study of host-pathogen interactions. Extra- and intracellular life forms of this bacterium result in a complex initiation of innate and adaptive immune responses which is yet poorly understood.

An integrated approach has been applied to gain a deeper understanding of early infections (J. Spaargaren, MD, Municipal Health Service, Amsterdam)

and late complications in women (J. Land, MD, PhD, Department of Gynaecology and Obstetrics of the Academic Medical Center of Maastricht). Fundamental aspects have been investigated with murine-based experimental models (J.M. Lyons, MSc, and J.I. Ito, MD, PhD, Department of Infectious Diseases, City of Hope, National Medical Center and Beckman Research Institute, Duarte, CA, USA) and cellular biological studies (Y. Pannekoek, PhD, Department of Medical Microbiology, Academic Medical Center, Amsterdam). We hope that this approach will contribute to gaining better insight into the pathogenesis of this infection and contribute to the development of a vaccine. This may in turn lead to the eradication of *C. trachomatis*, the most common sexually transmitted bacterial pathogen worldwide.

In this mini-symposium, following the an introductory lecture by Prof. M. Ward, the first session will highlight expert opinions on *C. trachomatis* infection. The second session will summarise ongoing PhD research on this pathogen in the Netherlands and Belgium. Finally, a State-of-the-Art lecture on Toll-like receptors as recognition mechanisms of innate immunity, given by M. Netea, MD, PhD, will bring the symposium to a close. After a short break, Joseph Lyons will defend his thesis entitled, "An integrated approach to the study of *Chlamydia trachomatis* infection of the female urogenital tract" in the Vrije Universiteit.

In closing, we wish to express our gratitude to Prof. S.A. Danner, Head of Internal Medicine of the VUmc Amsterdam, who is actively supporting the immunogenetic research in infectious diseases.



A. Salvador Peña

Head of the Laboratory of
Immunogenetics
VUmc Amsterdam



Servaas A. Morré

Research Co-ordinator
Immunogenetics, Infectious
Diseases
VUmc Amsterdam

Programme

10:00-10:30 **Registration**

10:30-10:45 **Introduction**

Prof. Chris J.L.M. Meijer, Director, Department of Pathology
Prof. A. Salvador Peña, Head of the Laboratory of Immunogenetics
Servaas A. Morré, PhD, Co-ordinator Research Line, Immunogenetics of Infectious Diseases

10:45 - 12:30 **Session 1: Expert Opinions on *Chlamydia trachomatis* Infection**

Chlamydial research and researchers: changing priorities, a personal view *page 7*
Prof. Michael Ward, MD, PhD

Chlamydial protein synthesis and polymorphism in IncA
Yvonne Pannekoek, PhD *page 8*

Selective screening for *Chlamydia trachomatis* is needed in the Netherlands *page 10*
Ton Coenen, MSc, MPM

Lymphogranuloma venereum proctitis: an emerging STD in HIV-positive men in the Netherlands *page 11*
Roos Perenboom, MD, PhD

Pathogenicity of *Chlamydia trachomatis* serovar E genital infection in specific pathogen-free piglets *page 12*
Daisy Vanrompay, PhD

12:30-13:15 **Lunch**

Session 1

13:15-14:30 **Session 2: Presentation of PhD Research**

Session 2

Developing a feasible, acceptable and evidence-based strategy for selective, opportunistic screening for *Chlamydia trachomatis* infection in women in general practice in Flanders
Veronique Verhoeven, MD page 13

Epidemiology, pathogenesis and immunogenetics of *Chlamydia trachomatis* infections in the human urogenital tract
Joke Spaargaren, MD page 14

Chlamydia trachomatis in the upper genital tract
Janneke E. den Hartog, MD page 15

Immunogenetic aspects of *Chlamydia trachomatis* infections
Sander Ouburg, MSc page 16

Determinants and consequences of *Chlamydia trachomatis* infection for pregnant women and their offspring
Ingrid Rours, MD page 17

Acquired and innate immune response of the urogenital tract to *Chlamydia trachomatis*
Juliëtte Severin, MD page 19

