## ESCMID News

### ESCMID

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Dear Colleagues

The ESCMID continuously expands its repertoire of scientific and educational activities in the infection disciplines. This year, the ESCMID School will be organised in Santander, Spain and a variety of post-graduate courses will be held across Europe to provide updates on hot clinical and laboratory topics. This issue will find many of you attending the 16th ECCMID in Nice, which once again promises to offer the best opportunity to present and discuss the latest scientific findings in the infection field on this side of the Atlantic. Andreas Voss has led the ECCMID Programme Committee with his characteristic enthusiasm to prepare an outstanding and well-balanced scientific programme. In addition, the popular Educational Workshops will provide close interaction with leading experts from ESCMID Study Groups. I am confident that this 16th edition will build upon the success of previous ECCMIDs staged under the leadership of Patrick Francioli, revisited in this issue from an historical perspective.

Beyond scientific meetings and educational courses, exchange visits between research institutions are also very helpful for young scientists in developing their career and building international collaborations. This is testified in this issue by two ESCMID grant recipients who report on their training visits to foreign laboratories. We wish to further promote these research training visits and are considering new ways to facilitate similar exchanges for young physicians during their clinical and laboratory training.

A rewarding responsibility of the Past President is to chair the Awards Committee. I take this opportunity to thank my colleagues Catherine Cordonnier, Jordi Vila and Johan Van Eldere who sat on this Committee for their support in selecting and recommending this year’s awardees. The number and quality of the applications received made our task difficult. It will be a pleasure to welcome and congratulate the awardees of the ESCMID Award for Excellence, Young Investigator Awards, bioMérieux-ESCMID Award, and Research Fellowships. I wish to encourage you to submit nominations for next year’s ESCMID Awards competition.

Marc Struelens
ESCMID Past President
Editor and Chairman, Publication Committee

Front page:
Transmission electron microscope image of a pair of Staphylococcus aureus cells. S. aureus is the world’s most common cause of hospital-contracted infections. In addition, methicillin-resistant (MRSA) strains are an increasing problem in the hospital and community settings. In this context see the article by Hugh Pennington on MRSA and other unlearned lessons on page 25 of this issue.
The beginning of 2006 has again reminded us of the risk of a new influenza pandemic. To a large extent, this is a consequence of the spread of the H5N1 influenza A strains to eastern Turkey by migrating birds and the reports that several humans have contracted the infection. There has been an increased fear of a massive outbreak caused by a mutated H5N1 virus that can spread between humans. However, H5N1 is not the only influenza A virus and there is an unchanged risk that we will experience a “normal” pandemic similar to the Asian or the Hong Kong flu.

Another aspect of the massive press coverage of the bird flu outbreaks is that there now seems to be a markedly increased political interest in development of national plans for an influenza pandemic. Simultaneously, WHO, the EU Commission and ECDC have emphasised the importance of a rapid increase in the capacity to produce influenza vaccines as well as the urgent need for a prototype vaccine for H5N1. These organisations have also advocated increasing the stores of antiviral compounds such as oseltamivir and zanamivir.

Even if H5N1 is, and should be, a major item on the agenda for improved preparedness for infectious diseases we must not forget the other infections, which still are more important than influenza as causes of death. It is important to remember that every 16th second someone dies from diarrhoea and every eighth second a respiratory-tract infection kills a human being. Most of those who die will be children in the world’s poorest countries and most of the infections could have been prevented by simple and inexpensive measures such as improved hygiene, effective antibiotics and better coverage of the vaccination programmes. To these figures the deaths caused by malaria, tuberculosis, HIV and measles should be added.

The ESCMID members, clinical microbiologists and infectious disease physicians, have a key role in the fight against the infections which annually cause the death of more than 17 million people worldwide.
Agenda

1 Welcome and President’s report (R. Norrby)
2 Report of the Secretary General (P. Francioli)
3 Presentation of the ESCMID Research Fellowships (M. Struelens)
4 Financial report of the Treasurer (E. Nagy)
5 Approval of the accounts (vote) (R. Norrby)
6 Report of the Education Officer (J. Garau)
7 Report of the Professional Affairs Officer, Clinical Microbiology (E. Nagy)
8 Report of the Professional Affairs Officer, Infectious Diseases (R. Read)
9 Report of the Scientific Affairs Officer (J. Vila)
10 Report of the Chair of the Publication Committee (M. Struelens)
11 Report of the President of the 16th ECCMID (P. Dellamonica)
12 Report of the Chair of the 16th ECCMID Programme Committee (A. Voss)
13 Approval of the Statutes (vote) (R. Norrby)
14 Proposal of new membership fees (vote) (R. Norrby)
15 Formal approval of the actions of the Executive Committee (vote) (R. Norrby)
16 Other business (R. Norrby)

Ad 13: Approval of the Statutes

Formal confirmation of the current Statutes including previously approved amendments. Please refer to the website (www.escmid.org/society) for the full text.

Ad 14: Proposal of New Membership Fees

In 2006 the annual Clinical Microbiology and Infection (CMI) page budget will increase from 1056 to 1200 pages. This leads to increased costs for the editorial office and especially for the production by Blackwell. The ESCMID Executive is therefore proposing an increase of the membership fee by EUR 3 or EUR 1 for CMI print & online or CMI online, respectively:

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<th>Membership Category</th>
<th>Current Fee (EUR)</th>
<th>New Fee (EUR)</th>
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<tr>
<td>Regular, full rate</td>
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<tr>
<td>– CMI print &amp; online</td>
<td>85</td>
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<td>57</td>
<td>58</td>
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<td>Regular, reduced rate (≤ 35 years, retired)</td>
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<tr>
<td>– CMI print &amp; online</td>
<td>65</td>
<td>68</td>
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<tr>
<td>– CMI online</td>
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5th ESCMID School of Clinical Microbiology and Infectious Diseases

Santander, Spain, 10 – 16 June 2006

A one-week course dedicated to postgraduate and continuous medical education. The programme covers a broad range of relevant topics in Clinical Microbiology and Infectious Diseases, thus being of interest to young MDs at the end of their specialty training as well as to pharmacists, biologists, PhD students and postdoctoral fellows working in the infection field. For details and registration see the ESCMID homepage at: www.escmid.org/education.

Organised by the ESCMID Education Committee

Under the auspices of the University Hospital Marqués de Valdecilla and the University of Cantabria, Santander, Spain
ESCMID Awards and Fellowships 2007

ESCMID Award for Excellence in Clinical Microbiology and Infectious Diseases

The European Society of Clinical Microbiology and Infectious Diseases will present the ESCMID Award for Excellence in Clinical Microbiology and Infectious Diseases in the year 2007 to honour a senior scientist for his/her overall achievements in these fields.

**Purpose**
The purpose of this award is to recognise and reward an outstanding lifetime contribution in the areas of science, education or professional affairs in Clinical Microbiology and/or Infectious Diseases.

**Award**
The award of EUR 10'000 will be presented by the president of ESCMID at the 17th ECCMID/25th ICC 2007 in Munich. The recipient will be honoured at the occasion of a 45-minute lecture to be given by the awardee. The name of the recipient will be published in the Final Programme, ESCMID News and on ESCMID’s website.

**Eligibility criteria**
Nominees for the award must be senior scientists who are professionally active and expected to write a review paper reflecting their field(s) of research in Clinical Microbiology and/or Infectious Diseases.

- A biographical sketch of the nominee (maximum two pages, plus an abstract of 150 words)
- A summary and analysis of the nominee’s major contributions to research in the fields of Clinical Microbiology and/or Infectious Diseases
- A list of the major original publications in refereed journals
- The complete postal and e-mail address, phone and fax number, and a colour photograph of the nominee (on paper or electronic)
- In addition, two letters of support from individuals outside the nominating institution should be mailed directly or together with the nomination to the ESCMID Award Committee.

Seven copies of the nomination package must be received by 1 October 2006.

The recipient of the award will be asked for a manuscript on the research field to which she/he mostly contributed for publication in CMI.

**Selection procedure**
The recipient will be determined by the ESCMID Awards Committee and notified by 28 February 2007 at the latest. No correspondence beyond that necessary for the nomination will be accepted. Self-applications will not be considered.

Please send your nomination to:
ESCMID Membership Office
Hainbuchenstrasse 65
D-82024 Taufkirchen / Germany
Phone +49 89 6126162
Fax +49 89 6128176
Email birgit.menzemer@escmid.org

ESCMID Young Investigator Award for Research in Clinical Microbiology and Infectious Diseases

The European Society of Clinical Microbiology and Infectious Diseases will sponsor up to two ESCMID Young Investigator Awards for Research in Clinical Microbiology and Infectious Diseases in 2007 to recognise outstanding research by younger colleagues in these fields.

**Purpose**
The purpose of these awards is to acknowledge excellence in research, and to stimulate further research of the highest scientific level.

**Awards**
The awards of EUR 7500 each, which should be used to support further research, will be presented by the Chair of the ESCMID Awards Committee at the 17th ECCMID/25th ICC in Munich on the occasion of a 20-minute lecture to be given by the awardees on topics of their main field of research. In addition, the awardees are expected to write a review paper reflecting their field(s) of research in Clinical Microbiology and Infection (CMI). The names of the recipients will be published in the Final Programme, ESCMID News and on ESCMID’s website.

**Eligibility criteria**
Nominees for the award should be born on 1 January 1967 or after. Appropriate research may be based on laboratory investigations, clinical studies, experimental animal studies, or a combination thereof. Nominees must have been employed in a European laboratory or hospital or have a future appointment in one. Members of the ESCMID Executive Committee are ineligible.

**Nomination procedure**
Nominations must be received no later than 1 October 2006. They must be submitted in writing together with proof of the nominee’s age, and include a CV, a complete list of publications as well as up to five original papers published in 2004, 2005 or 2006 or accepted for publication. The nominations should describe the candidate, his/her career, his/her research interests and personal contributions to the various research projects, in which he or she has been participating. At least two
additional supporting letters should be presented by individuals outside the nominating institution. Self-applications will not be considered. The complete postal and e-mail address, phone and fax number of the nominee must be included. Seven copies of all materials plus one colour photograph (on paper or electronic) must be sent to the ESCMID Awards Committee, who will select the recipients. The recipients will be notified of their awards by 28 February 2007 at the latest. No correspondence beyond that necessary for the nomination will be accepted.

Please send your nomination to:
ESCMID Membership Office
Hainbuchenstrasse 65
D-82024 Taufkirchen / Germany
Phone +49 89 6126162
Fax +49 89 6128176
Email birgit.menzemer@escmid.org

ESCMID Research Fellowships

The European Society of Clinical Microbiology and Infectious Diseases will sponsor the ESCMID Research Fellowships to support further research of young Society members in the fields of Clinical Microbiology and/or Infectious Diseases.

Purpose
The purpose of these awards is to encourage young investigators and to promote the development of research in the fields of Clinical Microbiology and/or Infectious Diseases.

Fellowships
Up to five fellowships, each consisting of a cash award of EUR 5'000 will be presented by the Chair of the ESCMID Awards Committee at the Assembly of Members taking place during the 17th ECCMID/25th ICC 2007 in Munich. The names of the recipients will be published in the Final Programme, ESCMID News and on ESCMID’s website.

Eligibility criteria
Awards will be made on the basis of a detailed research plan to be part of the application. Eligible individuals must be ESCMID members. They should be born after 1 January 1967 and not be more than five years beyond their training as post-doctoral students or fellows. Appropriate research may be based on laboratory investigations, clinical studies, experimental animal studies, or a combination thereof. Research must be carried out in a European research laboratory or department. If there are collaborators, applicants must make clear their personal role in planning, undertaking and supporting the planned project. Members of the ESCMID Executive Committee are ineligible.

