## ESCMID News

### ESCMID European Council 2003 – Minutes

### ESCMID Workshop on Challenges in CM and ID

### European Centre for Disease Prevention and Control: ESCMID Position Paper

### Meeting Report on the European Conference on Antibiotic Resistance

### Phagocytosis of rickettsiae by an endothelial cell (see page 8)

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### Phagocytosis of rickettsiae by an endothelial cell

(see page 8)
Research and innovation are the life-blood of any organisation claiming to represent those involved in the science and practice of microbiology and infectious disease. It is therefore gratifying to witness the expanding influence of ESCMID in this area. Firstly, the increasing quality of the Society’s annual ECCMID has been widely recognised. The programme has considerable depth and breadth and the quality of submitted abstracts continues to improve. In addition, the Society is increasingly influencing the European research agenda. Two examples are worth highlighting. Firstly, members are advising the European Commission on the research focus for successive calls within the Sixth Framework Research Programme. Secondly, the Society was given responsibility by the European Commission to co-organise the meeting in Rome on the “Role of Research in Combating Antibiotic Resistance”. At the time of writing, the programme has been defined and the resulting recommendations will hopefully influence future research direction in Europe. Both of these examples are likely to ensure continued funding for research into topics of microbiological and infectious disease interest. As Chairman of the Publications and Awards Committees, excellence in research impacts significantly on these two areas of the Society’s activities. Scientific publication has a particular relevance, even in a world of rapid change. The aphorism that “If it isn’t published it doesn’t exist!” remains true today as it did in the past. Scientific publishing has traditionally been taken out of the hands of the scientific community and placed in the hands of publishing houses, largely for economic reasons. Publishers have assumed responsibility for not only printing and distribution, but also non-scientific editing and journal promotion. Inevitably, the price of academic journals has been strongly influenced by this commercial arrangement, as indeed has the spiralling number of biomedical journals. Recognition that access to knowledge is a fundamental human right is beginning to challenge these traditional arrangements, and also happens to coincide with shrinking library budgets and rising subscription charges. All this has much greater impact on the transfer of scientific knowledge and technology in developing countries where even the internet revolution has still not solved this paradox of supply and demand. Here it is interesting to note a recent decision by the Public Library of Science to launch its first free journal. This is an exciting and challenging development. Professional and scientific societies, which publish journals, will need to examine the principles and economics that govern such activities. We are clearly in a new era, in which it will be necessary to address issues of copyright ownership, funding the peer review process and ensuring that the costs of electronic publishing can be met, thus facilitating the demand for easier access to knowledge. This edition of ESCMID News provides the regular features from the Society’s Officers, details of future activities, News in Brief and other articles of interest including a farewell message from Emilio Bouza, who, as Editor-in-Chief, has made an enormous contribution in driving the increasing success of Clinical Microbiology and Infection. There is also a challenging contribution concerning the position of microbiology and infectious disease as distinct disciplines in Europe by Fernando Baquero. In addition, this ESCMID News includes a presentation of and comment on the recently published FEMS European Declaration for Microbiology. Do provide feedback on any area of interest to the Society and its members.

Roger Finch
Past President
President Publication Committee
Message from the President

Dear Colleagues,

As 2003 has just come to a close when you are reading these pages, it is a pleasure to highlight three areas of ESCMID activities which are advancing the art and science of the combat against infectious diseases. In the field of science, ESCMID has co-organised the “European conference on the role of research in combating antibiotic resistance” in Rome, November 28-30 with the Directorate General Research and Technological Development of the European Commission (see report on page 21). I wish to express my sincere thanks to our Secretary-General, Giuseppe Cornaglia, as the organiser of this successful conference that attracted 160 delegates from 30 countries, including biomedical scientists, microbiologists, clinicians, epidemiologists and representatives from the pharmaceutical and biotechnology industry. Participants reviewed the current knowledge and identified gaps in our understanding of antimicrobial resistance in human pathogens in the broader context of microbial ecology and evolution and the epidemiology of infection caused by resistant pathogens.

The conference’s recommendations on research priorities and technologies to be developed to generate innovative treatment and prevention strategies will be published early next year in Clinical Microbiology and Infection. I am confident that these recommendations will provide information for both national research funding programmes as well as for future calls for proposals under the EC 6th Framework Programme for Research and Technological Development, which has identified combating resistance to drugs as one of its priorities. The conference participants also emphasized the problem of severe under-funding in this research area and recommended that the infectious disease and microbiology community should make the public and political policy-makers much more aware of the public health and economic costs of infectious diseases caused by resistant micro-organisms. We recognise that ESCMID has an important role to play in advocating the importance of this health problem and developing public awareness campaigns to this effect. It was also underlined that the time has come to foster a climate of active partnership between all stakeholders, health authorities, industry and academia. This dialogue is needed to strike a better balance between public health needs for new anti-microbial drugs on the one hand and the economic constraints of drug research and development on the other hand.

