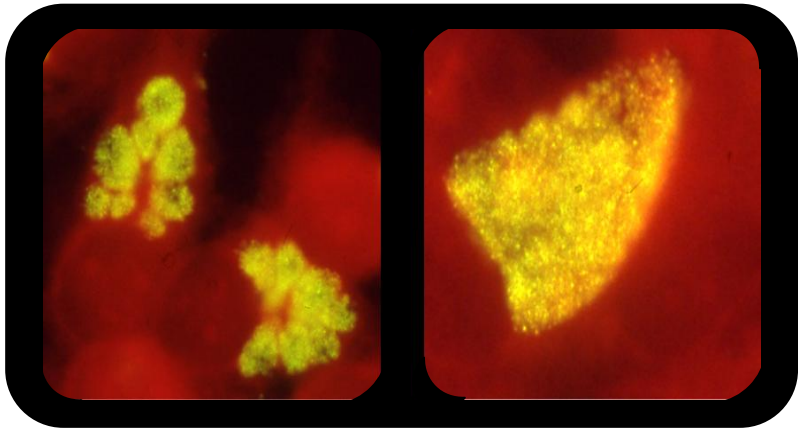


4th AACM

Fourth Annual Amsterdam

***Chlamydia* Meeting**



VU University Medical Centre
Amsterdam

13 December 2007
9.30 – 17.00

Preface

Welcome: this year we organize our symposium for the fourth time, but since we have included all *Chlamydiae* species including *C. pneumoniae* and *C. psittaci* we have renamed our symposium to the "Annual Amsterdam Chlamydia Meeting" (AACM; previously known as: "Mini-symposium *Chlamydia trachomatis* infections"). This year we have registered more participants than on previous occasions. Over eighty scientists are registered including participants from outside The Netherlands (19).

We are confident that our foreign key-note speakers: Prof. Andreas Pospischil (CH) and Prof Angelika Stary (AT), Prof David Mabey (UK), and Dr. Joe Lyons (US) with the Dutch speakers will spark the minds of both young as well as established chlamydiologists and trigger valuable discussions this day and enrich the Proceedings of this Symposium!

The Laboratory of Immunogenetics: it was established by Prof. A. Salvador Peña (Head) in 1992, and has become part of the Department of Pathology (Head Prof. Chris J.L.M. Meijer) in 2005. The Laboratory links fundamental scientific research and clinical applications (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, from 1st Jan 2008, Head of the Laboratory of Immunogenetics).

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 such as *Chlamydia trachomatis*, *C. pneumoniae* and *C. psittaci* infections in humans. Bacterial, environmental and host genetic factors determine the clinical course of the *Chlamydiae* infections and an integrated multi-disciplinary approach is used to study these factors.

Acknowledgements: We wish to express our gratitude to Prof. Sven A. Danner, Head of Internal Medicine of the VUmc Amsterdam, and Prof Cathrien A. Bruggeman, Head of Medical Microbiology of the Academic Hospital Maastricht, who actively support the immunogenetic research in infectious diseases. In addition, we would like to thank our main sponsor, Roche Diagnostics. We also like to thank the ten other sponsors and those involved in the organization of this meeting: Jolein Pleijster and Ouafae Karimi. We like to express our profound gratitude to Prous Science, in Barcelona, in particular to Dr. Joseph R. Prous, President, for the continuous support for Immunogenetics and for his contribution to make possible the publication of the Proceedings of the 4th AACM as a special supplement of the journal "Drugs of Today".



A. Salvador Peña

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Servaas A. Morré

Research Coordinator
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Sander Ouburg

Postdoc (ID)
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Programme

- 9.00 – 9.30 Registration to the symposium (Foyer)
- 9.30 – 9.40 Opening: Dr. Servaas Morr  & Prof. Salvador Pe a
- 9.40 – 11.10 Keynote speakers
- 9.40 Prof. Andreas Pospischil (CH)
From disease to etiology – historic aspects of Chlamydia related diseases in animals and humans
- 10.10 Prof. Angelika Stary (AT)
Chlamydia trachomatis diagnostics
- 10.40 Dr. Joseph Lyons (US)
Vaccine Development and Testing – The Ultimate Challenge for the Integrated Approach
- 11.10 – 11.40 **Coffee Break (Foyer)**
- 11.40 Dr. Jan van Bergen (NL) & Dr. Eline op de Coul (NL)
An internet-based Chlamydia screening project
- 12.10 Prof. David Mabey (UK)
Ocular Chlamydia trachomatis infections
- 12.40 – 13.40 **Lunch (Foyer)**
- 13.40 Prof. A. Salvador Pe a (NL)
Defects in innate immunity: From Crohn's disease to Chlamydia infections
- 14.10 Dr. Servaas A. Morr  (NL)
Chlamydia consortia
- 14.40 – 17.00 PhD students/fellows
- 14.40 *C. pneumoniae* Dr. Ellen Boelen (NL)
C. pneumoniae in the brain
- 14.55 Dr. Tryfon Vainas (NL)
C. pneumoniae and cardiovascular disease
- 15.10 – 15.50 **Coffee break**
- 15.50 *C. psittaci* Kristel Verminnen (BE)
Chlamydia psittaci zoonotic risk assessment on a Belgian turkey farm
- 16.05 Caroline Visser (NL)
Chlamydia psittaci in the Netherlands
- 16.40 *C. trachomatis* Elfi Brouwers (NL)
Chlamydia trachomatis infections in swingers
- 16.35 Arnold Catsburg (NL)
Chlamydia trachomatis infections
- 16.50 – 17.00 **Closing remarks**
- 17.00 – 18.00 **Drinks**



Andreas Pospischil, PhD

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Curriculum Vitae

Andreas Pospischil, born in Vienna, Austria in January 1948 moved with his parents to Munich in 1954 where he was raised, went to school and studied Veterinary Medicine at the University of Munich, Germany from 1968 to 1973. After a short period in veterinary large animal practice until 1975 he returned to the Veterinary Faculty at University of Munich, Germany to work on his DVM thesis in veterinary virology completed in 1977. In 1978 he joined the staff of the Institute of Veterinary Pathology at the Veterinary Faculty at University of Munich, Germany to be trained first in electron microscopy later in anatomic pathology and biopsy diagnostics. Infectious diseases of the gastrointestinal tract of animals evolved to be his main research interest leading to “Habilitation” with experimental mixed infections of calves with enterotoxigenic *E. coli* and Rota virus in 1984. This was followed by a postdoc period of 2 years at the National Animal Disease Center in Ames, Ia. USA, working on experimental infections on *Salmonella* carrier state in pigs. During these experiments the presence of *Chlamydia* in the gastrointestinal tract of pigs was recognized for the first time. Returning to Europe he joined the BASF AG at Ludwigshafen, Germany to set up an electron microscopy laboratory in the area of toxicologic pathology. In 1987 he had the chance to move to the University of Zurich, Switzerland to become head of Department Veterinary Pathology. Since that time *Chlamydia* and *Chlamydia* related diseases in animals and their zoonotic implications are his main research focus.