Application procedure
The deadline for submission is 1 October 2006. Applications must be submitted in writing together with a CV, a list of publications, and two supporting letters, including a specific description of the applicant’s present research and a detailed research plan. Applicants must include their complete postal and e-mail address, telephone and fax number and send seven copies of all materials plus one colour photograph (on paper or electronic) to the ESCMID Awards Committee, who will select the fellows. Applicants will be notified of the decision by 28 February 2007 at the latest. No correspondence beyond that necessary for the application will be accepted.

Please send your application to:
ESCMID Membership Office
Hainbuchenstrasse 65
D-82024 Taufkirchen / Germany
Phone +49 89 6126162
Fax +49 89 6128176
Email birgit.menzemer@escmid.org

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) is pleased to announce an award of EUR 10'000 sponsored by bioMérieux to recognise excellence and/or major contributions to progress in clinical microbiology by young scientists from Central and Eastern Europe.

Application
Nominations of central and eastern European scientists born in 1967 or later are to be submitted in writing. They must contain a description of the nominee's career, his/her postal and email address, place and date of birth, list of publications, research interests and major contributions to the development of clinical microbiology. Two supporting letters from outside the nominating institution must be included. Self-applications will not be considered. Seven copies of all materials, plus one colour photograph (on paper or electronic) must be sent to the ESCMID Awards Committee.

The selection of the recipient will be made by the ESCMID Awards Committee. Members of the ESCMID Executive Committee are ineligible. No correspondence beyond that necessary for the application will be accepted.

The deadline for submission is 1 October 2006. The recipient of the Award will be notified of the decision by 28 February 2007 at the latest. The Award will be presented at the 17th ECCMID/25th ICC 2007 in Munich.

Please send your application to:
ESCMID Executive Office
P.O. Box 6, Clarastrasse 57
CH-4005 Basel, Switzerland
Phone +41 61 686 77 99
Email peter.schoch@escmid.org
ESCMID Awardees 2006

Award for Excellence in Clinical Microbiology and Infectious Diseases

Roland Leclercq
born 1949 in Paris, France; MD, PhD, Professor of Microbiology, Head of the Department of Microbiology and of a research group at the University Hospital of Caen, France, in recognition of his outstanding contributions to our understanding of antimicrobial resistance mechanisms, especially in Gram-positive organisms, their epidemiology and clinical implications. He reported and elucidated resistance mechanisms to lincosamides, glycopeptides, aminoglycosides, macrolides and streptogramins, and demonstrated that multiresistance in Staphylococcus aureus from cystic fibrosis patients was due to hypermutable strains. In addition to being a successful researcher Roland Leclercq is a restless and dedicated teacher.

Research interests
Roland Leclercq’s research focus is on antimicrobial resistance in Gram-positive organisms. In particular, he reported the major types of resistance to glycopeptides in enterococci and a variety of new mechanisms of resistance to macrolides and related antibiotics in streptococci and staphylococci. More recently, he studied the adaptation of Staphylococcus aureus to its host via hypermutability and its influence on antibiotic resistance. He also participated in the development of new antimicrobials and anticipated development of resistance by describing mechanisms of resistance to some of these drugs in laboratory-generated mutants. Beyond the basic aspects of mechanisms of resistance to antimicrobials, his studies extend to the clinical relevance of the findings and epidemiological aspects.

ESCMID 1·2006

Young Investigator Awards for Research in Clinical Microbiology and Infectious Diseases

Gilbert Daniel Greub
born 1967 in Neuchatel, Switzerland; MD, PhD, researcher at the Institute of Microbiology, University of Lausanne, Switzerland, in recognition of his outstanding research accomplishments in the field of Chlamydia-like organisms. He described for the first time the developmental cycle of Parachlamydia, studied the genetic, evolutionary history, and interactions of this obligate intracellular organism with amoebae and macrophages, and demonstrated a role of Parachlamydia in pneumonia.

Research interests
Discovering new agents of pneumonia is the main objective of Gilbert Greub’s research group. To reach this goal, he uses amoebal coculture to selectively grow amoeba-resisting bacteria, which allows investigation of their pathogenicity. Gilbert Greub provided serological and molecular evidence suggesting a role of Parachlamydia in pneumonia. He showed that this Chlamydia-like organism resists against human macrophages. Furthermore, he demonstrated that Parachlamydia remains unrecognised by macrophages and is able to modulate the biogenesis of phagosomes. He also showed the existence of the crescent body, an infectious developmental stage only present in Parachlamydia. Recently, he discovered a F-like tra operon in a genomic island on the chromosome of a Parachlamydia-related bacteria. This is the first evidence of a putative conjugative DNA transfer among obligate intracellular bacteria. Further ongoing research is directed at elucidating the biology and pathogenicity of other amoeba-resisting chlamydiae such as Waddlia and Simkania.

ESCMID 1·2006

Stephan Jürgen Harbarth
born 1967 in Immenstadt, Germany; MD, MS, Senior Research Associate, hospital epidemiologist and attending physician at the University Hospital, Geneva, Switzerland, in recognition of his outstanding contributions in the field of infectious disease epidemiology, focussing on prevention and control of nosocomial infections and antimicrobial resistance in hospitals. In addition, he pioneered studies on the cultural and regulatory factors that influence antimicrobial use in different countries.

Research interests
Stephan Harbarth’s research interest is focussed on the epidemiology and prevention of antibiotic-resistant, healthcare-associated infections. In particular, his studies on the impact and control of nosocomial MRSA transmission have increased our understanding of the epidemiology of MRSA and improved our ability to combat this microorganism.

His other important contributions to the field of antibiotic resistance, which had an impact on policy making, are research on the adverse effects of prolonged antibiotic prophylaxis after surgery and on the ecological bias associated with group-level data analyses of antibiotic-use-versus-resistance relationships as well as several intervention studies. For instance, in a recently published article, Stephan Harbarth investigated the clinical usefulness of a rapid on-admission screening test for MRSA. A substantial decrease in MRSA infections was seen in a medical ICU after increasing compliance with on-admission screening and implementing a strategy that linked the rapid test to pre-emptive isolation of MRSA patients.

Complementary research interests include the molecular epidemiology of emerging pathogens such as community-acquired MRSA, the pharmaco-epidemiology of antibiotic use (including international analyses of macro-level determinants of antibiotic overuse), and improved and rapid diagnosis of severe infections in critically ill patients.

The Young Investigator Awards are sponsored by Pfizer.
ESCMID and bioMérieux Award for Advances in Clinical Microbiology

Maja Rupnik
born 1967 in Maribor, Slovenia; Assistant Professor at the Medical Faculty, University of Maribor and at the Institute of Public Health, Maribor, Slovenia, in recognition of her outstanding contributions to our understanding of the pathogenicity, epidemiology and genetics of Clostridium difficile. The toxino-typing scheme, which she developed for differentiating strains with variant toxin genes, is used throughout the world.

Research interests
The main research focus of the awardee are two large toxins (toxin A, TcdA and toxin B, TcdB), both considered as the major virulence factors of Clostridium difficile. Early research on variability of the toxin coding region resulted in establishment of toxino-typing – a PCR-based method for analysis of the entire PaLoc region. Later, her research focussed on epidemiology of variant C. difficile strains, in particular on TcdA-negative, TcdB-positive strains (A+B strains), and on strains that produce an additional toxin, binary toxin CDT. Another aspect of her research interests is the biology of C. difficile toxins. Here she studied the proteolytic processing of TcdB and the crystal structure of receptor-binding regions of TcdA. She promoted the discussion on the unification of the nomenclature of C. difficile toxins. The revised nomenclature is now supported by all major groups active in the field.

ESCMID Research Fellowships

Sofia K. Kasiakou
born 1975 in Athens, Greece; MD, Research Fellow at the Alfa Institute of Biomedical Sciences, Marousi, Greece and Resident in Internal Medicine at the Sotira General Hospital, Athens, Greece

Project
A multicenter, randomised, double-blind, controlled trial of the effectiveness and safety of intravenous colistin with or without intravenous meropenem in ICU patients for infections other than pneumonia due to colistin-only-sensitive bacteria

Research interests
The focus of Sofia Kasiakou’s research is on projects related to the effectiveness and safety of intravenous and aerosolised polymyxins for the treatment of patients with multidrug-resistant Gram-negative bacterial infections. Polymyxin B and polymyxin E (colistin), the two polymyxins used in clinical practice, are old antibiotics that were removed from clinical use for many decades because of toxicity concerns. However, the emergence of highly-resistant pathogens brought them back. In addition, she is interested in the investigation of alternative modes of intravenous administration of antibiotics, specifically the continuous intravenous infusion of antibiotics with time-dependent antibacterial activity, in order to optimise their pharmacokinetic and pharmacodynamic properties, and thus improve clinical outcomes.

Surbhi Malhotra-Kumar
born 1970 in Sirsa, India; PhD, post-doctoral fellow, Belgian Reference Centre for Group A Streptococcus, Department of Medical Microbiology, University of Antwerp, Belgium

Project
Analysis of novel genetic elements and resistance mechanisms, fitness costs and compensatory adaptations in macrolide-, ketolide-, and fluoroquinolone-resistant Group A Streptococcus

Research interests
The research of Surbhi Malhotra-Kumar is focussed on the molecular epidemiology and genetics of resistance to the macrolide-, ketolide-, and fluoroquinolone group of antimicrobials in oral streptococci, primarily Group A Streptococcus (GAS). Using the oro-pharyngeal flora in healthy individuals as a model, Surbhi Malhotra-Kumar has also analysed differences in selection pressure of various macrolides and the resulting impact on resistance. Continuing as a post-doctoral fellow in the laboratory of Herman Goossens, her current work includes: further analysis of novel and emerging genetic elements harboring macrolide resistance gene mutants, elucidating the basis of ketolide resistance in GAS, and the fitness costs of antibiotic resistance gene carriage.
Short History of ECCMID

Presentation by Patrick Francioli, ECCMID Programme Director 1998–2005 at the Opening Ceremony of 15th ECCMID 2005 in Copenhagen

Ladies and Gentleman, Dear Friends and Colleagues

I am most honoured and pleased to have been asked to give a short talk on the history of the Congress of our Society. My personal involvement with ECCMID started in 1997 as Scientific Chairman of the 7th ECCMID in Lausanne. In 1998, the Society created the position of an ECCMID Programme Director to ensure continuity of the format and content of our Congress, and I have been privileged to serve in that capacity since then, and thus to be involved in formulating the scientific programme of more than half of all ECCMIDs! Some of you might think that this is too much, I agree but I can reassure you: this one is the last one.

But let’s go back some 25 years. In the early 80s a group of prominent scientists and above all, friends, founded the European Society of Clinical Microbiology (ESCM). They were sharing their concern, not to say their frustration, about the high rejection rate they were experiencing with abstracts submitted to American meetings, a situation which, according to them, was absolutely unjustified! More seriously, they were convinced that Europe could also generate a high quality meeting. Thus the decision was made to proceed, and Professor Visconti organised the first European Congress of Clinical Microbiology (ECCM) in Bologna in 1983 (Figure 1). Supposedly, this choice of location had nothing to do with the reputation of the Italian cuisine! As a young fellow, I had the chance to witness the enthusiasm of this first European event which attracted almost 800 participants, and 270 submitted abstracts. Obviously this was a good start, and the decision was made to reconvene two years later in Brighton, clearly demonstrating that the attractiveness of the cuisine was not the driving force of the meeting!

Since then, as you all know, ECCMID has been travelling all over Europe (Figure 2). Among many adaptations to the evolving scientific world, some milestones deserve to be cited: first the Society and its Congress expanded its name: initially called ESCM, it became ESCMID in the late 80s, clearly showing the still valid and strong wish of the Society to foster closer ties between these two infection fields. Second, the Society decided to go from a biannual to an annual meeting, starting in 1999. In order to do that, major changes were needed to ensure continuity: a permanent Executive Office was created, and the Society was very fortunate to recruit Peter Schoch as Managing Director, who plays a key role in the Society and in the organisation of the congress. Moreover an international ECCMID Programme Committee was appointed by the Executive Committee to ensure the highest standards year after year. This proved to be of crucial importance, as evidenced by the consistently positive feedback of the participants. The commitment of industry to ECCMID under transparent rules has also been key in the success of the Congress. Finally, and most importantly, the number and quality of participating scientists presenting their original work at this meeting increased from year to year. At the most recent meetings, a record number of more than 2400 abstracts were received from more than 80 different countries, of which over 1600 were accepted for presentation after a blind review process. The evolution of attendance and abstract submission are shown in the Table below.