14:30-15:00 **State-of-the-Art Lecture**

Toll-like receptors as recognition mechanisms of innate immunity
Mihai Netea MD, PhD page 20

15:00-15:10 **Closing remarks**

A. Salvador Peña, MD, PhD

15:10-15:30 **Break**

15:45-17:15 **Doctoral Thesis Defence**

An integrated approach to the study of *Chlamydia trachomatis* infections of the female genital tract
Joseph M. Lyons

17:30-18:30 **Reception**



Chlamydial research and researchers: changing priorities, a personal view

Michael Ward, MD, PhD

School of Medicine, University of Southampton, UK

Michael Ward was formerly Professor of Medical Microbiology at the University of Southampton School of Medicine in the UK. He graduated in microbiology from University College, London University in 1967 and completed a PhD on gonococci in 1970 under Prof. Alan Glynn at the Wright-Fleming Institute of St Mary's Hospital, London. He moved the medical school at Southampton in 1972.

His early work, with Peter Watt, concerned the pathogenesis of gonococcal infection. Prof. Ward published the first electron micrographs of the in vivo adhesion of gonococci to human epithelia and described the process by which gonococci invade perfused human fallopian tube in vitro.

In 1979, he switched to chlamydial research. His was one of three groups which in 1981 co-discovered the chlamydial major outer membrane protein (MOMP). This was followed, in collaboration with Ian Clarke and others, by the initial characterisation of genes encoding various chlamydial surface or envelope antigens and, with Wayne Conlan, the high resolution mapping of neutralising epitopes on MOMP. A fruitful collaboration with David Mabey and Robin Bailey followed on the molecular epidemiology of trachoma in the Gambia, West Africa. His interest in gonococcal and chlamydial infections resulted in him serving for 6 years on the steering group of the WHO task force on infertility. More recently, together with cardiologist Yuk-ki Wong and others, he has published a series of papers challenging accepted thinking on the role of C. pneumoniae in coronary artery disease. He is the author of a large number of papers on chlamydial infections and contributed a chapter on chlamydial disease mechanisms to the American Society of Microbiology Book on Chlamydia (1999).

Prof. Ward retired from permanent employment with the University of Southampton in September 2004 and was awarded the title of Emeritus Professor. He continues to work for the University on an occasional basis.

The purpose of this talk will be to introduce chlamydiae and chlamydial research to those who are not familiar with the field and to reflect on some of the key assumptions and organisations on which chlamydial research is based.



Chlamydial protein synthesis and polymorphism in IncA

Yvonne Pannekoek, PhD

Department of Medical Microbiology, Academic Medical Center,
University of Amsterdam, The Netherlands

Yvonne Pannekoek specialised in molecular biology at the University of Amsterdam (UvA). In 1988 she began her PhD training at the Department of Medical Microbiology (Jos van Putten, MD and the late Prof. Jacob Dankert, MD, PhD), Academic Medical Center (AMC) of the UvA. Her research focused on molecular biology of heat shock proteins of *Neisseria*. During her PhD training she spent one year as visiting fellow at the Max-Planck-Institut für Infektionsbiologie (Thomas Meyer, MD) in Germany. In 1993, she successfully defended her PhD thesis entitled "Identification of Neisserial stress proteins". That same year she moved to Rochester, NY, USA, to join the laboratory of Patrik Bavoil, MD, as a post-doctoral fellow, and switched to the study of Chlamydia. In this laboratory she discovered the presence of the type-three secretion system in *C. psittaci* (awarded, with her co-workers, the prize for the best poster during the Third European Chlamydia meeting in Vienna, 1996). Back in the Netherlands, at the Department of Medical Microbiology, AMC, UvA, she continued her work on Chlamydia as an assistant professor, and started a fruitful collaboration with the Center for Reproductive Medicine, situated in the AMC (Prof. Fulco van der Veen, MD, PhD), investigating the relationship between Chlamydia infections and male infertility. In addition, she continued her work on the basic biology of Chlamydia, in close co-operation with her direct colleague Arie van der Ende, MD. Her current research is focused on inclusion proteins (in co-operation with Servaas Morré, PhD and Joke Spaargaren, MD) and methylation of peptide release factors of *C. trachomatis*.