Abstract

A first description of the aetiology of trachoma was published in 1907 by Halberstädter and von Prowazek. During expeditions to Java to study the transmission of syphilis, they infected orang-utans with conjunctival scrapings from trachoma patients. They called them “*chlamydozoa*” comparing them to the Greek term “mantle”. Descriptions of similar diseases have been found in ancient Chinese and Egyptian manuscripts (papyrus Ebers).

The first case of psittacosis was published by J. Ritter, a Swiss physician in 1879, he described a mini-epidemic in which 3/7 patients died identifying the source of infection (pet parrots & finches), determining the incubation period and

the non-transmissibility of the disease from human to human. The term psittacosis (Greek for parrot) was first applied in 1895. In 1893, Nocard isolated a gram-negative bacterium from parrots dying of psittacosis (*Bacillus psittacosis*). This organism was subsequently found in human or avian patients and was later diagnosed as *Salmonella*. The inconsistent bacteriological findings prompted a search for a filterable virus during the pandemic of 1929-1930. Almost simultaneously, Levinthal (1930), Coles (1930) and Lillie (1930) described small, filterable bodies in infectious material called "Levinthal-Coles-Lillie (L.C.L.) bodies". Bedson first suggested the bi-phasic development cycle in 1932 after having studied tissues from inoculated mice. In 1935, Burnet and Rountree propagated "the virus" on the chorioallantoic membrane of embryonated chicken. Until the proposal of Page (1966), there were at least seven attempts to define and name what we now know as *Chlamydiae*, as the various early clinical pictures made a clear taxonomical classification difficult. In 1958, the International Code of Nomenclature of Bacteria and Viruses was applied and the genus *Chlamydia* replaced *Miyagawanella* (Brumpt 1938), the genus name "*Chlamydia*" (Jones, Rake and Stearns, 1945) had precedence over *Bedsonia* (Meyer 1953) and *Rakeia* (Levaditi, Roger and Destombes, 1964).



Angelika Stary, MD, PhD

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Curriculum vitae

A. Stary was born in Vienna and graduated in medicine from the Medical University in Vienna. She got a special education on medical virology at the Institute of Virology (Univ. Prof. Dr. Christian Kunz) and moved afterwards to the Municipal Hospital in Vienna where she was subsequently trained in Dermatovenereology, working there for several years as senior doctor. In addition, A. Stary has been associated with the Ludwig Boltzman Institute of the Dermatological Department of the University Hospital in Vienna where she was responsible for the performance of scientific studies on STI epidemiology and diagnosis and established different methods for *Chlamydia* diagnosis. In 1995 she got the university degree as „Universitätsdozent“ and is since then lecturer at the University of Vienna. In April 2004 she got the title “university professor” from the University of Vienna, signed by the president of Austria. Since 1988 she is the head of the Outpatients` Centres for Diagnosis of Infectious Venero-Dermatological Diseases in Vienna, where patients are sent to for diagnostic evaluation of sexually transmitted infections or other infectious dermatological diseases. She has been reelected as the chair of the STD Council group of the Austrian Society for Dermatology and Venereology in November 2007, a position she held already from 1999 to 2005. She has a special interest in *chlamydial* infections and diagnosis of sexually transmitted infections, and organized and chaired the Third European *Chlamydia* Meeting in 1996 in Vienna. She has published results of several multicentre comparison studies on *chlamydial* diagnosis conducted in Europe and got practical experience with all available diagnostic *chlamydia* tests. She has been invited as speaker and chair to several international STI meetings and has been elected as Board Member of the ISSTD from 1999 to 2005 where she still holds the position as an ex officio member. From 2001 until 2005 she acted as the Regional Director of the European Branch of the International Union against Sexually Transmitted Infections (IUSTI) and has organized the IUSTI-Europe Congress 2002 in Vienna with about 500 participants. At the IUSTI world conference in Bangkok in November 2005 she was nominated as the worldwide president of the IUSTI and will hold this position until 2009 after her reelection in Seattle 2007.

Abstract

Nucleic acid amplification techniques (NAATs) are the new gold standard for *Chlamydia* diagnosis in men as well as in women. The number of NAATs has increased during the last years. In addition to DNA amplification by PCR

(COBAS Amplicor) and by strand displacement amplification (ProbeTec), the amplification of *chlamydial* RNA is used in the highly sensitive and specific Transcript Mediated Amplification assay (TMA assay). This assay qualitatively detects *Chlamydia trachomatis* only (APTIMA CT) or *Chlamydia trachomatis* together with *Neisseria gonorrhoeae* (APTIMA Combo 2) in endocervical and urethral swab specimens as well as in urine samples from symptomatic and asymptomatic individuals and is already FDA approved for testing vaginal swabs. A new real-time PCR-based assay for the detection of *C. trachomatis* and *N. gonorrhoeae* has been developed by Abbott Molecular Inc., which is designed for the Abbott m2000rt Instrument system. First comparison tests show a high concordance with other NAATs with a low hand-on time. These new technologies are a challenge for *Chlamydia* detection providing a high detection rate in different specimen types for symptomatic as well as for asymptomatic individuals. In a high number of studies including all different techniques for *Chlamydia* diagnosis, it has been proven that the most important advantage of NAATs is the high sensitivity reached by DNA or RNA amplification of the *Chlamydia* target. This can be achieved not only by using cervical and urethral samples but also by testing noninvasive specimen types such as urine, vaginal, and introital sample types. The evaluation of penile swabs as a noninvasive alternative sample has shown that this type of specimens can be recommended for high sensitivity-technologies. Using other than invasive specimens is an important issue for the acceptability of opportunistic screening of asymptomatic individuals who are at risk for being infected with *C. trachomatis*, such as male and female adolescents, men having sex with men, commercial sex workers, and contact persons. The emergence of a new variant of *C. trachomatis* is a further challenge for its detection by NAATs. As a consequence of the deletion of a 377 base pair in the region targeted by Roche and Abbott assays, false negative results were generated, influencing data on the epidemiological situation in Sweden. Although the detected number of the new strain variant is still restricted almost exclusively to Sweden, Abbott has already changed the target of their test system on the cryptic plasmid in order to increase its reliability. This observation underlines the need of careful epidemiological surveillance as well as the importance of using several test systems at a national level. For the future it might be important to consider a change of the targets used for the amplification technologies since genes on the plasmid, which are often chosen as the target sequence for NAATs, are not essential for survival.