ESCMID has also become a platform for the presentation of the work of many projects groups funded by the European Union in the field of infection, and the Society is honoured by the repeated participation of representatives of the European Commission in the Congress, showing that ESCMID has become a recognised partner.

A long time has passed since the first meeting in Bologna. However, despite the impressive evolution of ESCMID and ECCMID, some key elements, which were in the hearts of the founding members, are still present and fundamental to me: a magic mixture of good science, friendship and the flavour of European culture!

Thank you for your attention.

Patrick Francioli
Past ECCMID Programme Director

Figure 1. ESCM founding meeting in Munich in 1983. In the same year the 1st ECCM took place in Bologna with Arturo Visconti as Congress President. From left to right: Arne Forsgren, Mark Casewell, Jan Verhoef (standing), Jacques Acar, Arturo Visconti, Evelio Perea (standing), Tom Bergan, Ilja Braveny (standing), Eugène Yourassowski, Daryl Elder

Figure 2. ECCMID venues spread all over Europe

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<th>President</th>
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<th>Delegates*</th>
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<td>1st ECCM 1983</td>
<td>Bologna</td>
<td>Arturo Visconti</td>
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<td>?</td>
<td>1150</td>
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<td>Jan Verhoef</td>
<td>650</td>
<td>1450</td>
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<td>Nice</td>
<td>Jacques F. Acar</td>
<td>1400</td>
<td>3600</td>
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<td>5th ECCMID 1991</td>
<td>Oslo</td>
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* Approximate figures for early congresses
What’s New on the ESCMID Website?

As the Society grows and evolves, it becomes necessary to implement changes to our website. We are pleased to draw your attention to the following online improvements:

• You can now register or renew your ESCMID membership through the interactive membership form with the option to pay by credit card.
• It will soon be possible to order items online, such as publications, using the ESCMID online shop.
• Companies now have the opportunity to become corporate members. Corporate membership does not entitle companies to influence ESCMID’s activities beyond their regular voting right at the annual Assembly of Members.
• Since spring 2005 a condensed email version of ESCMID News, ESCMID Online News, is being distributed among ESCMID members and members of affiliated societies. It can also be downloaded from the ESCMID website, Publications section.
• To make ESCMID membership more attractive and to avoid further abuse of the ESCMID online membership directory by commercial interests, the directory has been moved to the protected zone. To log in members need their membership number and password*.
• Although it is not visible from the “outside”, a new release of the website management software has recently been introduced, which facilitates keeping our website up-to-date.
• In 2006 we have purchased new opinion poll software allowing rating scale questions and more flexibility in the design of opinion polls. If you are a trainee in Clinical Microbiology or Infectious Diseases please participate in the ongoing opinion poll on educational needs through the ESCMID website.

ESCMID Executive Committee

*Please note that if you have forgotten your membership ID number or password, you can contact Membership Services at birgit.menzemer@escmid.org.

Update on the ECDC

April 2005 to April 2006

ECCMID 2005 took place just a few weeks into the start-up phase of the European Centre for Disease Prevention and Control (ECDC). Zsuzsanna Jakab, the Centre’s first Director, took up her post on 1 March 2005 and made addressing ECCMID one of her first public engagements. One year on, what has been achieved?

In April and May 2006 ECDC rapidly recruited a core staff and on 20 May 2005 the Centre become operational, in the sense that it began monitoring the EU’s disease outbreak early warning and response system (EWRS) 24 hours a day seven days a week. EWRS is still run by the European Commission, but ECDC has become an increasingly significant player in this network.

By the autumn of 2005 ECDC’s senior management team was in place:
• Professor Johan Giesecke, who had been State Epidemiologist of Sweden and professor of Infectious Disease Epidemiology at the Karolinska Institute, was recruited to be ECDC’s Chief Scientist and to head its Scientific Advice Unit.
• Dr. Andrea Ammon, formerly State Epidemiologist of Germany, was recruited to head the Surveillance and Communication Unit.
• Dr. Denis Coulombier, erstwhile Head of the Department of Public Health Information Systems at the National Public Health Surveillance Centre in France became the head of ECDC’s Preparedness and Response Unit.
• Jef Maes, who had been Head of Administration at the European Environment Agency (EEA) became ECDC’s Head of Administration.
• Dr. Karl Ekdahl, Sweden’s Deputy State Epidemiologist, became the Strategic...
Advisor to the Director of ECDC and head of her cabinet.

Another key milestone attained on 1 October 2005 was that ECDC moved to permanent headquarters – the Tomteboda, on the campus of the Karolinska Institute. Finding a permanent base was of major operational importance. The Centre will be investing millions of euros over the coming years in developing its infrastructure. For example, ECDC needs to build a state-of-the-art emergency coordination centre and has also a major role to play in the future development of Europe-wide IT systems such as the Early Warning and Response System (EWRS) and networks for the sharing of surveillance data. It would not be possible to start building this infrastructure while in temporary offices.

The emphasis on making the ECDC operational quickly was well placed. Autumn of 2005 saw H5N1 avian influenza arrive in Europe’s neighbourhood. ECDC was called on to work with public health authorities across Europe to develop EU guidelines on the protection of people who might be exposed to infected poultry and an assessment of the risk H5N1 avian influenza posed to human health in Europe. ECDC was able to produce these documents rapidly thanks to the dedication and hard work of its management team and key scientific staff.

The start of 2006 saw human cases of avian influenza in Turkey and then in Iraq. In both cases ECDC epidemiologists played a key role in organising the international teams sent to assist these countries. From mid-February onward, H5N1 avian influenza started appearing in wild birds in the EU. ECDC issued further advice to Member States on populations in the EU that could be at risk – in particular, people who keep “backyard” poultry flocks – and suggested messages they could be given.

Public concern over H5N1 avian influenza has focussed political attention on the wider issue of preparedness against a flu pandemic. The Centre will be investing millions of euros over the coming years in developing its infrastructure. For example, ECDC needs to build a state-of-the-art emergency coordination centre and has also a major role to play in the future development of Europe-wide IT systems such as the Early Warning and Response System (EWRS) and networks for the sharing of surveillance data. It would not be possible to start building this infrastructure while in temporary offices.

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Public concern over H5N1 avian influenza has focussed political attention on the wider issue of preparedness against a human influenza pandemic. A joint team from ECDC, the European Commission and WHO visited six European countries last year to review their preparedness plans. A further six country visits are now taking place, with some initial results likely to be available by the joint EU / WHO workshop in Stockholm in May.

2006 is a preparatory year for ECDC’s surveillance activities. From 2007 ECDC will start taking over responsibility for producing European level surveillance data on the 46 diseases and disease groups that are notifiable at EU level. In October 2005 the Centre’s Management Board approved a strategy on the future of European disease surveillance. This sets out the principles and objectives which will guide the transition from the current situation, where there are just under 20 surveillance networks run as individual EU funded projects, toward a more integrated approach to surveillance cooperation. A first meeting between ECDC and the dedicated surveillance network (DSN) teams took place in November and a process of reviewing the work of the DSN – and the needs of ECDC for external support in disease surveillance – will get underway this year.

In the autumn of 2005 ECDC published an open call for nominations aimed at scientists wishing to be considered as members of its expert scientific panels. ECDC is planning to create ad hoc panels as the need for external scientific advice evolves. This will be especially necessary during the first years of existence, when the Centre staff will still be quite small. However, the Centre already started producing science in 2005: notably, its risk assessment on the human health implications of the arrival of H5N1 avian influenza in the European region and its guidelines on the protection of persons who may be exposed to infected birds. These documents were produced after intensive consultation with ECDC’s Advisory Forum, which brings together the public health institutes of the Member States.

By the end of 2005 ECDC had recruited a total of 29 officials. The Centre’s provisional budget for 2006 is €17.2 million and its head count is set to rise to 50 officials, with staff on detachment to ECDC from national public health authorities providing an additional resource. Around 15% of the provisional budget for 2006 is earmarked for buildings and infrastructure, €7.7 million is foreseen for salaries and the rest of the budget is allocated for projects, networks, scientific meetings and other such activities aimed at delivering on the Centre’s work programme.

Speaking in December 2005, just after ECDC’s Management Board approved the 2006 budget and reaffirmed the Centre’s work plan, Zsuzsanna Jakab, Director of ECDC said: “My ambition is that by the end of 2006 ECDC will have experts in place to cover all 46 of the infectious diseases that are notifiable at the EU level.”

Ben Duncan
ECDC Press Spokesman
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1 Greece, Poland and UK within the EU and Kazakhstan, Turkey and Ukraine in the wider Europe
2 France, Germany, Italy, Lithuania, Portugal, Slovakia
4 To access these documents see: www.ecdc.eu.int/avian_influenza/index.php
5 In February 2005 ECDC’s Management Board adopted a work programme for the Centre covering the years 2005 and 2006. This is available at: http://www.ecdc.eu.int/documents/pdf/ecdc_work_programme.pdf
EU Antimicrobial Resistance Strategy

Commission reports on the implementation of the Council Recommendation

At the end of last year, the European Commission published a report on the EU Member States’ implementation of Council Recommendation (2002/77/EC) on the Prudent Use of Anti-Microbial Agents in Human Medicine, after receiving feedback on their achievements. The report assesses the progress made, highlights shortcomings and proposes further actions. The overall evaluation of the actions executed by the Member States thus far is positive, while some particular areas of concern have been addressed in the report.

Evaluation of actions undertaken

The Commission’s report summarises and assesses each category of actions in the Recommendation that were undertaken by the Member States and by the Community as a whole. It finds that almost all Member States have national systems for surveillance of antimicrobial use and antibiotic consumption, have stepped up coordination mechanisms and have established guidelines for the appropriate use of antimicrobials. In addition, most Member States have a national programme for hospital hygiene and infection control, but the practicalities for the implementation of the programmes are not fully in place.

On the issue of promoting education and training of health professionals on antimicrobial resistance and informing the general public about the importance of prudent use of antimicrobial agents, the Commission found that all but six countries performed an awareness raising campaign in the last years although these were predominantly directed at the professional sector.

On the European Community level, the Commission has worked extensively on keeping the networks, committees and working groups up-to-date with developments in Member States. The EMEA, in cooperation with national authorities, is undertaking to revise and harmonise the information provided in the Summary of Product Characteristics, while criteria for authorisation of new products have been further developed to take into account the principle of containment of antimicrobial resistance. The EU has further financed a number of projects and networks for the collection of data and surveillance of antimicrobial consumption through the Health Action Programme and the 6th Framework Programme for Research and Technological Development.

However, the report highlights certain areas where action by Member States must be strengthened to achieve the main objective and goals of the Council Recommendation. It has found that National Strategies are not fully in place in all states and that even in the countries that have implemented them, legal and financial arrangements are usually inadequate. Lack of effective coordination mechanisms as well as of exchange of data and information on best practices hinder the success of the Community strategy. A serious problem for many countries is the availability of antibiotics without prescription, which is even more alarming because the volume of such OTC sales can hardly be estimated.

The Commission thus calls on Member States to tackle antibiotic self-medication and enforce a prescription only approach. Actions should be taken to further ensure that Member States have appropriate coordinating mechanisms in place, which will cover all relevant sectors and have adequate means to carry out their tasks. In addition, it suggests that all countries should adopt and put into effect guidelines on appropriate antimicrobial treatment, at least for the most common illnesses, and that information and education available to citizens on antimicrobials should be improved.