A second aspect that I find important for the society to address and in fact by all of us as medical professionals and citizens is public health policy. Control of communicable infections is a pressing public health challenge of global proportion. In this context, we warmly welcome the proposal by Commissioner Byrne to establish the European Centre for Disease Prevention and Control by 2005. As the Union is about to enlarge to 25 member states and a population of 450 million citizens this represents a timely step toward better co-ordination of surveillance and control of communicable diseases in Europe and beyond.

Effective infection control and prevention requires close co-operation between laboratory scientists, epidemiologists and public health practitioners. ESCMID holds the view that developing laboratory facilities at the level of the European CDC would provide a more credible capacity to respond to emerging and re-emerging infectious diseases. Furthermore, establishing central European laboratories to support communicable disease surveillance and provide international training would greatly facilitate the development of common responsibility among professionals across countries. There is a clear historical opportunity to boost this approach by physically linking the establishment of the European CDC to that of new centres of networks of excellence in infectious diseases and anti-microbial resistance research. I invite you to read the ESCMID Position Paper on the Commission’s proposal (page 18 in this issue) as our contribution to the current political discussions taking place in the European Parliament and Council of Ministers. Once again, your feedback is welcome on this and other policy issues that will shape our future ability to manage the microbial threat in Europe.

A last field of activity that I would like to bring to your attention is education, our major mission as a learned society. The second session of the ESCMID School has been held successfully last summer, as reported on page 12 of this issue, as well as several post-graduate education courses that have furthered scientific and clinical excellence across Europe. The needs are much greater and new educational initiatives are being developed. These will begin with pre-congress courses and workshops to be offered in Prague prior to the 14th ECCMID, to which I encourage you to register early to take benefit of the exciting scientific programme (see www.escmid.org/eccmid2004) and make sure that your original research findings receive the international attention that they deserve.

I wish you a fulfilling New Year at both the personal and professional levels.

Marc Struelens
President, ESCMID

Marc Struelens
ESCMID
Larger monthly issues with more pages and more content: In addition to an increase in the number of pages per issue, a new format in conjunction with systematic editing for conciseness will allow the inclusion of additional papers per issue, with an associated reduction in acceptance-to-publication times.

Pre-publication: Papers will be published online, in an officially citeable format, immediately upon final approval of proof pages, and will subsequently appear in hard copy.

Resolution of publication delays: The current backlog of accepted papers will be steadily reduced to normal proportions during 2004. Our aim for 2004 is to publish papers online within 60 days of acceptance, and in hard copy within six months of acceptance. A “fast-track” process for topical papers of exceptional quality will allow earlier publication in hard copy.

Online editorial process: The implementation of Manuscript Central has made it possible for papers to be in the hands of reviewers within hours of submission and for authors to have ongoing access to information about the status of their submission within the process.

E-proofing: Authors will shortly receive proof pages via a website rather than as email attachments. This is consistent with the online editorial system and a natural extension of the traditional pdf proofing system, with a number of advantages including increased speed of proof delivery to authors.

Reprints: As an upgrade from the traditional allowance of a limited number of complimentary hard-copy reprints, corresponding authors will now be provided with a pdf of the final published version, allowing all authors of the paper to create reprints for personal use.

Supplements Editor: The appointment of an Editor solely responsible for Supplements will allow a greater emphasis on topical and special interest publications and should result in more issues for the same subscription fee.

Decentralised Editorial Board: Granting Editors direct responsibility for soliciting Reviews will bring broadened competency into the editorial process, and placing Editors in direct communication with Authors will allow more people from more countries to actively participate in establishing editorial policy and in making editorial decisions.

Augmented Impact Factor: The timely publication of a greater number of quality papers will surely improve an Impact Factor which already places CMI among comparable journals in our field.

Finally, a new cover design for the Tenth Volume will accompany CMI into its second decade.