Yvonne Pannekoek is an active member of the Dutch Group for Chlamydia Research, initiating, organising and hosting meetings of this "society". Besides conducting research, she also teaches medicine, biology and students of higher laboratory schools. The fact that one of her students was awarded the prize for the best student report of higher educational schools in the Netherlands in 2000 reflects her approach to education.



Lymphogranuloma venereum proctitis: an emerging STD in HIV-positive men in the Netherlands

Roos Perenboom, MD, PhD

Department of Internal Medicine, VU University Medical Center,
Amsterdam, The Netherlands

A specialist in internal medicine and infectious diseases, Dr. Perenboom was trained at the Radboud University Hospital in Nijmegen, the Netherlands. She worked for many years in Tanzania, as medical officer in a mission hospital and later as a university lecturer and specialist in internal medicine at the Muhimbili Medical Centre in Dar Es Salaam. She has been a staff member of the Department of Medicine at VUmc since 1996. In both Tanzania and the Netherlands, her involvement was and continues to be in the area of infectious diseases, patient care, and teaching.

A recent outbreak of lymphogranuloma venereum (LVG) proctitis caused by *Chlamydia trachomatis* serovar L2 has been detected in HIV-positive men in the Netherlands and Belgium. This sexually transmitted disease (STD), which is well known and of frequent occurrence in tropical countries, was quite unusual in Europe until 2003. STDs with ulcerative lesions, such as LGV, facilitate transmission of other microorganisms, including HIV and hepatitis C. This in combination with risky sexual behaviour, such as unprotected anal sexual intercourse or use of sex toys, increases the risk of blood-blood contact and hence the risk of contracting multiple STDs. Two patients will be presented who in a short time period contracted multiple STDs, including LGV proctitis. The clinical picture, diagnostic procedures and treatment of LVG will be discussed.



Pathogenicity of *Chlamydia trachomatis* serovar E genital infection in specific pathogen-free piglets

D. Vanrompay, PhD¹, S.A. Morré, PhD² and E. Cox³

¹Ghent University, Laboratory of Immunology and Animal Biotechnology, Ghent, Belgium; ²VU University Medical Center, Laboratory of Immunogenetics, Section Immunogenetics of Infectious Diseases, Amsterdam, The Netherlands; and ³Ghent University, Laboratory of Veterinary Immunology, Merelbeke, Belgium

Daisy Vanrompay graduated as a Doctor in Veterinary Medicine from the Faculty of Veterinary Medicine, Ghent University, Belgium, in 1990. In the same year, she started her doctoral research fellowship on avian Chlamydia psittaci strains and their pathogenicity for turkeys at the Department of Veterinary Pathology, Bacteriology and Poultry Diseases of the Faculty of Veterinary Medicine at Ghent University. She finished her PhD as Doctor in Veterinary Sciences in 1994 and continued to work on chlamydiosis in poultry as a member of the assisting academic staff at the same department. In 1996, she started her postdoctoral research fellowship at the Department of Animal Production, Laboratory of Gene Technology and Laboratory of Physiology and Immunology of Domestic Animals of the Faculty of Agriculture and Biological Sciences at University of Leuven. In 2000, she obtained the position of assistant professor at the Department of Molecular Biotechnology, Faculty of Bioscience Engineering, Ghent University where she continues her scientific work on Chlamydiaceae.

Despite intensive research on chlamydial pathogenesis and host immune responses, vaccine development has been hampered by incomplete understanding of the virulence factors and the critical factors governing protective immunity. It is unknown why certain *Chlamydia trachomatis* serovars cause asymptomatic or symptomatic infection or ascend to the upper genital tract. Former studies have used non-primate monkey, mice or guinea-pig infection models. However, pigs are genetically and physiologically related to man and are susceptible to chlamydial infections. The main objective of the present study was the validation of the pig as an alternative animal model for *C. trachomatis* female genital tract infection.