The dissemination and exchange of this information and of best practices in prescribing methods is a point that needs to be especially highlighted and enhanced, according to the Commission. Finally, public health institutions are strongly advised to step up infection control measures to counter the spread of “super-bugs” such as MRSA, while international cooperation (WHO) is also supported.

EU coordination functions

The Commission’s role in supporting Member States’ actions will of course continue in the future, but this will no doubt change compared to previous years due to the establishment of the European Centre for Disease Control and Prevention (ECDC). The Centre has already taken up surveillance and risk assessment, which formerly were in the remit of the Commission. As the Commission’s report states: “as laid down in the Regulation establishing the Centre for Disease Prevention and Control … the ECDC will have an important role to operate European surveillance also in the area of antimicrobial resistance. The ECDC should be able to assist the Commission in the future preparation of implementation reports and of recommendation proposals.”

Similarly, EMEA will have a significant role to play in promoting new effective antibiotics and issuing market authorisations, as mentioned above.

Procedural aspects – practical next steps

The publication of the Commission’s report signals its transmission to the Council for approval. From that stage on, it will be up to the Austrian and Finnish Presidencies to take the matter forward during 2006.

Furthermore, antimicrobial resistance will continue to feature highly on the 2006 Work Programme of Commission General Directorate for Public Health (DG SANCO). A specific priority in this work plan is the “sharing of best practices on patient safety issues, in particular management and control of healthcare-associated infections and antimicrobial resistance”, as well as “activities on controlling adverse effects (from vaccines, chemicals, antivirals, other medicines and medical devices) in cooperation with the EMEA”.

Finally, as the process of adopting the 7th Framework Programme for Research and Innovation (2007–2013) as well as the new Community Action Programme for Health (2007–2013) continues in the course of 2006, there will be scope for future funding of related projects. The European Parliament has recently approved the first draft of the Action Programme for Health, which includes a recital on the importance of fighting resistance to antibiotics and nosocomial infections as they pose a serious threat to health in Europe and thus calls for new research into new antibiotics as well as for the proper use of the existing ones and the collection and analysis of relevant data.

Elli Tsiiligiani
Interel
EUCAST Is Making Progress

EUCAST, the European Committee on Antimicrobial Susceptibility Testing is making progress. Breakpoints for several classes of antibiotics have been harmonised and breakpoints for two new drugs have been determined as part of the EUCAST/EMEA process.

Harmonised breakpoints for existing antimicrobial agents

The harmonisation of European breakpoints for existing antimicrobial agents is a major objective for EUCAST. EUCAST European harmonised breakpoints are now available for aminoglycosides, fluoroquinolones, glycopeptides and linezolid (see www.eu-cast.org). Harmonised breakpoints for aztreonam, carbapenems and cephalosporins will be available after 16th ECCMID in April 2006. A preliminary table of penicillin breakpoints has just been sent for consultation with the National Breakpoint Committees in Europe. The EUCAST Subcommittee on Antifungal Susceptibility Testing has almost completed European breakpoints for fluconazole.

Breakpoints for new antimicrobial agents

A Standard Operating Procedure (SOP) has been developed by EUCAST, the European Medicines Evaluation Agency (EMEA) and the pharmaceutical industry. Following the procedures in this SOP, EUCAST addressed two new antimicrobials during 2005. Daptomycin was registered by EMEA in late autumn 2005 and the breakpoints are available on the EUCAST website (www.eu-cast.org). Registration of tigecycline is still in process and breakpoints will be made available as soon as the drug is approved by EMEA.

The EUCAST Subcommittee on Antifungal Susceptibility Testing (EUCAST AFST)

The EUCAST AFST has collected large numbers of MIC-distributions for antifungal agents active against Candida spp. in preparation for setting breakpoints on antifungal drugs. The MIC distributions for fluconazole will soon be made available on the EUCAST website. The subcommittee is preparing for EUCAST consultation about the proposed European breakpoint of Fluconazole. This consultation will involve the EUCAST General Committee as well as the pharmaceutical and device manufacturing companies.

EUCAST workshop in Rome

On 23 November 2005 a EUCAST workshop took place next to St Peter’s Square in Rome with the participation of the EUCAST Steering Committee, members of the EUCAST General Committee, delegates from the European Antimicrobial Resistance Surveillance System (EARRS) and 25 representatives of pharmaceutical companies and susceptibility testing device manufacturers. There were wide-ranging discussions, including the views of industry on the process of setting EUCAST breakpoints for bacteria and fungi in Europe and their implementation. Various aspects of problems in antimicrobial susceptibility testing and interpretation were also examined. During the following two days EUCAST and EARRS arranged a joint workshop for EUCAST and EARRS delegates, in which aspects of antimicrobial resistance surveillance of common interest were discussed.

EUCAST at 16th ECCMID in Nice

EUCAST has organised a satellite workshop on antimicrobial susceptibility testing to be held on Saturday, 1 April 2006 10.30–12.30 at the Acropolis Conference Centre in Nice. Attendance will be limited to members of the National Breakpoint Committees, the EUCAST General Committees, members of the EUCAST Subcommittee on Antifungal Susceptibility Testing and members of the pharmaceutical and susceptibility testing device manufacturing industries. The workshop will deal with the need for speciation in antimicrobial susceptibility testing.

On the afternoon of Saturday, 1 April 2006 the annual business meeting of EUCAST will be held. This is an open meeting, during which the current activities of EUCAST will be reviewed. All are welcome to attend.

On the afternoon of Tuesday, 4 April 2006 the EUCAST symposium for ECCMID on The clinical implications of low-level resistance will take place. Please see the ECCMID programme for details.

EUCAST and CLSI

For several years the EUCAST chairman has represented ECCMID at the twice yearly Antimicrobial Susceptibility Testing Subcommittee and working group discussions of the CLSI (formerly NCCLS). I and on several occasions, other EUCAST Steering Committee members have taken an active part in the discussions, including those on new cephalosporin breakpoints for Enterobacteriaceae, vancomycin breakpoints for Staphylococcus aureus, fluoroquinolone breakpoints for staphylococci, breakpoints for Acinetobacter spp. and revised breakpoints for Neisseria meningitidis. The work of the Enterobacteriaceae working group has recently been suspended until FDA and CLSI have sorted out their differing viewpoints on procedures for revising breakpoints. A new working group which has been established to revise the M23 document about the procedure of determining breakpoints by CLSI will complete this task. Unfortunately all other working groups involved in much needed revisions of breakpoints are on hold while the discussions between CLSI and FDA are ongoing and the M23 working group is in session. EUCAST strongly believes that there is a need for an internationally-agreed process for setting and revising breakpoints, perhaps under the auspices of the International Standards Organization. This will be pursued by EUCAST.

EUCAST Technical Notes (ETNs) in CMI

Beginning in 2006 a series of EUCAST Technical Notes will be published in Clinical Microbiology and Infection. The ETNs will summarise the background data, on which decisions are made on breakpoints for individual new agents (e.g. daptomycin and tigecycline) or harmonised breakpoints for groups of agents (e.g. aminoglycosides, fluoroquinolones and glycopeptides). The technical notes are based on the more detailed rationale documents produced by EUCAST for each of the antimicrobial agents subjected to the processes of harmonising or setting breakpoints. The rationale documents will be available on the EUCAST website (see www.eu-cast.org).

EUCAST wild type MIC distributions on the internet

EUCAST wild type MIC distributions for all organism-antimicrobial agent combinations, for which EUCAST has published new or harmonised breakpoints, are
available on the EUCAST website (see www.eucast.org). The MIC distributions are the combined data from many data sources, which are checked for consistency before incorporation into the database. Some distributions are now based on close to 100,000 MICs. The data are presented as tables and histograms of MIC distributions. Wild-type MIC distributions have several benefits — they assist in setting breakpoints that do not divide the wild-type distributions, which would prevent reproducible susceptibility testing; they are used to define epidemiological cut-off values (microbiological breakpoints) that separate the wild-type from the non-wild type microorganisms; they provide a reference for those who need to calibrate susceptibility testing systems or products; and they provide a reference to the expected MIC value for an organism that has not developed resistance to an agent.

**EUCAST and VetCast**

In December 2004 the Veterinary Committee on Antimicrobial Susceptibility Testing (VetCast) was initiated in Copenhagen at a meeting of representatives of European veterinary reference laboratories. In the EU it is mandatory for all Member States to monitor antimicrobial resistance annually in organisms of public health concern. This monitoring is primarily focused on Salmonella spp and Campylobacter spp from food-producing animals, but may include other organisms. In order to harmonise the results of these monitoring activities in Europe, uniform breakpoints are essential. Hence, setting wild type distributions is very relevant for veterinary laboratories. Through VetCast and the existing network of veterinary reference laboratories close to 1668 MIC data sets, covering a substantial range of organisms and agents of relevance to the veterinary field, have been collected. In January 2006 a Community Reference Laboratory (CRL) was designated for antimicrobial resistance (DFVF, Denmark). The CRL will have a major role in the future implementation of epidemiological cut-off values and breakpoints.

Gunnar Kahlmeter
EUCAST Chairman

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**Authority among equals**

From a young age, we grant to our peers a great deal of authority, to a different degree and of a different nature than that inherent in traditional authority figures. This probably because one way of seeing ourselves is through the eyes of, or in the context of, our peers - those doing the same thing, those behaving the same way, those in the same situation, those with whom we wish to be associated.

Up to a certain point, we have the luxury of deciding who our peers are, based on an understanding of ourselves, or an aspiration. Those who wish to publish in scientific publications, however, are more restricted. Nonetheless, peers remain a mainstay of self-judgment and peer review has become an established institution.

The First International Congress on Peer Review in Biomedical Publication took place in 1989, and the Fifth took place last year. This initiative on the part of the JAMA has been fostered, among others, by the BMJ and the Lancet.

In an editorial following the Second Congress, Drummond Rennie, Deputy Editor at JAMA, explained that the point of the initiative is to stimulate and present research on peer review and the integrity of the publication process, an area of research that seems unlikely to some. According to pre-and post-congress questionnaires, the vast majority of respondents (95% pre-congress and 92% post-congress) agreed that peer review improves the quality of published manuscripts. Prior to the congress survey, 68% of respondents thought journals should adopt more uniform standards for peer review and 81% were of this opinion after the congress. The majority of respondents concurred that editors should contribute to an effort to establish baseline data on the prevalence of scientific fraud (75% pre-congress and 85% post-congress) [1].

Peer review, according to Richard Smith, former editor of the BMJ, currently CEO of United Health Europe and board member of The Public Library of Science (PLoS), is held "absolutely sacred" in a field where people rarely accept anything on "blind faith". Still, there is evidence of the "downside" of peer review. “Even the very best journals have published rubbish they wish they’d never published at all. Peer review doesn’t stop that.” And the process can lead to misjudgments in the other direction, failures to recognise promising work; some of the most highly cited papers were initially rejected. Peer review is a “lottery to some extent” says Smith; “it’s very unscientific, really” [2].

Others, however, believe that the process of peer review could be precisely scientific. Richard Horton, Editor of the Lancet, in a presentation at the Second Congress, suggested that a method of argument analysis [3], if applied to the scientific research paper, offers an opportunity for a systematic and logical approach to peer review. In brief, the relation between (1) the primary data and (2) the interpretation of these data (the argument) is determined by (3) the justification or reasonable grounds for the study. Reviewers should focus initially on the validity of the core argument made by the authors to determine whether the study is even warranted. Thus, reviewers should look for a justification for the study (3) before considering the data (1) and the interpretation (2); only then does it make sense to consider the probability (4), the degree of random and systematic error (5) and the ‘generalisability’ (6). Horton proposes these six criteria as an alternative to the usual checklist, which provides ‘a crude normative framework’ for reviewers. Doing so would lead the reviewer through a logical process that would limit the risk of unacknowl-
edged bias and should result in a useful review [4].