With all good wishes for the New Year,

Judith Crane

On behalf of the Editorial Team
Farewell Message from the CMI Editor-in-Chief

As I reach the end of my term (June 2000–December 2003) as Editor-in-Chief of Clinical Microbiology and Infection, on behalf of the Madrid team and myself, I would like to say goodbye to our readers and authors. During this period, CMI was offered considerably more scientific material for publication and our rejection rate has been adjusted accordingly. Therefore we have increased the number of pages published. We have produced many monographic issues and supplements that have been welcomed by our readership. Finally, the first Impact Factor for CMI was announced this summer, with a rating of 1.2.

None of this would have been possible without the dedicated and continuous work, which we have carried out to the best of our ability, and which would not have been possible without the contributions and loyalty of our authors and readers.

The Journal now faces new challenges such as, in my opinion, the use of a totally electronic editorial system. Increasing the number of pages will allow CMI to accept and publish more quickly the large quantity of good scientific material received.

The appointment of Kevin Towner as Editor of the monthly issues and Carl Eric Nord as Editor of supplements is an excellent decision and represents the Society’s firm belief in the future of the Journal. According to a recent survey among members, the Journal is one of the most valued assets of our Society.

We should like to conclude by expressing our satisfaction and our gratitude. We thank the Society and the Executive Committee for their faith in us during this period, the authors for their contributions and criticism, and the readers for their encouragement.

The opportunity to serve ESCMID and its members has been an honour and privilege we shall never forget.

Thank you.

Emilio Bouza Santiago
CMI Editor-in-Chief

Microbial Typing Technologies:
Practical Course with Theoretical Support
24TH ESCMID POSTGRADUATE EDUCATION COURSE
WARSAW, POLAND, APRIL 25–30, 2004

This course is organised by ESGEM. It is aimed at clinical microbiologists who have little theoretical knowledge of DNA-based typing and wish to acquire the practical and theoretical skills for both pulse-field gel electrophoresis (PFGE) and polymerase chain reaction (PCR)-based methods.

For further information please contact: Dr Joanna Empel, Phone +48 22 851 43 88, Email jempel@il.wwaw.pl or consult the ESCMID website (www.escmid.org), Courses & Workshops.

Measuring, Auditing, and Improving Antimicrobial Prescribing
27TH ESCMID POSTGRADUATE EDUCATION COURSE
PRUHONICE, CZECH REPUBLIC, APRIL 29–MAY 1, 2004

This course is organised by ESGAP and will take place directly before the 14th ECCMID 2004 and is intended for medical doctors, scientists and clinical pharmacists, who are involved in antibiotic policy activities. The topics are: the measurement of antimicrobial consumption in the community and in hospitals, the relation of consumption/antimicrobial prescribing with resistance, audit methodologies for monitoring the quality of antimicrobial prescribing and possible interventions.

For further information please contact: Dr. Vlastimil Jindrak, Phone +420 25727 2280, Email vlastimil.jindrak@homolka.cz or consult the ESCMID website (www.escmid.org), Courses & Workshops.
ESCMID EUROPEAN COUNCIL 2003

Minutes

MEETING DURING 13th ECCMID 2003, GLASGOW, SCOTLAND, UK MAY 11, 2003

1 WELCOME AND PRESIDENT’S ADDRESS

Roger Finch welcomed the participants to the meeting of the European Council 2003. He especially welcomed the representatives of the Hospital Infections Society of Turkey and the Interregional Association for Clinical Microbiology and Antimicrobial Chemotherapy of Russia. These societies were accepted as new member organisations during the past year. A total of 98 country representatives, representatives from the associated specialist societies and study group chairpersons were invited, 50 thereof attended.

The meeting agenda was distributed on time and the meeting minutes for 2002 were published in ESCMID News 3-2002.

Roger Finch paid tribute to Professor Arturo Visconti who passed away a few days ago at the age of 79. Arturo Visconti was one of the founding members of ESCM, which developed later into ESCMID, and the President of the 1st ECCM in 1983 in Bologna. Many will remember his style and aptness in Clinical Microbiology.

The mission of ESCMID is to promote excellence in CM and ID. From the many activities in 2002 devoted to this goal he mentioned only a few. For a more detailed account he referred to his message in ESCMID News 1-2003:

i) Education: The 1st ESCMID School, a one-week interactive course devoted to postgraduate and continuous medical education in CM and ID, took place in summer 2002 in Lausanne. Twenty-seven participants attended. The 2nd ESCMID School will take place in 2003 in Utrecht.

ii) Professional affairs: Main concerns were the accreditation of CME activities with UEMS and the promotion of the recognition of CM and ID as independent specialities in those countries where this is not the case.