Developing a feasible, acceptable and evidence-based strategy for selective, opportunistic screening for *Chlamydia trachomatis* infection in women in general practice in Flanders

Veronique Verhoeven, MD

General Practice Department, Antwerp University, Belgium

Veronique Verhoeven studied medicine at Antwerp University in Belgium and worked as a GP for two years. In 2000, she started conducting research at the General Practice Department of Antwerp University. Her main project was to develop a strategy for selective, opportunistic screening for urogenital chlamydial infection in general practice. This screening model was implemented in Flemish general practice in May 2004. Other research projects are on Chlamydia-human papilloma virus (HPV) interactions, and on self-sampling for HPV in the prevention of cervical cancer. In addition to her research work, she teaches at Antwerp University, and she works as an emergency medicine doctor and occasionally as a GP.

Our aim was to develop a feasible, acceptable and evidence-based strategy for selective, opportunistic screening for *Chlamydia trachomatis* infection in women in general practice in Flanders. Until recently, screening was uncommon and untargeted in the absence of valid screening criteria. We conducted a large prevalence and risk factor study, from which a screening algorithm was derived. This algorithm was validated in a new sample at a later date. Furthermore, we examined which conditions influence successful implementation of screening. A tool to facilitate GP-patient communication was developed and evaluated in a cluster randomised, controlled trial. After a pilot implementation study focusing on feasibility and quality improvement issues, the screening model was disseminated among all Flemish GPs.



Epidemiology, pathogenesis and immunogenetics of *Chlamydia trachomatis* infections in the human urogenital tract

Joke Spaargaren, MD

Municipal Health Service, Public Health Laboratory,
Amsterdam, The Netherlands

Joke Spaargaren worked as a senior research technician at the Department of Blood Coagulation at the "Centraal Laboratorium van de Bloedtransfusiedienst" (CLB) in the Netherlands from 1979 to 1985. She worked on the pathogenesis of arterial thrombosis and atherosclerosis, which resulted in seven scientific publications in international journals. In 1985 she initiated her studies in medicine at the University of Amsterdam. During this time she worked at the National Cancer Institute (with M. Kast, PhD and Prof. C.J.M. Melief, PhD) on the cellular immunology of a lethal Sendai virus infection in a murine model. In 1991 she graduated and continued to specialise in microbiology in Leiden (Prof. C.P.A. van Boven, PhD, MD; Prof. A.C. Kroes, PhD, MD) at the Leiden University Medical Centre. During her specialisation she was trained in the laboratory diagnostics of infectious diseases, and became registered in this speciality in 1998. In 1999, she began working at the Public Health Laboratory at the Municipal Health Service (Prof. R.A. Coutinho, PhD, MD) in Amsterdam. In charge of the laboratory, she started to work on the genotyping of sexually transmitted diseases, e.g., *Neisseria gonorrhoeae*, *C. trachomatis* and *Treponema pallidum*.

In 2001 her research began to focus on the epidemiology, pathogenesis and immunogenetics of *C. trachomatis* infections in the human urogenital tract in close collaboration with Servaas A. Morré, PhD, and Prof. A.S. Peña, MD, PhD, FRCP. The results of this research will be summarised in her thesis to be defended in 2005 at the University of Amsterdam (UVA).

Bacterial, environmental and host factors are studied in the susceptibility to and severity of *Chlamydia trachomatis* infections in women attending the STD Clinic in Amsterdam. In addition, from both a health care and research point of view, the recently reported lymphogranuloma venereum outbreak among men having sex with men is characterised on an epidemiological level, and therapy and diagnostics approaches are being evaluated.



Chlamydia trachomatis in the upper genital tract

Janneke E. den Hartog, MD

Department of Obstetrics and Gynaecology,
Academic Hospital Maastricht, The Netherlands

Janneke E. den Hartog studied medicine at the University of Maastricht, the Netherlands, and graduated in 2001. In December 2001, she started her PhD program on *C. trachomatis* in the Department of Obstetrics and Gynaecology of the Academic Hospital Maastricht (supervisors Prof. J.L.H. Evers MD, PhD; Prof. C.A. Bruggeman PhD; and J.A. Land, MD, PhD). She is also an in vitro fertilisation doctor and will begin her residency in Obstetrics and Gynaecology after completing her thesis.