Joseph M. Lyons, PhD

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Curriculum vitae

Joseph M. Lyons, PhD, is a Support Scientist in the Department of Infectious Diseases at the City of Hope National Medical Center and the Beckman Research Institute. He attended San Diego State University, earning both Bachelor's (1969) and Master's (1972) degrees in Microbiology with a minor emphasis in Philosophy. He commenced his research career in the Department of Infectious Diseases at the University of California, San Diego, under the direct supervision of Professor Abraham I. Braude, MD, PhD. In this role, he was responsible for developing animal models of human infectious diseases and the methods needed to assess both the host and infectious agent factors that contribute to the pathology and immunology of infection. He held this position until 1983, when he accepted the position of Supervisor in the Department of Infectious Diseases Research Laboratory of James I. Ito, MD, at the City of Hope. In this capacity, he continues to develop animal models of human diseases with current efforts focused on *C. trachomatis* female genital tract infection and pulmonary aspergillosis in the immunosuppressed host. The aims of this research are to develop more effective diagnostic and therapeutic methods to prevent and treat infections with these agents, including traditional antibiotic approaches as well as the use of immune modulators and active immunization to provide protection against colonization and early events in the infection process. In 2004, Joseph earned his PhD from Vrije Universiteit Medical Centre in the Laboratory of Immunogenetics by successfully defending a thesis entitled: "An Integrated Approach to the Study of *Chlamydia trachomatis*" Infection of the Female Genital Tract. Since then, he and an increasing number of collaborators continue to promote and apply the integrated approach to: 1) identify and test candidate genes that are associated with susceptibility to and outcome of *C. trachomatis* infection; 2) promote the use of human urogenital serovars in animal models of female genital tract infection in order to assure the translational value of these efforts; and 3) to improve existing animal models of female genital tract infection to better mimic the pathogenesis of human infection with this agent, thus improving the translation value of research conducted using these models.

Abstract

Since its conception a decade ago, the integrated approach to the study of *Chlamydia trachomatis* (Ct) infection of the female genital tract has been successful in its initial applications: 1) of identifying and testing candidate genes that are associated with susceptibility to and outcome of infection; and 2) in promoting the use of human urogenital serovars in animal models in order to assure the translational value of these efforts. However, with a number of Ct vaccine candidates ready for pre-clinical safety and efficacy testing, the ultimate challenge for the integrated approach will be to suggest and, if necessary, develop the appropriate animal models for use in this effort. At a minimum, these models must mimic the essential features of transmission and disease progression that contribute to the severe outcomes associated with upper genital tract infection with this agent, in order to eliminate the risk of inadvertently promoting these sequelae following vaccination. To date, animal models whether mouse, pig or non-human primate have been based on the generally accepted premise that upper genital tract infection, when it occurs, is a late event in a linear retrograde process that originates with a cervical infection. As a result, the models are static with respect to the issue of transmission of Ct between partners during intercourse, with the direct installation of elementary bodies into the vagina being considered an adequate representation of this event. However, what this simple paradigm overlooks are many features of reproductive anatomy, physiology, and immunology that could influence the spread of Ct within the female genital tract. In fact, a review of the literature strongly suggests that many natural processes associated with human reproductive biology are likely to have a dynamic influence on the distribution and spread of Ct within the female genital tract both coincidental to intercourse and during a localized cervical infection. This presentation will describe some of the likely effects that the menstrual cycle and coitus related phenomena have on the susceptibility, course and outcome of female genital tract infection with Ct. Although the new paradigm of pathogenesis that emerges from this more comprehensive and integrated understanding raises concerns about the adequacy of existing animal models; it also suggests ways to modify these models in ways that better mimic the very real complexities of human infection, and therefore serve as adequate models in which to test the safety and efficacy of vaccine candidates against *Chlamydia trachomatis* (Ct) infection of the female genital tract.



Jan van Bergen, MD, PhD

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Curriculum vitae

Jan van Bergen was born in Landgraaf (the Netherlands) and studied medicine at the Radboud University Nijmegen, graduated as a master of Public Health at the London School of Hygiene and Tropical medicine and did his PhD at the University of Amsterdam. He worked as a district medical officer and consultant in Africa and Latin-America. He was involved in several studies on STI, particularly on *Chlamydia trachomatis* in the Netherlands. He is program manager at Soa Aids Nederland and involved in quality assurance, research and educational programmes on STI. He is editor of the Dutch STI journal (SOAIDS Magazine) and coordinator of the *Chlamydia* Screening Implementation Project. He still works part-time as a general practitioner in a multicultural and low-income neighbourhood in Amsterdam South-East.

Abstract

The *Chlamydia* Screening Implementation (CSI) Project is a large-scale intervention, piloting sustainable, selective, systematic and internet-based *Chlamydia* screening in the Netherlands. Between 2008 and 2010 all 315.000 sexually active 16-29yr citizens of Amsterdam and Rotterdam are invited two times in a three year period to participate in the screening; in the lower prevalence area S-Limburg only if they match a certain risk-profile. Eligible persons are retrieved from the population register and receive a letter either from the Public Health Service (PHS) or from their GP. Via the internet site www.chlamydiatest.nl they will be able to get information, do pre-test interviews online, order sampling materials, view instruction video's, get test results and download treatment guidelines for their health provider. Also partner treatment and counselling will be included at the website. The PHS implements the screening; STI AIDS Netherlands coordinates the project.

The large scale design of this programme makes it possible to offer screening to the total eligible population in the region. It provides not only individual benefits (early detection and treatment to prevent complications) but also enables studying the impact of screening on population prevalence.



Eline op de Coul, PhD

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Curriculum vitae

Eline Op de Coul was born in Veldhoven, the Netherlands (1969). After she graduated at the Agriculture University in Wageningen, she worked on the molecular epidemiology of HIV-1 at the Amsterdam Public Health Service (GGD). After she finished her PhD thesis in 2001, she started working as an epidemiologist in the field of HIV/STI surveillance at the Centre for Infectious Disease Control at the National Institute for Public Health and the Environment (RIVM).