I have attended the third (Prague), fourth (Barcelona) and fifth (Chicago) congresses and the following highlights reflect a sample of the presentations in two subject areas at the last congress, with reference to CMI.

Criteria for authorship and conflict of interest

The guidelines for authors who submit to CMI, as those for most other journals, set forth criteria for authorship in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, generally known as the Vancouver Style, which were first published in 1979 following a meeting in Vancouver in 1978. The initial group expanded and evolved into the International Committee of Medical Journal Editors (ICMJE), which meets annually and has broadened its scope to include ethical principles related to publication in biomedical journals.

In the case of CMI, anyone named as an author should have made a significant contribution to the overall design of the study and to the execution of the work described, and all authors are held responsible for the content of the entire paper (i.e., individuals who merely provided facilities, strains or reagents, completed questionnaires, or critiqued the paper do not have a claim to authorship) – clearly impossible to enforce but it makes sense to remind authors (and non-authors) of their responsibilities.

As Rennie expressed during an Authorship Task Force meeting, if each author would ask himself ‘would I be embarrassed if put to the test of my claim to authorship or my disclaimer concerning conflict of interest?” a great deal would be accomplished.

A number of journals require a signed disclosure of each author’s contribution, which is not required of authors submitting to CMI. Apparently, the structure of contribution disclosure forms significantly influences the number of contributions reported by authors. Recent studies report a discrepancy between two declarations from corresponding authors about their own contributions to the same manuscript when asked on separate occasions [5].

This discrepancy might be explained, in part, by the degree to which ICMJE criteria are understood. Authors seem to understand intuitively three of the ICMJE criteria for authorship: substantial contributions to conception and design of a study; analysis and interpretation of data; and drafting of the article. They seem to be unclear, however, about the other three criteria: acquisition of data; critical revision of data for important intellectual content; and final approval of the version to be published [6]. As each author is expected to meet all six conditions, problems in the authors’ perception of their responsibility clearly arise.

The second issue concerning disclosure is that of conflict of interest, and this applies not only to authors, but also to editors and reviewers. One’s own interests become so much a part of oneself that disclosure of a potential conflict is not always forthcoming, or – to be fair – not always deemed necessary. For this reason, although simply a suggestion for good practice and fair behaviour, the ‘would I be embarrassed test’ may be more reliable than formal declarations which are most often signed without reflection.

In the case of CMI, a significant number of authors declare financial support in the acknowledgement section, which is expected according to the guidelines for authors. It is less common for authors to declare that no financial support was received or that no conflict of interest exists, but some authors do so.

Although authors usually disclose a source of funds, they almost always fail to disclose the role of the funding source in the study or in the preparation of the manuscript. It is rare that authors disclose a potential conflict of interest. However, affiliations and potential conflicts may be discovered during the editorial process, including peer review, and respective disclosures may then be introduced in the published text [7]. Unlike policies for authors, journals infrequently have conflict of interest policies in place for reviewers and editors, and even less commonly publish such disclosures [8].

In the case of CMI, it is not uncommon for reviewers to declare a certain type of conflict of interest, e.g., collaboration with the authors or previous review of the authors’ work. Conflicts of interest that involve professional competition or financial affiliations which may affect assessment of a given paper, however, are typically not disclosed.

Apparently the relative emphasis on conflict of interest, both professional and financial, varies across disciplines. Conflict of interest policies are common in journals reporting general medicine and multidisciplinary science, although these policies usually do not clearly define the several types of conflict of interest, but they are less common in journals representing other scientific disciplines [9]. One study concludes that conflicts of interest actually exist in a minority of submissions to biomedical journals and almost one-third of disclosed conflicts concern institutional relationships with industry, most frequently relating to grants, consultations and honoraria. It is noteworthy that manuscripts with professed conflicts do not appear to be rejected more frequently than those without [10].

The peer review process: identity of reviewers

CMI offers submitting authors the opportunity to suggest four potential reviewers and to exclude two. A minority chooses to make suggestions, and even fewer exclude reviewers.

It appears that reports submitted by author-suggested reviewers do not differ in quality from editor-selected reviewers; however, according to the same two studies, author-suggested reviewers tend to make more favourable recommendations for publication [11, 12]. Another study found a higher rate of acceptance in papers by authors who chose to exclude reviewers, and concluded that suggesting reviewers had less of an influence on acceptance than did excluding reviewers [13].

The question of blinded review remains open and controversial, not so much because its merit is questioned, but for practical reasons. It has proven impossible to successfully blind reviewers to the identity of authors, mainly due to reference lists and the format of research papers in which authors frequently refer to themselves or their institutions in the first person. What has proven to be possible and acceptable in the review of congress abstracts has not been accomplished in the context of journal submissions.

A reasonable conclusion is that the identity of reviewers should be likewise transparent. Rennie maintains that signing a review makes it better. Among the most outspoken advocates for research in the field of peer review, he finds this concept a given, for which even he does not need research data to be convinced. “I’ve always signed every review because I know if I sign something, I’m more accountable.” Juries are not anonymous, he argues, so why are peer reviewers? Always willing to put his opinions on the line, Rennie pre-
dicts that anonymous reviewers will be considered ‘quaint in 20 years’ and as rare as an anonymous letter to the editor [2].

A policy of disclosing reviewer identity has not been embraced by the majority of journals, however, including CMI. The original Editorial Board debated the idea, and some members were strongly in favour, but it was not adopted. In the past, reviewers for CMI did have the option of signing their comments for the authors, and some did so. The Nature journals give reviewers an opportunity to make their identity known, but according to Bernd Pulverer, editor of Nature Cell Biology, less than one percent take advantage of the opportunity, which he understands as the competitive nature of scientific publishing interfering with something that, in principle, should work. Other editors are less optimistic. Peter Lawrence, an editor of Development and former editorial board member of Cell, believes that anonymity helps reviewers stay objective at a time when authors are going to desperate measures to get their results accepted by top journals and an increasing number of scientists are spending time networking with editors. Donald Kennedy, editor-in-chief of Science, maintains that “candour flourishes” when referees know that not all of their comments will reach the authors [2].

The separation of comments for authors and confidential comments for editors, however, need not eliminate the possibility of making the reviewer’s identity known. The reviewer, knowing that his identity will be revealed, has complete control over the content of his comments for the authors, yet has the opportunity to make further comments that will remain confidential. The online journal, BioMed Central, actually requires authors to suggest four reviewers when making a submission and authors and reviewers know each other’s identity, as do readers, since reviews, with the exception of confidential comments for the editors, are published alongside accepted articles [9]. Similarly, in recent years, the BMJ has revealed the identity of reviewers, but maintained a policy of allowing confidential comments for the editors. Smith, then editor, claims that there were no serious problems following the decision, and the only ‘adverse effect’ involved authors who brought to light a reviewer’s potential conflict of interest, which is actually a ‘good thing’ [2].

Those responsible for making editorial decisions are familiar with the discrepancy among reviewers’ comments and must of course distinguish between the constructive and the simply critical review. Some reports are much more thoughtful than others, and thus more useful to both the authors and the editors. If there are self-serving reviewers among the whole, they are few and their intentions are usually obvious to the point of discouraging further invitations to review. In my experience, reviewers in general (who are in turn authors) have been remarkably generous and willing to dedicate a great deal of time to assessing and commenting on the work of their peers, which surely merits recognition. The sort of reviewers who are truly valued may even appreciate the additional recognition implied in making their identity known.

The institution of peer review seems to be intact for several reasons: most people are flattered to be asked for an opinion; most clinicians and researchers are genuinely interested in the work they do; most people are willing to give advice and some are even adept at imparting information when it relates to their own area of experience. This is very good news in the general context of character and seems also to explain why the process of peer review succeeds, for the most part, in improving the quality of published papers.

Judith Crane
CMI Managing Editor

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Who Has Won the Battle?

Recently, avian influenza attracted world-wide attention when a highly pathogenic strain of the subtype H5N1 gained enzootic status in poultry throughout Southeast Asia and traversed interclass barriers when transmitted from birds to mammals. With the increased spread of avian flu in the wild bird population, further outbreaks along and between overlapping migratory flyways from inner Asia towards the Middle East and Africa have hit Turkey, Romania, Croatia, and the Crimean peninsula. The emergence of avian flu in Turkey, Europe’s eastern door, first brought the virus closer to Europe than ever before. In this article, we attempt to share the Turkish avian flu experience.

The status quo in Turkey

Geographically speaking, Turkey is a bird haven, providing a home for 456 different species, 376 of which may be encountered on a regular basis while another 80 species are known to originate from Siberia, Africa and North America. The shift of the world’s attention to the avian flu cases in Southeast Asian countries has prompted intensive worldwide preparation against the avian flu, including Turkey. After January 2004, follow-up of flu cases was done under the strict supervision of the Ministry of Health, and by 16 March 2004, physicians and veterinarians alike were informed in writing regarding the signs and symptoms of the disease.

The first case of avian flu in Turkey was discovered on 8 October 2005 in turkeys in the Kiziksa county (western Turkey). Two thousand turkeys died in one night alone. A team of experts was promptly dispatched to the area; poultry within a protection radius of 3 km were culled, and those within the designated observation radius of 7 km were thoroughly screened. In addition, teaching programs were implemented, aimed at educating and increasing awareness among health personal and in the community. Pamphlets were circulated, and chemoprophylaxis was given in a very restrictive manner to individuals who had contact with live or dead birds. Meanwhile, an order was placed for one million boxes of Tamiflu®.

15 December 2005 marked the death of winged animals in the county of Igdir (eastern Turkey). Samples were obtained from the dead animals, and a temporary quarantine was put in place. By 26 December 2005, H5N1 was established as the cause of death, and samples were sent to the Reference Laboratory of the European Union in the UK to confirm these findings, as well as to determine the genetic structure of the virus. After confirmation of the H5N1 strain, 359 birds in the region were culled, and 11 individuals with a history of close contact with infected birds were given prophylaxis with Tamiflu®. Quarantine and decontamination efforts were maintained throughout the region.

On 31 December 2005, four children from the same family living in Dogubeyazit (very close to above-mentioned Igdir province) area were referred to the Yuzuncu Yil University in Van with one week of high fever and breathing difficulties. The children, between 9-15 years of age, were hospitalised for leucopenia and pneumonia. According to the accounts of both parents, chickens which they were raising, fell sick on 21 December 2005. When the birds started dying, two were slaughtered by the eldest children and the feathers were picked by two other siblings. The birds were eventually cooked and consumed mainly by the family’s and neighbour’s children. Upper respiratory tract secretions obtained from the four siblings on 1 January 2006 were sent to the reference laboratory for further investigation. ELISA and PCR analysis failed to detect the avian flu virus. However, by the 4th of January the virus was found in respiratory secretions of the 14-year-old who was dead by then as well as from his 15-year-old sister. Samples were sent to the WHO’s reference laboratory in the UK, and the presence of the H5N1 strain was verified. The eldest sister died on 6 January 2006.

Until the end of February 2006, there were 21 confirmed cases (17 children) of avian flu in Turkey, the last of which was reported on 17 January 2006. Nine were from Agri, three from Ankara and two each from Van and Kastamonu. Corum, Samsun, Sivas, Siirt and Sanliurfa had one reported case each (see Figure). The only deaths were the four children in Dogubeyazit. The local tradition of housing domestic winged animals indoors during the cold season could result in the clustering of cases in the east of the country. Similarly, the young are usually entrusted with the care of poultry, which may explain why the children were most affected by the virus.

Measures in Turkey

Veterinarian measures (surveillance, outbreak control)

Aiming to break the chain of transmission from wild birds to domestic birds (backyard poultry) as well as human be-
ings, about 2.3 million domestic birds have been destroyed so far, and their owners compensated. The plan is to destroy all backyard poultry over the entire country in time, starting from the infected provinces. According to the estimates of the Ministry of Agriculture and Rural Affairs this includes about 10 million birds. This strategy excludes the integrated poultry farms where strict protective measures are being conducted. The sale of all live backyard poultry species in local markets has been prohibited. The press is regularly informed, so that public awareness is being raised and, in addition, training sessions are being conducted particularly in high-risk provinces. The infected districts have been placed under quarantine; no animals are allowed to move in or out of the provinces. Culling operations are currently under way.