Other projects related to the cooperation with the European Commission in organising a Conference on the Role of Research in Combating Antibiotic Resistance in November 2002 in Rome.

iii) Science: Convener and support of EUCAST which is undertaking a new start under the leadership of Gunnar Kahlmeter with the goal of achieving harmonisation of methodology and breakpoints across Europe. Two applications for EU research grants from DG Research (6th Framework Programme) and DG Sanco (Public Health Programme) have been submitted.

iv) Clinical Microbiology and Infection: editorial transition from Emilio Bouza, Madrid to Kevin Towner, Nottingham for the monthly issues and Carl Erik Nord, Stockholm, for the supplements.

2 COOPERATION BETWEEN EUROPEAN SOCIETIES

Roger Finch started by referring to his statement of the previous year that the current multiplicity of European congresses with similar topics is wasteful of resources and hard to justify.

ESCMID has started together with FESCI and ISC a process of convergence and reached a state of negotiating a detailed proposal for a joint ECCMID/ICC in 2007. If successful, the model could be extended to joint ECCMID/ECcs in the following years. It is self-evident that the final proposal, which needs to be agreed to by the ESCMID membership, must guarantee an income stream for ESCMID sufficient to carry on with its agenda. In summary: The spirit of cooperation is real but progress slow.

Questions from the floor:

1 Which European congresses should be integrated with ECCMID? Roger Finch responded that the current focus is on ICC. A successful model of cooperation could probably be easily applied to both ICC and ECC. Another occasional Congress in Infectious Diseases taking place in Europe is ICID. The initial proposal to organise a joint ECCMID/ICID in 2006 in Europe however was unsuccessful.

2 Is there a feedback from sponsors concerning joint congress organisation? According to Roger Finch all companies, which have been asked strongly support the concept of a single European Congress of Clinical Microbiology and Infectious Diseases.

3 COOPERATION WITH NATIONAL SOCIETIES IN THE EXPANDING EU AND OTHER COUNTRIES

Roger Finch reported that in December 2002 a delegation of the ESCMID Executive was invited to Moscow for discussions with representatives of the Russian Ministry of Health and the Russian Academy of Medical Sciences (RAMS). The visit resulted in a Memorandum of Collaboration between RAMS and ESCMID in the field of educational conferences and workshops, publication and study groups.

4 AFFILIATION OF EUROPEAN SPECIALIST SOCIETIES

Affiliation is a process whereby European specialist societies and ESCMID cooperate to promote the wider interests of both organisations as described by Peter Schoch. Since 2001 a pilot scheme with the British Infection Society, the Swiss Society for Infectious Diseases and the Italian Association of Clinical Microbiologists has been in operation. Benefits for the national societies include the provision of ESCMID News, electronic mailings, discount at ECCMIDs and CMI subscription at the same preferential rate as ESCMID members. The cost has been set at EUR 5 per member per year. The Executive recently assessed the current affiliation programme with the following results:

i) Professional cooperation of the infection societies across Europe must be strengthened, ESCMID is the natural platform for this.
ii) The current pilot affiliation scheme however has been too attractive in comparison with regular membership. ESCMID has not only incurred a budget deficit but is also losing members.

Proposed actions: The Executive is seeking feedback from the pilot societies about strengths and weaknesses of the current scheme and will then formulate new proposals that support the general principles of affiliation. The revised scheme must be cost neutral for ESCMID. It will be discussed with the European Council after which their constituent societies will be invited to become affiliated with ESCMID under the new scheme.

Questions from the floor:
1 What is the relationship with FEMS? Peter Schoch responded that a Memorandum of Collaboration is currently being worked out. It will mention joint activities in the fields of education and research fellowships.

2 What are the models for new affiliation schemes? The discussion about new models has just started with no definite proposal yet, but it will be important, as generally agreed, that affiliation results in an increase of ESCMID’s membership and not a loss.

3 An electronic ESCMID News would allow lowering the membership fee and help protect ESCMID’s membership base. Are there plans along these lines? An electronic newsletter is an option for affiliated members. Within the Executive there is agreement that we need an additional non-scientific output channel that is more comfortable than the internet as downloading and printing out newsletters is too cumbersome. Cost limitations should be achieved by limiting the number of pages and avoiding colour.