The *Chlamydia* Research Group Maastricht focuses on the late sequelae of *C. trachomatis* infections in women: tubal pathology and subfertility. The *Chlamydia* Research Group of Maastricht consists of members of the research institutes Maastricht Infection Centre (MINC) and Growth and Development (GROW), and the departments of Medical Microbiology and Obstetrics and Gynaecology.

The predictive value of different serological *Chlamydia* antibody tests (CAT) for tubal pathology has been studied. Furthermore, potential markers of persistent *C. trachomatis* infections as risk factors for tubal pathology have been evaluated. Future research will focus on the spread of *C. trachomatis* in the genital tract and its detection in the fallopian tubes and endometrium of subfertile women. At the moment, a pilot study is underway, in which paraffin-embedded endometrial tissue is tested for the presence of *C. trachomatis* using immunohistochemistry.



Immunogenetic aspects of *Chlamydia trachomatis* infections

Sander Ouburg, MSc

VUmc Amsterdam, The Netherlands

Sander Ouburg studied medical biology at the Universiteit van Amsterdam (UvA) and graduated in August 2002. As an undergraduate student, he worked on the regulation of IL-12Rb2 by IL-13 in the Department of Cell Biology and Histology, Academic Medical Centre (AMC), Amsterdam (H.H. Smits, MSc; Prof. M.L. Kapsenberg, PhD). The second internship focused on the role of IL-1B and IL-1RN gene polymorphisms in the susceptibility and severity of human urogenital *Chlamydia trachomatis* infections at the Public Health Laboratory, Public Health Services (Prof. R.A. Coutinho, PhD; J. Spaargaren, MD; S.A. Morré, PhD). Finally, his internship essay discussed the immunogenetics of human urogenital tract infections (J. Spaargaren, MD; S.A. Morré, PhD). He is currently working on the immunogenetics of infectious diseases with special attention to gastric atrophy disorders (Prof. A.S. Peña, MD, PhD, FRCP; S.A. Morré, PhD; Prof. C.J.J. Mulder, MD, PhD; E.C. Klinkenberg-Knol, MD, PhD). Sander Ouburg is an AstraZeneca fellow.

This presentation will focus on the candidate genes used in the integrated approach to the study of *Chlamydia trachomatis* infections in the female urogenital tract, as described in the thesis of Joseph Lyons. Special attention will be given to genes involved in the innate immune responses to *C. trachomatis* infections, such as Toll-like receptors, and to those involved in the Th0→Th1 routing, such IFN- γ and IL-12.



Determinants and consequences of *Chlamydia trachomatis* infection for pregnant women and their offspring

Ingrid Rours, MD

Department of Medical Microbiology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands

G. Ingrid J.G. Rours obtained her medical degree in 1990, at the Faculty of Medicine, University of Amsterdam (UVA), the Netherlands. As an undergraduate student she did field research in north-east Brazil concerning breastfeeding and malnutrition in infants for the Royal Institute of Tropical Medicine (Prof. J. Kusin) in Amsterdam. She also worked at the Department of Paediatrics of the Dhaka Institute of Child Health (Prof. Akbar) in Bangladesh and participated in research on shigellosis at the International Centre for Diarrhoeal Disease Research in Dhaka.

After graduation, she worked as a medical officer, followed by a specialisation in paediatrics at the Chris Hani Baragwanath Hospital in Soweto, and in the Johannesburg General Hospital and Coronation Hospital in Johannesburg, South Africa. She obtained an MMed Paediatrics Degree in 1998 at the Witwatersrand University in Johannesburg for her research work on Chlamydia infections in mothers and their infants, in collaboration with the Department of Obstetrics and Gynaecology and the Department of Paediatrics at the Johannesburg General Hospital (Prof. A.D. Rothberg) and the Department of Sexually Transmitted Diseases in the South African Institute for Medical Research (Prof. R. Ballard). She then worked in general paediatrics at the Johannesburg General Hospital and at the child abuse clinic of the Transvaal Memorial Institute in Johannesburg.