Enhanced human surveillance

Samples (nasopharyngeal swap, tracheal aspirate, etc.) are obtained from persons admitted to health care centers with a history of contact with dead or sick poultry and from those who deal with slaughter, picking feathers, butchering, and preparation of poultry for cooking or consumption of the diseased animals and their products (eggs). The samples are examined in National Reference Laboratories in Ankara and Istanbul. Rapid test, ELISA and PCR are being conducted. 2152 samples have been studied so far.

Social awareness measures

Ever since 2004, both the printed and visual media have been collaborating with scientists and representatives from the Ministries of Health and of Agriculture and Rural Affairs, and as a result, programmes aimed at increasing public awareness have been developed. A curb has been put on the sale of live winged animals in most of the country, and the general public has been encouraged to consume packaged winged-animal products, including eggs, that have undergone thorough health inspection. The importance of properly cooking winged-animal products has also been advocated.

Risk communication

Joint meetings are being held with EU, ECDC, WHO, FAO, OIE in order to review the existing situation and determine measures to be taken. We are sharing our data and information with relevant international organisations in a transparent manner.

Conclusions

Turkey, being along the migration routes of several bird species, will always remain under threat for avian flu. Enforcement of a transparent policy in Turkey, as well as the use of a scientific approach have made the fight against avian flu a success. However, even though there is no evidence supporting human-to-human transmission in any of the cases in Turkey, it is certain that such transmission would pose a serious threat in the near future should it occur. For this reason it is still prudent for the whole world to work in unison against this common threat.

Turkish isolates have new mutations

The first mutation involves a substitution in one sample of an amino acid at position 223 of the haemagglutinin receptor protein. This protein allows the flu virus to bind to the receptors on the surface of its host’s cells. This mutation has been observed twice before - in a father and son in Hong Kong in 2003, and in one fatal case in Vietnam last year. It increases the virus’s ability to bind to human receptors, and decreases its affinity for poultry receptors, making strains with this mutation better adapted to infecting humans.

The same sample also contained a mutation at position 153 of the haemagglutinin protein. Finally, both samples from the Turkish teenagers show a substitution of glutamic acid with lycine, at position 627 of the polymerase protein, which the virus uses to replicate its genetic material. This mutation has been seen in other flu sequences from Eurasian poultry over the past year. It was also present in the one person who died during an outbreak of H7N7 in the Netherlands in 2003, and in a few people in Vietnam and Thailand. The Turkey strains are the first, in which the polymerase and receptor-binding mutations have been found together. They could make it easier for humans to catch the virus from poultry. But they might also favour human-to-human transmission. This is because the polymerase change helps the virus to survive in the cooler nasal regions of the respiratory tract, and the haemagglutinin mutation encourages the virus to target receptors in the nose and throat, rather than lower down in the lungs. The virus is thought to be more likely to spread through droplets coughed from the nose and throat than from infections lower in the respiratory tract.

Change in virus infectivity compared with Southeast Asian situation

Although we do not have enough data to compare the virus infectivity with the Southeast Asian situation. However, molecular phylogeny indicated that the HA gene is most similar to that of recent isolates from Qinghai, Ukraine (99.5% identity), Novosibirsk (99.2% identity) and the 2005 isolates from Turkey (98.9 identity). Sequencing and molecular phylogeny of the NA gene indicates that it is most similar to recent isolates from Qinghai (99.8% identity).

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Tolerance of *Listeria* to pH Stress

Research Report of a Trainee

Efstathios Giotis

My research visit to the Illinois State University (School of Biological Sciences) lasted from the end of July 2005 to the end of January 2006. Training took place under the supervision of Professor Brian Wilkinson and Dr Arunachalam Muthaiyan. The main focus of my studies was:

- to examine the role of the membrane fatty acids in alkaline and acid stress and in particular the role of the branched chain fatty acids in the alkaline tolerance of *Listeria monocytogenes* using gas chromatography,
- to find out the gene expression alterations that take place during short-time (alkaline shock) or a long-term (alkaline adaptation) using oligo microarrays,
- finally, to validate microarray results using such methods as Northern Blot and quantitative Real Time Polymerase Chain Reaction (RT-PCR).

**Background**

*Listeria monocytogenes*, a causative agent of both sporadic and epidemic foodborne infection, emerged as an important human pathogen in the 1980’s (1). *L. monocytogenes* is ubiquitous in nature and is resistant to diverse environmental conditions such as low pH, high NaCl concentrations, low oxygen level, and is able to grow at very low temperatures (2 to 4°C) (1). The resistance of *L. monocytogenes* to stresses is of particular concern especially when mild treatments are used for food preservation in the industry because survival and subsequent growth of even a single contaminating cell could result in bacterial numbers that exceed the infectious dose, on subsequent portioning and packaging of the food (2). Alkaline stress is of great significance, as *Listeria* is often exposed to such conditions in food processing environments cleaned with alkaline detergents or in the mildly alkaline pH values which prevail within engulfing phagolysosomes. Few insights have been presented on the role of membrane fatty acids in the regulation of the membrane structural state under acid and alkaline adaptation in *L. monocytogenes*. Kaneda (1991) noted that growth pH affects the fatty acid profile of *Bacillus subtilis*, a bacterium with similar fatty acid composition to *L. monocytogenes*. The pH stress is associated with membrane disintegration and it is presently unknown whether Listeria is able to change and regulate its membrane fatty acid composition within the growth pH range and if that offers a special competitive advantage in environments with frequent fluctuations in pH such as the food processing settings.

**Methods**

For the fatty acid analysis, cells of *L. monocytogenes* 10403S and its sigB mutant were grown to mid exponential phase at different growth pHs (5.0, 5.5, 6.0, 7.0, 8.0, 8.5 and 9.0) and cells were harvested with centrifugation and washed three times with distilled water. The fatty acids in the cells (wet weight) were saponified, methylated and extracted. The resulting methyl ester mixtures were separated by an Agilent 5890 dual tower gas chromatograph. Fatty acids were identified by the MIDI microbial identification system (Sherlock 4.5 Microbial Identification System). Transcription profiling of *L. monocytogenes* 10403S was carried out at 15, 30 and 60 min in order to capture an early, an intermediate and a prolonged expression response to alkaline shock using complementary DNA arrays from the Pathogen Functional Genomic Research Centre (US). Additionally, the transcriptome was checked after a long exposure in alkaline pH in order to compare short- and long-term cellular adaptations. To verify the microarray results the regulation of gene expression was confirmed by quantitative RT-PCR. Purified labelled complementary DNA was hybridised with *L. monocytogenes* genome microarray version 1.0 (PFGRC). The full genome array consists of 6347 70-mer oligonucleotides representing 2843 Open Reading Frames (ORFs) from *L. monocytogenes* reference strain EGD-e, and 1884 unique ORFs from strain F22365 (serotype 4b), 705 unique ORFs from strain H7858 (serotype 4b) and 915 unique ORFs from strain F6854 (serotype 1/2a) which are not present in the EGD-e strain’s annotated gene complement. The full 70-mer complement is printed twice on the surface of the microarray. TIFF images of the hybridised arrays were analysed using TIGR spotfinder (www.tigr.org/software) software, the data set was normalised by applying the LOWESS algorithm and using the TIGR-MIDAS software, significant changes were identified with SAM (significance analysis of microarrays; www-stat.stanford.edu/~tibs/SAM/index.html) software. Several controls were employed to minimise the technical and biological variations and ensure that the data obtained were of good quality. First, each ORF was present in triplicate in the array. Second, each RNA preparation was used to make probes for at least two separate arrays for which the incorporated dye was reversed. Finally, three independent RNA batches from each point were used.

**Results**

The fatty acids distributions varied at the acid and alkaline adaptation of the cells. An increase of the overall sum of branched chain fatty acids and a decrease of the straight chain acids occurred at alkaline adaptation and the opposite happened at the acid adaptation. The proportion of anteiso branched fatty acids significantly increased with the alkalinity of the medium on the expense of the iso fatty acids proportion. A mirror trend was found at acid pH values. However, little changes occurred at the mar-
Transfection in the Study of Malaria Parasites

Introduction

The malaria parasite

Malaria has plagued humans throughout recorded history and results in the death of between 1.5 and 2.7 million people per year – mainly young children - in Sub-Saharan Africa alone. Four species of the protozoan parasite *Plasmodium* are infective to humans, and two of them, *Plasmodium falciparum* and *Plasmodium vivax*, are the most prevalent. *P. falciparum* causes the most severe form of malaria in humans. Genetically, *P. falciparum* is related to *P. reichenowi*, which causes chimpanzee malaria, while *P. vivax* clusters with simian malarias. The non-human primate malaria, caused by *P. knowlesi*, a natural parasite of *Macaca fascicularis*, has a relatively broad host range extending to humans, where it causes a mild disease. The parasite is closely related to *P. vivax*, and many genes identified in *P. vivax* have homologues in *P. knowlesi*.

Transfection

“Transfection” is the introduction of recombinant DNA into cultured cells and has become an important tool for studying gene function and regulation. The development of transfection technology for blood-stage malaria parasites is of great importance in the postgenomic era. It provides a direct way in which to correlate genotype (the genetic makeup) with phenotype (the observable physical or biochemical characteristics of an organism), and this enhances the further understanding of parasite biology. The aim is to facilitate rational design of new vaccines and drugs, which are urgently needed to fight the malaria epidemic.

Current Knowledge

Genome and proteome decoded

During the past ten years, our understanding of many aspects of the biology of malaria parasites has increased dramatically. In particular, the complete genome sequences of *P. falciparum* and *P. yoelii* (rodent malaria parasite), the availability of transcriptome and proteome profiles, and the establishment of transfection techniques for asexual-stage malaria parasites all represent major achievements from the past decade. Now we are truly in the post-
Two ring-form *Plasmodium vivax* trophozoites within red blood cells are shown in this thin-film Giemsa-stained micrograph.

Drug resistance

Chemotherapy has become one of the major control strategies for *P. falciparum*. The development of drug resistance to virtually all of the currently available drugs, however, is causing a crisis in the use of these compounds for prophylaxis and treatment of this disease. In a recent review Cowman (2) discusses strategies to identify novel genes involved in the molecular mechanisms used by the parasite to circumvent the lethal effect of current chemotherapeutic agents.

Numerous approaches have been employed to identify the molecules responsible for drug resistance in *P. falciparum*. However, it was not until the recent development of stable transfection in this parasite that it became possible to prove the role of particular genes in drug resistance and characterise the nature of the specific mutations that contribute to the resistance phenotype. In a further review, Crabb (3) describes the contribution of various molecular genetic approaches to the dissection of drug resistance in *P. falciparum* as well as future possibilities in this field.

Transfection studies

Electroporation, or electropor permeabilisation, is a significant increase in the electrical conductivity and permeability of the cell plasma membrane caused by an externally-applied electrical field. It is usually used in molecular biology as a way of introducing some substance inside the cell: by loading it with a molecular probe or bringing in a drug or piece of coding DNA that can change the cell’s function. The development of an electroporation-based transfection method for *P. falciparum* has been very successful for the study of some genes but its efficiency remains very low. While alternative approaches have been documented, electroporation of infected red blood cells generally remains the method of choice for introducing DNA into *P. falciparum*. Skinner-Adams *et al.* compared four published transfection techniques in their ability to achieve stable transfections (4).

Methods to transiently and stably transfect blood stages of the human malaria parasite *P. falciparum* have been developed and adapted for gene-knockout, allelic replacement, and transgene expression in this organism. Crabb *et al.* (5) detail these methods, as well as approaches used to monitor transfectants during the selection process. The different plasmid vectors that are currently used for gene targeting and transgene expression are also described.