Abstract

Objectives: In 2007, a three-year screening intervention for *Chlamydia trachomatis* (Ct) will start in Amsterdam, Rotterdam and South-Limburg. In these areas, the sexually active population will be invited in two screening rounds to participate in an internet-based screening by using home-sampling kits. This project aims to evaluate a) the feasibility, b) effectiveness and c) cost-effectiveness of the *Chlamydia* Screening Implementation (CSI). In particular, we will investigate the feasibility of internet-based screening and differences between a general and a selective screening approach for populations in different areas.

Methods/results: (a) In two areas with a high population density (Amsterdam/Rotterdam) systematic screening of all 16-29 year olds will be conducted and in Limburg (lower population density) participation in CSI will be based on a self-administered risk-profile. In all locations, respondents will be recruited by mail and invited for Ct-screening by internet. In-depth non-responder studies will be conducted to evaluate determinants of participating in internet-based screening.

(b) To evaluate the effects of screening on the population prevalence, a phased implementation of screening for randomly selected groups will be implemented. The phased implementation (stepped wedge design) will allow analysis of time trends in the participation rate in screening in those groups who are offered an extra third screening round. It will offer an opportunity for obtaining a pre-screening prevalence estimate that can be compared with earlier population-based prevalence estimates and with Ct-positivity rates. Furthermore, we



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Curriculum Vitae

David Mabey is a physician specialising in Infectious and Tropical Diseases. After training in the UK, he went to work at the Medical Research Council unit in The Gambia, West Africa in 1978, and was in charge of clinical services there from 1982-86. He joined the London School of Hygiene & Tropical Medicine as a Senior Lecturer in the Department of Clinical Sciences in 1986, and was made Professor of Communicable Diseases in 1994. He is an Honorary Consultant Physician at the Hospital for Tropical Diseases in London. He became interested in trachoma, caused by ocular infection with *Chlamydia trachomatis*, and in genital *C. trachomatis* infection, while working in the Gambia. Since the early 1980s he has been involved in research on both trachoma and sexually transmitted infections, with many international collaborators. Most of the field work has been done in The Gambia and Tanzania, and laboratory work on the pathogenesis and immunology of trachoma has been done in London and The Gambia.

Abstract

C. trachomatis remains the leading infectious cause of blindness. The World Health Organisation (WHO) estimates that some 80 million people are currently suffering from active trachoma, caused by serotypes A-C of *C. trachomatis*, and about 8 million are suffering from potentially blinding sequelae of the disease. 1.3 million are blind, representing just under 4% of the total global burden of blindness. Trachoma disappeared from Europe and North America in the 20th century as living standards improved, and is now mainly a disease of the rural poor in Africa and Asia. It causes blindness through a scarring process affecting mainly the conjunctival surface of the upper eyelid which develops after repeated infections over many years, causing the lashes to turn inwards and rub against the cornea. Ocular *C. trachomatis* infection can be cured with a single dose of azithromycin, and mass treatment of affected communities can eliminate infection. Mass treatment programmes and improved living standards have reduced the prevalence of trachoma in many countries in recent years, leading



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Curriculum vitae

General: Amado Salvador Peña is Professor of Gastrointestinal Immunology at the VU University VU Medical Center (VUmc) in Amsterdam, the Netherlands since 1991. He is Head of the Laboratory of Immunogenetics in the VUmc since 1992, first under the umbrella of the Dept. of Gastroenterology and since the 1st February 2005 in the Dept. of Pathology in order to cover immunogenetic research in other disciplines with patients suffering from chronic inflammation. He is a senior staff member of the Dept. of Gastroenterology. His main interest in research is Translational research in Immunogenetics of chronic inflammatory and autoimmune diseases. Dr. Peña obtained the Educational Council for Foreign Medical Graduates Certificate (ECFMG) in 1966 and obtained a PhD degree (D. Phil. Oxon) in the University of Oxford, UK in 1971. He was trained in gastroenterology in Oxford, England, with Dr. Sidney C. Truelove (1966-1971) and in Leiden, the Netherlands with Prof. A.J. Charles Haex. He worked in an academic position in the University of Leiden, Leiden, The Netherlands (1971-1991). He trained in immunology in Bethesda, U.S. at the National Institutes of Health with Dr. W. Strober (1975-1976). He is a registered Immunologist and a registered Gastroenterologist in the Netherlands and in Spain. He is a regular reviewer for several journals in gastroenterology, immunology and genetics.

Professional Memberships: He is a member of several societies of gastroenterology and immunology, including the American and Dutch Societies of Gastroenterology. He is an Honorary Member of the Spanish Society of Gastroenterology, the "Asociación Castellana de Aparato Digestivo (ACAD)" as well as the Hungarian Society of Gastroenterology (Honorary Membership). He is Medical Patron of the European Federation of Crohn and Colitis Associations (EFCCA). In 1998 he has been elected "Fellow of the Royal College of Physicians" (London, U.K.).

Honors: He was made a "Knight of the Order of the Netherlands Lion" in September, 2000 on the merits of his dedication in celiac disease research and patient care. He received the "Joanna and David B. Sachar", International Award and Visiting Professorship in Inflammatory Bowel Disease at the Mount Sinai, New York, USA in 2003. He has been appointed as "visiting professor" in the University of Alcalá de Henares, Spain January - May 2006. On the first of May 2006 he was elected as Fellow of the American Gastroenterological Association (AGAF). On the 13th of October 2007 he was elected Professor Honoris Causa of the Catholic University of Cordoba, Argentina.

Recent Extramural Funding: European Gastric Cancer Research (EURGAST) FP5 European Union 2001-2004; INFOBIOMED, FP6 European Union 2003-2006. IBDChip FP6 European Union 2006-2009, EpiGenChlamydia FP6 2007 - 2009.

Publications and Thesis Director: Over 250 publications in PUBMED and director of 16 PhD theses

Abstract

Chronic inflammatory diseases called Th1-Th17 diseases in mammals and in invertebrates such as corals, are influenced by a symbiotic relationship with a metabolically active bacterial population. Host genetic susceptibility in the form of a defective mucosal barrier function and/or abnormal bacterial killing of a defective autophagic process can lead to enhanced exposure to luminal bacteria and defective immunoregulation to lack of appropriate immunosuppression. Some of these diseases have been classified as “barrier diseases” and result from the lack of integration of symbiotic microorganisms, pathogens, and the mucosal immune system.

Learning from coral disease: Scientists working in the field of coral microbiology have shown the complex coral structure supports an enormous diversity of (micro) organisms. Stress factors that contribute to coral disease are climate change, water pollution and over-fishing. Corals contain a diverse microbial population in their mucus and tissues. It appears that coral-associated microbial populations are very susceptible to rapid changes in the environment. Although they have no adaptive immune system, corals can develop resistance to pathogens and be as models for understanding the innate immune response.