After returning to the Netherlands, she worked in general paediatrics in the Maasland Hospital, Sittard. This was followed by a subspeciality in neonatology at the Department of Neonatology of the UMC St Radboud Hospital, qualifying in 2000 at the University of Nijmegen. Subsequently, she worked in the Paediatric Outpatient Department and ran the Child Abuse Clinic at the Sophia Children's Hospital in Rotterdam, where she did a fellowship in paediatric infectious diseases. At present she is working on her PhD thesis in collaboration with the Department of Paediatrics (Prof. R. de Groot) and Department of Medical Microbiology and Infectious Diseases (Prof. H.A. Verbrugh) at the Erasmus University in Rotterdam.



Acquired and innate immune response of the urogenital tract to *Chlamydia trachomatis*

Juliëtte A. Severin, MD

Department of Medical Microbiology and Infectious Diseases, Erasmus MC, University Medical Center, Rotterdam, and Department of Microbiology, Reinier de Graaf Gasthuis Hospital, Delft, The Netherlands

Juliëtte A. Severin began her medical training at the Faculty of Medicine, University of Leiden, the Netherlands, in 1994. As an undergraduate student she worked at the Department of Medical Microbiology, University of Leiden on the molecular epidemiology of *Acinetobacter* spp. (L. Dijkshoorn, PhD) and at the Universidade Federal de São Paulo in São Paulo, Brazil on the interaction of AIDS and tropical diseases (Prof. A.C. Pignatari, MD, PhD). After receiving her medical degree in 2001, she was a resident in internal medicine at the Reinier de Graaf Gasthuis Hospital in Delft (E. Maartense, MD, PhD). Since November 2001 she has been working as a resident in Medical Microbiology at the Erasmus MC, Rotterdam (Prof. Verbrugh, MD, PhD) and the Reinier de Graaf Gasthuis Hospital, Delft (R. Vreede, MD, PhD).

Research activities focusing on elucidating the innate immune response of the urogenital tract to *Chlamydia trachomatis* infections in order to reveal the pathogenic mechanisms and protection will be discussed. In the first project, the profile of cytokines as produced by (primary) epithelial cells on *C. trachomatis* infection has been studied in detail. Future projects will include other aspects of innate immunity.



Toll-like receptors as recognition mechanisms of innate immunity

Mihai Netea

Radboud University, Nijmegen, The Netherlands

After completing his medical education in Cluj-Napoca, Romania, Mihai Netea carried out his PhD studies on modulation of the synthesis of proinflammatory cytokines in infection models, and defended his thesis at the Radboud University, Nijmegen, the Netherlands. His interest in the field of cytokines and sepsis continued after his PhD defence, leading to important insights in the biology of proinflammatory cytokines IL-1 and IL-18. Recently, his interests have shifted towards the mechanisms of bacterial recognition, to which he made an important contribution in the field of fungal recognition by Toll-like receptors.

Innate immunity uses recognition of conserved bacterial structures called pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors as the first mechanism of activation during infection. Toll-like receptors (TLRs) are probably the most important class of pattern-recognition receptors. Recognition of PAMPs by TLRs, either alone or in heterodimerisation with other TLR or non-TLR receptors, induces signals responsible for the activation of genes important for an effective host defense, especially those of proinflammatory cytokines. In addition, TLRs expressed on specialised antigen-presenting cells, such as dendritic cells, are responsible for signals modulating the development of adaptive immune response. Recent studies also suggest that pathogenic microorganisms can modulate or interfere with the TLR-mediated pattern recognition, and use TLRs as escape mechanisms from host defense. Thus, TLR is both the major recognition mechanism of innate immunity, and a bridge linking the innate and adaptive immune responses.

Symposium co-ordinator:

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