The apicoplast† and mitochondrion of the malaria parasite *P. falciparum* are important intracellular organelles and targets of several anti-malarial drugs. In recent years researchers have begun to piece together the metabolic pathways of these organelles, with a view to understanding their functions and identifying further anti-malarial targets. Tonkin *et al.* (6) describe a novel series of *P. falciparum* transfection vectors used to localise proteins involved in isoprenoid biosynthesis and the posttranslational processing of apicoplast-encoded proteins to the apicoplast, and a protein putatively involved in the citric acid cycle to the mitochondrion. To confirm the localisation of these proteins, they have developed a new immunofluorescence assay protocol using antibodies specific to the apicoplast and mitochondrion.

Transfection of *P. falciparum* has remained difficult and laborious due to a lack of suitable reporter genes* and low transfection efficiency. Militello *et al.* (7) evaluated the luciferase gene of *Renilla reniformis*, a sensitive mammalian reporter gene, and found that it can be expressed in *P. falciparum* and is easily detected by luminometry. Moreover, both firefly and *R. reniformis* luciferase genes can be co-expressed in *P. falciparum* and their respective enzyme activities can be measured from the same sample. Thus, the *R. reniformis* luciferase gene can be used as an experimental reporter gene and/or used in conjunction with the firefly luciferase.

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† The apicoplast is a plastid organelle, homologous to chloroplasts of plants, that is found in apicomplexan parasites such as *Plasmodium* spp. Like plant chloroplasts, apicoplasts are semi-autonomous with their own genome and expression machinery. In addition, apicoplasts import numerous proteins encoded by nuclear genes. The exact role of a plastid in parasites is uncertain but early clues indicate synthesis of lipids, heme and isoprenoids as possibilities. The various metabolic processes of the apicoplast are potentially excellent targets for drug therapy.

* Reporter gene (often simply reporter) is a gene that researchers attach to another they wish to study in cell culture, animals or plants. Researchers use a reporter to easily identify those that have taken up the gene, or which have incorporated it in the desired way into their chromosomes. A common reporter codes for an enzyme luciferase, which catalyses a reaction with a luciferin to produce light.

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gene where one gene would be used to control transfection efficiency.

Other transfection techniques developed for malaria parasite blood stages include episomal** transfection and targeted integration with linear constructs for the rodent parasite P. berghei, episomal transfection and targeted integration with circular DNA for the human parasite P. falciparum, and episomal transfection for the nonhuman primate malaria parasites P. knowlesi and P. cynomolgi.

### Experimental Research in a Monkey Model

Molecular biological studies on P. vivax are mainly hampered by the lack of a continuous in vitro cell culture. As P. vivax can only invade reticulocytes (immature red blood cells) in the human blood, the in vitro cell culture is restricted to a few cycles. To circumvent this difficulty, scientists use fresh blood from either humans or monkeys. One of us (JP) was given the opportunity to work in the laboratory of Dr. John Barnwell at the Center for Disease Control in Atlanta, Georgia. Dr. Barnwell’s laboratory is one of few to utilise the best characterised primate models: Aotus and Saimiri monkeys for P. vivax research. For transient transfection experiments, two splenectomised Saimiri boliviensis boliviensis monkeys were successfully infected with P. vivax isolate Sal I. When parasitemia peaked (typically between 1–3%), 4–5 ml whole blood were taken from the animal and the mainly trophozoite-infected erythrocytes were enriched using a cushion of 50% Percoll. The P. vivax-infected erythrocytes were then mixed with one of two luciferase markers under the control of the P. falciparum hrl3 5’ and hrl2 3’ or under the control of the P. falciparum cam 5’ and 3’ region of the genome. The mixture was then electroporated in order to give the highest parasite viability. The samples were maintained in an ex vivo culture for 22 hours before extracts were prepared and analysed for luciferase activity. Importantly, extracts from transfected P. vivax-infected erythrocytes showed clear luciferase activities for both types of luciferase, while no detectable luciferase activity was observed in the control experiments. The results were confirmed for each construct in two independent experiments. These data clearly indicate expression of both firefly and Renilla luciferase by P. vivax despite these reporter genes being under the control of P. falciparum regulatory elements. This suggests that P. falciparum and P. vivax, although phylogenetically distinct, share common motifs which influence gene expression and are recognised by a conserved machinery.

In a further experiment P. vivax-infected erythrocytes were challenged with the T. gondii dhfr-ts gene which confers resistance to pyrimethamine. After electroporation, the cells were then injected back into the animals. At the end of the experiment, pyrimethamine-resistant parasites were not observed in the animals.

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**Episome: unit of genetic material composed of a series of genes that sometimes has an independent existence in a host cell and at other times is integrated into the chromosome, replicating itself along with it.

### Conclusion

The development of transfection technology for blood-stage malaria parasites is of great importance in the postgenomic era, as it provides a direct way in which to correlate genotype with phenotype, in the understanding of this parasite’s biology. The hope is to facilitate rational design of new vaccines and drugs, which are urgently needed to fight the malaria epidemic. This is all the more important in view of the resistance, which the malaria parasites developed against virtually all currently available antimalarial drugs, thus causing a crisis for prophylaxis and treatment of this disease.

The recent development of stable transfection in malaria provides a gateway to the elucidation of the role of particular genes in drug resistance and to the characterisation of the nature of the specific mutations that contribute to the resistance phenotype, offering much hope for the future.

### Acknowledgement

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Air Travel and Foodborne Disease

The 344 passengers on the flight from Anchorage to Copenhagen had just finished a hearty breakfast and gotten comfortable in their seats. Then one of the travellers had a strange feeling in his abdomen. He reached the lavatory just before having to vomit. Within an hour a dozen passengers also developed gastrointestinal problems. The passengers complained of nausea, vomiting, abdominal cramping and diarrhoea. The lavatory was constantly occupied and more and more passengers reported being sick to the flight personnel – some of whom obviously also did not feel well.

When the Boeing 747 landed in Copenhagen after a stopover in Paris, the hygienic conditions in the airplane were catastrophic. Airsickness bags filled to the brim lay between rows of seats, the floor of the aisles was covered with vomitus, and the toilets were contaminated with faeces. Altogether during the 9-hour flight, 196 passengers (57%) became ill with an acute gastroenteritis. Of those infected 88% had developed diarrhoea, 82% vomiting, 74% abdominal cramps and 68% nausea. Canadian, Danish, and American infectious disease specialists identified the cause to be an omelette topped with two ham slices that had stood at room temperature for over 14 hours and had been stored for another 14 hours at 10°C. Phage typing from samples taken from the ham and the omelette as well as from stool and vomit of ill passengers identified Staphyloccocus aureus phage group III. The same phage group S. aureus was isolated from a sore on the right hand of the cook who had prepared the omelette. In addition, Staphylococcus enterotoxin was detectable in the remains of the dangerous breakfast. Therefore, the diagnosis of staphylococcal food poisoning was definitively confirmed.

This episode from the year 1975 is not an isolated case. 17 years later on board a flight from Lima to Los Angeles an even greater medical catastrophe was initiated. Out of 336 passengers 75 (22%) became ill with acute diarrhoea and vomiting one to six days after their arrival in Los Angeles. Stool samples showed the presence of V. cholerae 01, the same type of pathogen that was causing a fulminant epidemic in Peru and its surrounding countries at the same time. Ten passengers required hospitalisation and one of them died. A salad containing seafood, which a catering company in Lima had prepared, was identified as the source of the infection.

Every year around one billion people entrust themselves to air travel, 50 million of which start in developing countries with poor hygienic conditions. How many passengers become ill from the flight itself is unknown. A recently-published article came to the conclusion that the risk of a common-vehicle infection during a flight is considerably higher than with other forms of pathogen transmission such as contact, airborne, or vector borne. Salmonella, Shigella, vibrios, Norwalk-like agents and enterotoxin-producing staphylococci were up until now identified as the cause of in-flight meal common-source epidemics. Since 1947 there has been documentation of a total of 41 epidemics with more than 5,000 cases and a total of 11 deaths. Salmonella-caused enteritis was the most frequent type of illness (approximately 4,000 cases and seven deaths). Eight epidemics were caused by Staphylococcus aureus enterotoxins, three by vibrios, one by Shigella and one by Norwalk-like agents.

The actual incidence is presumably much greater, for it is often difficult to recognise an in-flight foodborne outbreak. There are several reasons: once the passengers reach their destination airport, they depart in all directions. If they became ill with enteritis a few days later, the relationship to a flight is seldom made by the attending physician. More often it is presumed that the cause was an intestinal infection contracted during the stay in the departure country, particularly when the passenger had been staying in a developing country. Even if a cluster of illnesses exists, it is often difficult to obtain data from the remaining flight passengers and to obtain adequate sample material. Furthermore, it is usually impossible to identify the source of infection in retrospect, since following the end of the flight the incriminating food usually lands among tons of garbage.

The difficulty for the infectious disease specialist to clarify an in-flight foodborne epidemic can be seen in the example of a recent Staphylococcus enterotoxin poisoning. A catering company from Illinois had delivered a chocolate dessert to different intercontinental flights departing from Los Angeles. On two different flights to London eight and four passengers became ill (including the captain, who had to be hospitalised in London.) Another 14 passengers became ill on a flight to Tokyo. Since the beginning of the illness stretched over three days, the correlation to a common event was extremely difficult. Only when it became clear that the affected passengers of all three flights had eaten in economy class was it possible by comparing the menus to identify the dessert as the source of infection. Remains of the chocolate cake contained >10^6 S. aureus colony-forming units per gram, and the phage typing of the dessert and of the stool samples of the patients revealed the same phage group.

How often the food served in an airplane is bacterially contaminated can only be conjectured. A survey of in-flight foods conducted in the UK in 1989 showed 24% of 1,013 samples to be significantly contaminated with pathogens, from Salmonella to E. coli and Bacillus species.

Catering companies that specialise in airline meals have large kitchens that produce several tens of thousands to 100,000 meals per day. Before the meals are served to the passenger in the air on simple plastic to fancy porcelain dishes, they have undergone a lengthy and complex production and variably long transport time in possibly strongly fluctuating outdoor temperatures. Warm meals are basically prepared on the ground, cooled after cooking and reheated in the airplane galley. The capacity to keep the individual meals cooled on board is limited. The counter space available for galley activities is minimal and is concurrently used for snacks, main dishes, desserts, drinks, glasses, etc. Garbage has to be stored in a minimal amount of space. These are all critical factors for good food hygiene. Presumably the long transportation time, lack of cooling and inadequate cooking time during the food preparation are the significant risk factors for an in-flight common-source epidemic. New trends in flight catering augment the risk even further.

The competition among the airline companies has lead to more exquisite menus – at least for the passengers in business and first class. Thus, there are transatlantic flights with a renowned cook on board, who gives the prepared meals the finishing touch, whether it be shrimp cocktail, veal fricassee, bamboo shoots or filet of sole. Without a doubt these are culinary
delicacies, but onboard an airplane they should be enjoyed cautiously due to the difficult microbiological conditions. Obviously, the more elective and sophisticated in-flight meals become, the higher are the requirements for correct food handling.

An underestimated problem up to now is the relatively weak food hygiene knowledge of the flight attendants. During a routine check a controller ascertained that, for lack of any other space, a flight attendant had temporarily placed a tray of sushi on the toilet! Only recently have flight attendants systematically been trained in food hygiene. The training ranges from goods receipt storage and cleaning to re-heating and serving, and from critical ice handling to refuse disposal.

Moreover, although temperature control is crucial to all food safety, there is no existing post-dispatch documentation system. Ten of good receipt temperatures, storage or re-heating. A further problem is that the flight personnel themselves eat and drink at different locations day after day, possibly having been exposed to contaminated food, and likely becoming an asymptomatic carrier of pathogenic microorganisms.