Learning from Crohn's disease: Modern genotyping techniques have made it possible to perform genetic studies in large series of patients. Mutations and gene polymorphisms at five different levels appear to be involved in the susceptibility to suffer from Crohn's disease: 1) Mutations that control the integrity of the intestinal epithelium and permeability in Crohn's disease; 2) Mutations affecting the mucosal transport of different ions, cations and drugs. In Crohn's disease mutations have been reported in sodium dependent-organic cationic transporters SLC22A4 (OCTN1) and SLC22A5 (OCTN2); 3) Mutations involved in the sensing of the microbial flora: TLR4 and CARD15. In Europe circa 15% - 40% of patients with Crohn's disease have mutations in the *CARD15* gene. Patients with Crohn's disease of the colon have less beta defensins as a result of lesser “copy number variation” (CNV) polymorphism in the beta-defensin 2 gene (HBD-2). 4) Mutation in genes that regulate autophagy: “autophagy-related 16-like 1”(ATG16L1) and the ‘immunity-related GTPase family, M’ (IRGM) and 5) Mutations in genes involved in the regulation of the acquired immunity such as HLA and the interleukin 23 receptor (IL23R). These complex genetic regulation affecting the barrier of our organism may be modified by altering the microflora in a much shorter time than by the classical Darwinian mutation and selection. The lessons that we can draw from these diseases and the approaches followed to define the basic defects may serve as a lead to understand the pathology induced by *Chlamydiae* and suggest new areas of therapeutic targeting.



Servaas A. Morré, PhD

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Curriculum vitae

Servaas A. Morré, PhD, who is working on *Chlamydia trachomatis* for 12 years, graduated at the VU University, the Netherlands, in Biochemistry and Molecular Biology in 1994. He worked on plat genetics at The Zaadunie (NL), on Drosophila genetics in Potugal (Universidade Do Porto, Laboratório de Genética Molecular), and on the on the processing of ribosomal RNAs in *Saccharomyces cerevisiae* (VU University, NL). His PhD thesis performed in Department of Pathology (VU University) was on the epidemiology, diagnostics and immunopathogenesis of human urogenital *Chlamydia trachomatis* infections. As a postdoc, he extended *Chlamydial* research in the Department of Infectious Diseases, The City of Hope Medical Center, California, USA (Dr. Jim Ito and Dr. Joseph Lyons). The 1st of November 2001, he joined the Laboratory of Immunogenetics, VUmc. His research is focused on the immunogenetics of infectious diseases including HPV, sepsis, and periodontitis, but with still special attention to *Chlamydia trachomatis*. Together with Prof. Salvador Peña and Dr. Sander Ouburg, he organizes for the 4th time the "Annual Amsterdam Chlamydia Meeting" in Dec 2007. In July 2005 he was a member on the ISSTDR Scientific Committee and organized amongst others the workshop "Immunogenetics of *Chlamydia trachomatis* Infections". He is organizing Committee member of 6th Meeting of the European Society for *Chlamydia* Research, University of Aarhus, Aarhus, Denmark, July 1-4, 2008. He is coordinator of the International *Chlamydial* ICTI consortium and since 2007 he is Scientific Consortium Director, of the European Framework Programme 6 (FP6) "Contribution of molecular epidemiology and host-pathogen genomics to understand *Chlamydia trachomatis* disease (Acronym: EpiGenChlamydia). From the first of January 2008 he will be head of the Laboratory of Immunogenetics.

Abstract

There are clear differences in the clinical course of *Chlamydiae* infections which can be explained by the interaction between the host (host factors) and the pathogen (virulence factors), an interaction which will be influenced by environmental factors like co-infections. The critical evaluation of host, bacterial, environmental, clinical and epidemiological data and the results of experimental



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Curriculum vitae

Ellen Boelen was born in Genk, Belgium (1980) and graduated in Biology from the Catholic University Leuven in 2002. Thereafter, she moved to the Maastricht University where she started her PhD project, focusing on the effect of *Chlamydia pneumoniae* infection on brain cells, at the departments of Medical Microbiology and Cellular Neuroscience. Since July 2007, she is working as a postdoctoral fellow at the department of Medical Microbiology (Maastricht University), further exploring the role of infections and inflammation in neurodegenerative disorders.

Abstract

An increasing amount of basic and clinical evidence indicates that infections with subsequent inflammation and glial activation could be an important feature in the pathogenesis of neurodegenerative diseases like Alzheimer's disease (AD). Apart from direct effects of pathogens on neuronal cells, it can be hypothesized that inflammatory molecular mechanisms, like the production of pro-inflammatory mediators by resident glial cells, may result in neurotoxicity, neuronal death, or neuronal dysfunction.

Therefore, we first investigated the direct effects of a *Chlamydia pneumoniae* (Cpn) infection, a pathogen which has recently been associated with AD, on various brain cell lines: a murine microglial (MMC), an astrocyte (MAC) and a neuronal (NB) cell line. Secondly, the inflammatory response in MMC and MAC cells was examined following Cpn infection. We also determined whether these inflammatory responses were sufficient to cause neuronal cell death in vitro. Finally, we investigated whether Cpn infection resulted in the aggregation of amyloid beta, one of the hallmarks of AD, in the brain of normal Balb/c mice.

(frequent concurrent partners) they are able to accelerate the STD epidemic in the population. Efforts for STD-prevention and enhanced active case finding are needed just like is the case for every common risk group.



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Curriculum vitae

Tryfon Vainas read medicine at the medical faculty of Maastricht University. In 1998 he followed an elective clinical and research attachment for 3 months at the department of vascular surgery, Leicester Royal Infirmary, Leicester, UK. After graduation the author accepted a position as PhD-student at the department of Surgery, Maastricht University Hospital and Cardiovascular Research Institute of Maastricht. In that period he worked under supervision of Professor CA Bruggeman trying to elucidate the role of *Chlamydia pneumoniae* in the development of atherosclerotic disease. This work culminated in the defense of his thesis entitled 'On the inflammatory and infectious aspects of atherosclerosis'. In May 2003 he started his training in General Surgery at Maastricht University Hospital and is currently completing his surgical training at the department of Surgery of Catharina Ziekenhuis Eindhoven. Tryfon has switched his scientific focus towards the identification of biomarkers for the improved pre-operative selection of patients with aneurismal or obstructive atherosclerotic disease.

Abstract

Following Saikku and colleagues, who first described an association between *Chlamydia pneumoniae* (Cpn) antibodies and coronary artery disease, a large number of sero-epidemiological studies exploring the relation between Cpn serology and atherosclerotic disease with conflicting results has been published. Despite the large numbers of sero-epidemiological trials suggesting an association between Cpn and atherosclerosis, no correlation has been found between the presence of Cpn DNA or proteins in vascular tissue and atherosclerotic plaque histology. Furthermore, no correlation between Cpn antibodies and presence of Cpn DNA and/or proteins in atherosclerotic vascular tissue has been established.

The fact that Cpn serology is associated with clinical manifestations of atherosclerotic disease whereas any sign of infection, whether serologic

(antibodies) or histologic (vascular presence of DNA/proteins), does not seem to be related to atherosclerotic plaque histology may suggest that in humans, Cpn does not stimulate advanced atherosclerotic lesion progression via in situ processes but rather through systemic effects of (non)vascular Cpn infection and/or by the host response to Cpn infection. We have shown in this respect that Cpn serology is associated with hypercoagulability but not with histological plaque instability in patients with carotid artery disease.

The interaction between individuals and the microbiological environment is more complex than traditionally anticipated, especially in the case of chronic degenerative diseases such as atherosclerosis. Taking into account the high incidence of Cpn antibodies in the general population, it seems likely that genetic factors may affect individual susceptibility for the pro-atherogenic effects of infections and, thus, determine the outcome and severity of chronic degenerative inflammatory diseases. We have demonstrated that among patients with peripheral arterial disease the carrier trait *TLR4* G-allele & *CD14* TT-genotype, rather than individual polymorphisms, is associated with extent of atherosclerotic disease.

The sero-epidemiological and experimental data suggesting a possible association between Cpn infection and atherosclerosis triggered the interest of (cardio)vascular clinicians for the role of anti-*chlamydial* antibiotics as a new treatment modality for patients with atherosclerotic vascular disease. A plethora of data has been produced showing that (antichlamydial) antibiotics offer no cardiovascular benefit in patients with coronary artery disease. Similarly, we have shown that a short term antibiotic prophylactic treatment did not offer any benefits in terms of clinical events or (changes in) ankle-brachial pressure index in patients with peripheral arterial disease.

In light of the strong evidence in favour of involvement of Cpn in the development of atherosclerosis, the negative results of the clinical trials may be related to the inability to select patients with clinically relevant (vascular) Cpn infection, to insufficient study medication, or to wrong timing of antibiotic treatment during the course of atherosclerosis development.



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Curriculum vitae

Kristel Verminnen was born on February 6th 1980 in Rumst (Belgium). In 1998 she finished high school and in the same year she started her studies at Ghent University where she obtained in 2003 the diploma of Bio-Engineer option cell and gene biotechnology with thesis title: "*Chlamydophila psittaci* DNA vaccination and recombinant MOMP vaccination in turkeys". From 2003 on, she is PhD student at Ghent University in the laboratory of Immunology and Animal Biotechnology. Under the leadership of her promotor Prof. dr. Daisy Vanrompay, she does research about *Chlamydophila psittaci* zoonosis and development of DNA formulations for mucosal immunization of turkeys. Kristel Verminnen is author and co-author of different scientific publications.

Abstract

Reports on zoonotic transmission of *Chlamydophila psittaci*, originating from poultry are incidentally published. During recent studies in European turkeys we isolated *Chlamydophila psittaci* genotypes A, B, D, E, F and E/B, all considered potentially dangerous for humans. This encouraged us to analyze the zoonotic risk on a Belgian turkey farm, from production onset until slaughter using a *Chlamydophila psittaci* diagnostic platform. Twenty individually marked hens as well as the farmer and 2 scientists were monitored medically. Bioaerosol monitoring, serology, isolation and nested PCR demonstrated chlamydiosis on the farm leading to symptomatic psittacosis in all 3 persons involved. Outer membrane protein A (ompA) sequencing confirmed the zoonotic transmission of *Chlamydophila psittaci* genotype A. Strangely, two different antibody MIF tests remained negative in all infected persons. Results demonstrate the value of the currently used diagnostic platform in demonstrating *Cp. psittaci* infections in both birds and humans, but raise questions on the MIF test for diagnosing human psittacosis.



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Curriculum vitae

Caroline Visser, MD, PhD, is a clinical microbiologist working at the department of Medical Microbiology in the Academic Medical Centre in Amsterdam. In 1997 she defended her PhD thesis on the role of mesothelial cells and macrophages in peritonitis in peritoneal dialysis patients (Vrije University Amsterdam). The following 4 years she was trained as a clinical microbiologist at the department of Medical Microbiology of the LUMC in Leiden. From 2001 to 2004 she worked as an all-round clinical microbiologist in the Reinier de Graaf Gasthuis in Delft. From 2004 till now she's been working in the AMC. More or less by coincidence she got involved in the field of *Chlamydophila psittaci* research when one of the trainees, Edou Heddema, had the opportunity to investigate an outbreak of psittacosis among veterinarian students. This was the start of further studies on psittacosis in general and genotyping in particular. Edou Heddema defended his thesis on these studies in March 2007.

Since then a collaboration was initiated to optimize the genotyping of *Chlamydophila psittaci* strain.

Abstract

Psittacosis is a zoonosis caused by *Chlamydophila psittaci*. Until recently diagnosis of this sometimes severe disease was based on serology. Therefore, a real-time PCR was developed to detect the bacterium in various clinical materials. This technique proved its worth during an outbreak of psittacosis in veterinarian students who contracted the disease while working with parrots and pigeons. To distinguish which birds were responsible a PCR was developed to genotype the bacterium in direct clinical material. Furthermore the infection rate of feral pigeons in Amsterdam was studied to determine the infection risk in the general population. All this work has led to better diagnostic tools and therefore a better understanding of the clinical syndrome and the epidemiology of psittacosis.



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Curriculum vitae

Elfi E.H.G. Brouwers is a PhD-student on the public health aspects on *Chlamydia trachomatis* at the public health Service South Limburg, department of Infectious Diseases. She is master of sciences in health-sciences and currently working as a junior projectleader on the Dutch *Chlamydia* Screening Implementation. The CSI project is a three-year large scale *Chlamydia trachomatis* (Ct) Screening project among 16-29 year-olds in two areas with a high population density (Amsterdam and Rotterdam) and the eastern part of South-Limburg (lower population density) in the Netherlands. The screening implementation, that is internet-based by using home sampling kits, is repeated in two consecutive periods of one year.