Experts suggest dividing foods into different risk classes, strictly banning those with the highest risk of infection from flights. The category of dangerous items includes products that may constitute a risk either as such or due to improper heating on board, such as raw milk, undercooked poultry, raw and undercooked eggs, as well as raw sprouts, meat, fish, and shellfish. The high-risk class includes items that are intensively handled after heating, for instance de-boned, peeled, or stuffed. The lowest risk lies in acidified foods, fruits that can be peeled, canned fruit, bread, and dry baked foods.

Since food contamination can never be completely ruled out despite all safety precautions, the captain and co-pilot should at least receive a different menu than the passengers. The author is reminded in horror of the long-distance flight with a Russian carrier, on which the flight attendants brought the first meal to the cockpit—long before the passengers had been served. If staphylococcal enterotoxins had been part of the menu, the captain and co-pilot would have become index cases of an in-flight foodborne epidemic infection.

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How clean are surfaces in commercial aircrafts?

In a recent study from the San Diego State University C.J. McManus and S.T. Kelley sampled armrests, tray tables, toilet seats, bathroom sinks, floors, handles on the outside of lavatories and inside door knobs by wiping these surfaces with Kimwipes at the end of domestic and international flights. The DNA was extracted and PCR clone libraries were made from the DNA samples using bacterial-specific 16S ribosomal DNA. Using the evolutionary-conserved bacterial small subunit rDNA, PCR clone libraries were created and matched against sequences documented in GenBank. Samples collected from the cabin surfaces had an undetectable level of DNA and produced no PCR products. However, bacterial diversity was high on lavatory surfaces such as indoor handles, toilet seats, sink faucets and paper towels. In this environment 58 different bacterial genera were identified including Streptococcus, Staphylococcus, Corynebacterium, Propionebacterium and Kocuria. These findings highlight the importance of strict food hygiene for food stored and prepared in the aircraft, as pathogens might be spread from the toilet to other compartments of the aircraft.

MRSA and Other Unlearned Lessons

This article is being reprinted in a shortened version with permission from: Don’t pick your nose, Hugh Pennington on MRSA: London Review of Books 2005, 27 (24).

MRSA is a very British abbreviation. M stands for methicillin, first called BRL1241 because it was developed during the 1950’s in the Beecham Research Laboratories at Betchworth in Surrey. R stands for Resistant; the development of methicillin resistance in a hospital was first detected in October 1960 at Guildford, also in Surrey. And S stands for Staphylococcus aureus, discovered in the late 1870’s at Aberdeen by Alexander Ogston, surgeon at the Royal Infirmary. William Duguid Geddes, the Professor of Greek at Aberdeen, suggested “Staphylococcus” to Ogston – Greek kokkos = grain and staphyl = bunch of grapes – because it described what he had seen in pus under the microscope. Ogston published the name in 1882. And Alexander Fleming was studying Staphylococcus when he discovered penicillin in 1928, and the first patient to be treated in the first clinical trial of the new antibiotic at Oxford was infected with it.

Penicillin revolutionised the treatment of staphylococcal infections. But its power over them began to wane soon after its general introduction. Britain led again. The first naturally occurring penicillin-resistant staphylococci were noted by Alexander Fleming in 1942. In April to November 1946, 12.5% of Staphylococcus aureus strains isolated at the Hamme-smith Hospital in London were penicillin-resistant. By early 1947 the percentage had tripled. The bacteriologist Mary Barber showed that this rise was not due to the development of resistance while patients were being treated. It was caused by the spread of a penicillin-resistant strain in the hospital.

Methicillin was developed in response. Optimism was very high. In the 1960 Lancet paper describing it, its discoverers wrote “resistance to BRL 1241 comparable to that which exists to penicillin G would require the ability to inactivate BRL 1241 by a new penicillinase. Since cultures have not been encountered showing this property, it seems unlikely that the selection and proliferation of resistance strains will take place rapidly, if at all”. The logic
was impeccable – but only if the destruction of penicillin by penicillinase was the sole way a staphylococcus could become penicillin resistant. It was not. Less than a year after the publication of the optimistic prediction in the Lancet, the first MRSA were described. Two years later, in 1963, there was the first British hospital outbreak. It was in Surrey. An MRSA strain at Queen Mary’s Hospital for Children at Carshalton spread to eight of the forty-eight wards, infecting 37 patients and killing one.

The evolution of MRSA continued. Its progress followed the ‘Barber effect’, in which new antibiotic-resistance characters add on to previously acquired resistances in staphylococci good at spreading in hospitals. But in Britain about a decade went by before MRSA became a widespread problem needing specific action. There were hospital outbreaks in the 1970s; by the early 1980s MRSA epidemics were being described in Australia, Ireland and London.

Surrey has appeared often enough in the early history of MRSA for common sense to identify to it as the ultimate source of all our current crises. But it was not. The MRSA of today have no recent source of all our current crises. But it was sense to identify to it as the ultimate early 1980s MRSA epidemics were being described in England, Ireland and London.

There is a striking historical hospital infection parallel: “It is no question of unsanitariness or of overcrowding….or of the other factors that have been proposed. They are only side issues, important in their way, but side issues all the same. It is the actual infection that matters; it is the chronic cases, the carriers, who keep the…infection going…. They form the keynote of the problem, and must be detected and isolated before any permanent good can be done.”

There is much to be learned from this. One is that the history of hospital infection is not just a story of the infectious agents. It is also a story of the people who work in hospitals, and of the ways in which they interact with each other and with the patients they treat.

One of the most important lessons is the importance of communication. In the early days of MRSA, there was little communication between hospitals. This was a mistake. It is now clear that MRSA can spread from one hospital to another very quickly. The key to controlling MRSA is to ensure that all hospitals are aware of the patients who are infected, and that they take steps to prevent the spread of MRSA.

Another important lesson is the importance of education. It is not enough to control MRSA by simply isolating infected patients. We also need to educate all hospital staff about the risks of MRSA, and about the best ways to prevent its spread.

Finally, we need to remember that MRSA is not the only problem that hospitals face. There are many other problems, and we need to address them all. To do this, we need to work together, and to remember that we are all part of a larger community.

In conclusion, the history of MRSA is a cautionary tale. It shows us that we need to be constantly vigilant, and to ensure that we are doing all we can to prevent the spread of MRSA.

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The risk of hospital acquired infection from 
Staphylococcus aureus has not had the attention it deserved because its list of famous victims is so short. Even famous illnesses caused by it have escaped bacteriological attribution. Queen Victoria’s armpit abscess in 1871 poured pus for days after it was cut open by Joseph Lister. All that is remembered is the carbolic acid spray getting into her eyes. Rommel’s swollen nose caused him to leave North Africa just before the battle of el Alamein to recuperate. Monty gets all the credit still. Failure to recognise the importance of Staphylococcus aureus has not been confined to hospital chief executives, journalists and members of the public. Their hand hygiene habits show that many hospital staff have been unaware of it as well.

Since 2000 UK Health Departments have responded to MRSA by announcing many initiatives. In contrast their current target of reducing MRSA bacteraemias by half by 2008 is very modest. The number of MRSA bacteraemias is a surrogate measure for non-trivial infections. Reducing them by half means the same for lethality. Achieving this target means that MRSA will still be killing more people than all the microbial causes of food poisoning put together; Salmonella, Campylobacter, Listeria, E.coli 0157 and noroviruses are just some in the list. So there is a paradox. The outbreak of MRSA concluded “lastly, and most important, patients harbouring these rare strains must be isolated, vigorously treated, and preferably should be sent out of hospital as soon as possible.” The words of Jean Bradley and her colleagues describing in 1985 a two-year-long MRSA outbreak at the Royal Free Hospital in London were prophetic: “several authors have reported failure to contain MRSA infection without an isolation unit: hospitals without such facilities, or as at this hospital, unable to finance the staffing of a unit may find that this epidemic MRSA will pose a considerable threat to their clinical practice.”

When EMRSA appeared beyond their borders the Dutch decided to keep them out by a policy of “search and destroy”. Infected and colonised patients are segregated in strict isolation, and colonised staff treated and kept away from patients. Vigorous screening, and properly staffed isolation facilities have been key features of this policy. Its success has shown that Barber and Stewart and Bradley were right. But search and destroy was never adopted country-wide in the UK, and for MRSA, Britain has become the sick man of Europe.

The National Audit Office (NAO) Progress Report Improving patient care by reducing the risk of hospital acquired infection (The Stationery Office, July 2004) opens with a map showing the proportion of Staphylococcus aureus bacteremia isolates resistant to methicillin in various European countries. At 43.9% the UK has the highest; in France it was 32.8%, Germany 18.7%, and in the Netherlands 1%.

Only in the 21st century has Staphylococcus aureus, as MRSA, attracted much attention from British politicians. The death of Michael Howard’s mother-in-law from a hospital infection at its beginning may be relevant. He made its control an issue in the 2005 General Election Campaign. Risk theorists claim that top level support for safety spending is much greater for air travel than for oil refineries because chief executives use the former a lot but never go near the latter. Personal involvement counts. Staphylococcus aureus has not had the attention it deserved because its list of famous victims is so short. Even famous illnesses caused by it have escaped bacteriological attribution. Queen Victoria’s armpit abscess in 1871 poured pus for days after it was cut open by Joseph Lister. All that is remembered is the carbolic acid spray getting into her eyes. Rommel’s swollen nose caused him to leave North Africa just before the battle of el Alamein to recuperate. Monty gets all the credit still. Failure to recognise the importance of Staphylococcus aureus has not been confined to hospital chief executives, journalists and members of the public. Their hand hygiene habits show that many hospital staff have been unaware of it as well.

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Not an Easter egg but …

What appears to be a fluorescent Easter egg is actually an oocyst of Isospora belli. Infections with Isopora belli and Cryptosporidium spp. are an important cause of diarrhoea in HIV-infected individuals including children. The use of Auramine O to stain the sample allows the rapid and easy detection of these coccidian parasites. Photograph courtesy of Thomas Hanscheid, Lisbon.

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More detailed information about ESCMID courses and conferences as well as general information about other events can be found on the ESCMID website at www.escmid.org under Courses & Workshops, ECCMIDs & Conferences, or Calendar of Events, respectively.

ESCMID events

15–16 May 2006
35th ESCMID postgraduate education course: Update in paediatric respiratory tract infections
Place: Vilnius, Lithuania
Contact: Conbaltas UAB
Phone: +370 5 212 0003
E-mail: course@balticconference.com
Internet: www.escmid.org/education

26–28 May 2006
36th ESCMID postgraduate education course: Detection and characterisation of metallo-beta-lactamases
Place: Verona, Italy
Contact: Marco Moschin
Phone: +39 041 52 62 530
E-mail: icc@icorganization.it
Internet: www.escmid.org/education

29–31 May 2006
ESCMID conference on ESBLs
Place: Venice, Italy
Contact: ICO
Phone: +39 041 52 62 530
Email: icc@icorganization.it
Internet: www.escmid.org/conferences

18–24 June 2006
39th ESCMID postgraduate education workshop: Mechanisms of antimicrobial resistance. A practical approach
Place: Palma de Mallorca, Spain
Contact: Sebastián Alberti
Phone: +34 971 173535
Email: sebastian.alberti@uib.es
Internet: www.escmid.org/education

25–28 November 2006
41st ESCMID postgraduate education course: ESCMID-SHEA training course in hospital epidemiology 2006
Place: Baden/Vienna, Austria
Contact: Alice Haindl
Phone: +43 2236 46541 116
Email: alice.haindl@aesculap-akademie.at
Internet: www.aesculap-akademie.com

Contact: Irja Roots
Phone: +372 737 4170
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Phone: +372 737 4170
E-mail: irja.roots@ut.ee
Internet: www.escmid.org/education

Endorsed by ESCMID

7–9 September 2006
XIX international workshop on helicobacter and related bacteria in chronic digestive inflammation
Place: Wroclaw, Poland
Contact: European Helicobacter Study Group (EHSG)
Internet: www.helicobacter.org/2006/

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