The project aims to evaluate a) feasibility, b) effectiveness, and c) cost-effectiveness

Moreover, she is involved in a point-of-care study for *Chlamydia trachomatis* antigen detection and in a regional study to assess prevalence and risk factors of *Chlamydia trachomatis* and assess efficacy of a self triage card among vocational school students.

Abstract

We wanted to estimate the prevalence of STD in swingers in the Netherlands. Swingers are heterosexual couples who have sex with other heterosexual couples (different concurrent sexual partners). Couples date via internet, via partner exchange clubs or they invite other couples at their home. Part of the men and women have bisexual contacts.

Urogenital samples were tested for the presence of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC) by NAAT. Serum samples were tested for the following infection markers: antiHIV, HbsAg and, anti-HBc, HIV and TPPA Swingers are an unrecognized and underreported risk group while they show high STD risk behaviour and high prevalence of CT and GC compared to well-known risk groups like adolescents, CSW and MSM. With their risk behaviour



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Curriculum vitae

Arnold Catsburg was born in 1977 and is working at the Department of Medical Microbiology and Infection Prevention, VU University Medical Center, Amsterdam since 2001. His internship was on Real-Time PCR (TaqMan) for qualification and quantification of *Bifidobacterium*, *Propionibacterium* and *Streptococcus* in mucosal biopsies from patients with Inflammatory Bowel disease and controls. After his internship he continued to work in the field of molecular microbiology. He developed diagnostic and typing strategies for amongst others *M. tuberculosis*, *Mycoplasma* and *Chlamydia*. He was also involved in the MOVB project, a study by the Dutch government after an airplane crash in "De Bijlmer", Amsterdam. Recently he has, besides his current task, started to work on his PhD thesis with a major focus on *Chlamydia trachomatis* infection.

Abstract

His presentation will focus on bacterial and host studies on *Chlamydia trachomatis*. In the part on bacterial studies the development of a Real Time PCR assay for the detection of the Swedish variant *C. trachomatis* will be discussed. In the second part of his presentation host studies will be discussed with a major focus on Mannose Binding Lectin (MBL). MBL is a lectin involved in the innate immune response. There are 6 different mutations described responsible for lower efficiency of this molecule. The development of an assay to detect all six mutations, and the role in the *Chlamydia trachomatis* susceptibility will be discussed.



Symposium Organizer Servaas A. Morré

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Curriculum vitae

Servaas A. Morré, PhD, who is working on *Chlamydia trachomatis* for almost 12 years, graduated at the VU University, the Netherlands, in Biochemistry and Molecular Biology in 1994. He worked at The Zaadunie, Department of Cell biology on plant genetics: polyploidization of *Brassica oleracea* (Cauliflower) during cell culture (M. Tan, PhD) and at the Department of Biochemistry and Molecular Biology VU on processing of ribosomal RNAs in *Saccharomyces cerevisiae* (Prof. H. Raué, PhD, R. van Nues PhD).

As an Erasmus Fellow he studied at the Universidade Do Porto, Laboratório de Genética Molecular, Portugal, on POLO: an essential kinase for mitosis in *Drosophila melanogaster* (Prof. C. Sunkel, PhD). His PhD thesis performed in Department of Pathology (VU University) was on the epidemiology, diagnostics and immunopathogenesis of human urogenital *Chlamydia trachomatis* infections. As a postdoc, the Van Coeverden Adriani Foundation made it possible to extended *Chlamydial* research in the Department of Infectious Diseases, The City of Hope Medical Center, California, USA, in collaboration with Dr. Jim Ito and Dr. Joseph Lyons, specialists in murine modeling. From the 1st of November 2001, he joined the Laboratory of Immunogenetics, VUmc. His research is focused on the immunogenetics of infectious diseases with still special attention to *Chlamydia trachomatis*, and also HIV (Prof. S. Danner & Dr. M. Agtmael)), periodontitis (collaboration with ACTA) and sepsis (collaboration AZM). Studies on Human Papilloma Virus (HPV) infections have been initiated together with Prof. C.J.L.M. Meijer in 2006. He organized together with Prof. Salvador Peña in December 2004 the "First Mini-symposium *Chlamydia trachomatis* Infections" and in December 2007 we organize already our fourth "Annual Dutch *Chlamydia* Meeting". In July 2005 at the 16th Biennial meeting of the International Society for Sexually Transmitted Diseases Research (ISSTD) he was a member on the Scientific Committee and organized amongst others the workshop "Immunogenetics of *Chlamydia trachomatis* Infections", with Prof. David Mabey (London, UK, Trachoma research). He is organizing Committee member of 6th Meeting of the European Society for *Chlamydia* Research, University of Aarhus, Aarhus, Denmark, July 1-4, 2008 and at this meeting also session organizer:

"Immunogenetics of *Chlamydia trachomatis* infections". Together with Tjaco Ossewaarde and Yvonne Pannekoek, he coordinates the Dutch *Chlamydia* Working Party. He is coordinator of the International *Chlamydial* consortium ICTI (Integrated approach on *Chlamydia trachomatis* Infections) and since 2007 he is Scientific Consortium Director, of the European Framework Programme 6 (FP6) grant (LIFESCIHEALTH FP6, Co-ordination Actions (CA)) in functional genomics research entitled: "Contribution of molecular epidemiology and host-pathogen genomics to understand *Chlamydia trachomatis* disease (Acronym: EpiGenChlamydia)" with 20 European, African and US groups. This consortium had his first meeting a day ago on 12 December 2007. As a partner he is participating in two other European FP6 programmes. Finally, together with Prof. Paul Savelkoul (Medical Microbiology and Infection Control, VUmc), he is co-founder and co-director of a VUmc spin-off company called Microbiome Ltd (Sept 2005), a company specializing in Microbiological diagnostics, typing and laboratory consultancy. From the first of January 2008 he will be head of the Laboratory of Immunogenetics.

An overview of PhD work in The Netherlands on *Chlamydia trachomatis*

Table I: *PhD theses in the Netherlands*

2007 Denise A.M. Perquin	University of Leiden / Medical Center Haaglanden
2006 Sander Ouburg	VU University Amsterdam
2006 Joke Spaargaren*	University of Amsterdam and VU University Amsterdam
2006 Tanja P. Gijsen*	Maastricht University
2006 Hannelore M. Götz*	Erasmus University Rotterdam
2005 Jan E.A.M. van Bergen*	University of Amsterdam
2004 Joseph M. Lyons*	City of Hope Medical Center, CA, USA, and VU University Amsterdam
2003 Laura S. Murillo	VU University Amsterdam
2002 Monica Molano Luque	VU University Amsterdam
2001 Irene G.M. van Valkengoed*	VU University Amsterdam
1999 Servaas A. Morré*	VU University Amsterdam
1999 Johannes W. Trum	University of Amsterdam
1999 Bernardus W.J. Mol	University of Amsterdam
1998 Yvonne T.H.P. van Duijnhoven	University of Amsterdam
1997 Marita J.W. van de Laar	University of Amsterdam
1995 Jar Lan*	VU University Amsterdam
1994 Josina van Ulsen	Erasmus University Rotterdam
1994 Jacobus M. Ossewaarde*	University of Utrecht
1993 Hans J.H. Theunissen*	Erasmus University Rotterdam
1992 Johannes T.M. van der Schoot*	University of Amsterdam
1992 Arent J.P. Boeke and Janny H. Dekker	VU University Amsterdam
1992 André H. van der Willigen	Erasmus University Rotterdam
1991 Eric C.J. Claas	VU University Amsterdam
1990 Gijsbertus J.H.M. Ruijs*	Rijksuniversiteit Groningen
1989 Henk J. Vonsée	Rijksuniversiteit Limburg
1987 Kie H. Tjiam*	Erasmus University Rotterdam

**Chlamydia trachomatis* is the major focus in the thesis.

Table II: *Current PhD fellows working (partially) on Chlamydia trachomatis.*

Janneke E. den Hartog	Maastricht University
Steven M. Westenberg	AMC, University of Amsterdam
Ingrid Rours	Erasmus University Rotterdam
Caroline J. Bax	University of Leiden / Medical Center Haaglanden
Arnold Catsburg	VU University Amsterdam
Vitaly Smelov	St. Petersburg State Medical University, Russia and VU University Amsterdam
Koen Quint	VU University Amsterdam
Laura van Dommelen	Maastricht University
Elfi E.H.G. Brouwers	Maastricht University
Esmée Lanjouw	Erasmus University Rotterdam

Attendants:

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4th Annual Amsterdam Chlamydia Meeting

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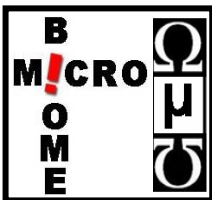


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Oxoid B.V. provides a wide range of Chlamydia serology kits including the IDEIA (PCE) Chlamydia and the IMAGEN Chlamydia kit.

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Goffin Meyvis Analytical & Medical
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Goffin Meyvis specializes in vitro diagnostics (IVD): Molecular Diagnostics RT & RT-Q-PCR, analysis, and point-of-care to large scale automation including software applications

José Tijsen
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HandiLab-C is a point of care and OTC rapid, non amplification self test for the detection of C. trachomatis.

Future STI / *Chlamydia* Meetings

- 6th German *Chlamydia* Workshop
February 27th – 29th, 2008, Ulm, Germany
<http://131.130.66.201/dcw/>
- 15th IUSTI – Asia-Pacific Congress
February 3rd – 6th, 2008, Dubai, UAE
www.iusti.ae
- 6th European *Chlamydia trachomatis* meeting
July 1st – 4th, 2008, Aarhus, Denmark
<http://www.chlamydia.au.dk>
- 18th ISSTD / BASHH Meeting
June 28th – July 1st, 2009, London, UK
www.isstdr.org
- IUSTI – AFRICA Regional Meeting
Early December 2009, Cape Town, South Africa
www.iusti.org/africameeting.html
- 5th Annual Amsterdam *Chlamydia* Meeting
December 2008, Amsterdam The Netherlands
- 12th International Symposium on Human *Chlamydia* Infections
2010

Announcement



5th

Annual Amsterdam *Chlamydia* Meeting

Mid December 2008



*Organiser: Servaas Morré
Laboratory of Immunogenetics,
Dept. of Pathology, VUmc, Amsterdam*

We hope to welcome you all in 2008

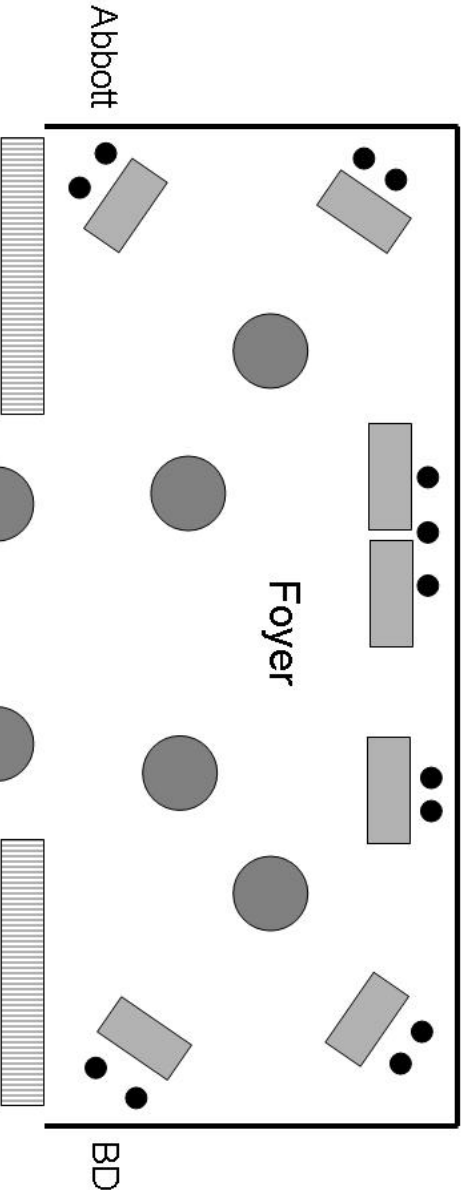
Floor plan

Greiner Bio-One

Roche Diagnostics

Registration desk

Clindia



Legend



Lunchtable



Table



Stand



Technical assistance:

Ouafae Karimi, MSc, PhD-fellow
Laboratory of Immunogenetics, Dept. of Pathology
VUmc, Amsterdam



Technical assistance:

Ing. Jolein Pleijster
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VUmc, Amsterdam



Assistant symposium coordinator

Lay out & design, odd jobs:

Sander Ouburg, PhD
Laboratory of Immunogenetics, Dept. of Pathology
VUmc, Amsterdam

This symposium is accredited with 5 points from the Dutch Society for Medical Microbiology (NVMM)

This symposium is accredited with 5 points from the Dutch Society for Dermatology and Venerology (NVDV)



VU university medical center