5 EBAID AND EBACM: TWO NEW CME ACCREDITATION BOARDS BY UEMS AND ESCMID

Peter Schoch referred to the new CME accreditation board EBAID (European Board for the Accreditation of CME in Infectious Diseases), which is a joint venture of the UEMS Section for Infectious Diseases and ESCMID. It is linked to EACCME, the European Accreditation Council for CME, which is an institution of UEMS. EBAID’s purpose is to assist EACCME in evaluating the quality of CME activities in the field of Infectious Diseases when national accreditation boards are not available. Further information and an online application form are available on ESCMID’s website www.escmid.org, CME / EBAID.

A related board is currently being set up with the UEMS Section for Medical Biopathology, Commission of Microbiology. It is called EBACM (European Board for the Accreditation of CME in Clinical Microbiology) and will be operational later this year.

6 ANY OTHER BUSINESS

Questions from the floor:
1 Why is Clinical Microbiology in UEMS a subspecialty of Medical Biopathology and not an independent speciality as in most European countries? Giuseppe Cornaglia could not explain when and why UEMS set up such a mixed specialty but referred to the fact that the legal authority to apply for a change is with the constituent organisations of UEMS, which are the national professional organisations of medical specialties. ESCMID has no power in this respect but would support any proposal by a UEMS member organisation towards establishing a UEMS Section of Clinical Microbiology.

2 Can you be more specific about ESCMID’s involvement in submitting EU research proposals? As explained by Roger Finch there were two proposals submitted up to now: One is CARRINE (Combating Antibiotic Resistance in Community-acquired LRTI), a Network of Excellence, led by Herman Goossens. ESCMID’s role would be the organisation of an educational platform. The second proposal was submitted to DG Sanco (Public Health Programme). It relates to funding EUCAST for the harmonisation of European breakpoints and was developed by Gunnar Kahlmeter.

3 What is the status of standardisation of Laboratory Guidelines in Clinical Microbiology? Roger Finch answered that such a standardisation does not exist but that, if there was general support, ESCMID could function as a repository for guidelines, both for assessment and communication.

The meeting adjourned at 13:45 h.

Basel, November 12, 2003

Roger Finch, ESCMID President

Peter Schoch, Managing Director
ESCMID Study Group for Coxiella, Anaplasma, Rickettsia and Bartonella (ESCAR)

ESCAR, formerly EUWOG, is the acronym for the ESCMID Study Group for Coxiella, Anaplasma, Rickettsia and Bartonella. What are the rationale and objectives for a Study Group in this field of infectious diseases and microbiology?

Rickettsiosis and related diseases are not only classical infectious diseases that caused thousands of deaths in previous eras. Currently, rickettsioses are emerging and re-emerging infections that cause many health problems not only in poorer countries but also in developed nations. The recent epidemic of typhus in Burundi with thousands of affected people, exemplifies re-emerging rickettsiosis. In some areas other classical rickettsioses as Mediterranean Spotted Fever, or Rocky Mountain Spotted Fever are endemic. Other infections caused by Ehrlichia, or Anaplasma sp. (ehrlichiosis), which have been recognised pathogens in mammals since the beginning of the 20th century in Europe. After the first European descriptions in humans, human granulocytic ehrlichiosis or human anaplasmosis was described Europe-wide, and we know that a large percentage of Ixodes ricinus ticks is infected by the etiologic agent Anaplasma phagocytophilum. Recently, a new species found in northern Italy has been described that could be a human pathogen (E. walkerii).

Bartonella infections are currently a significant problem worldwide. It has been demonstrated that B. quintana is the cause of new cases of “Trench Fever”, now called “Urban Trench Fever” because it affects urban homeless populations. This is an example of a re-emerging infection. We also know that B. henselae is one of the main etiologic agents of lymphadenopathy in children and young people and that Bartonella sp. are the main pathogens of culture-negative endocarditis. Sadly enough Rickettsia sp. and Coxiella burnetti are also “fashionable” bioterrorism threats. Although these agents are not easy to employ as biological weapons, they are still classified as Class B agents.

Obviously, almost all pathogens that we study in ESCAR also cause disease in other mammals, and they are of interest not only to physicians and microbiologists but also to veterinarians and other specialists.

The aim of ESCAR is to encourage basic and applied research in the field of rickettsiology and related diseases. ESCAR has approximately 300 members (medical doctors, microbiologists, scientists, veterinarians, pharmacists, etc.) from most European countries and many other countries around the world, including the USA, Japan, and Russia. Our main research fields are: epidemiology, genomics, taxonomy, diagnosis, physiopathology, immunology and therapy of rickettsiosis, bartonellosis, anaplasmosis, and coxiellosis in humans and animals.

We make recommendations on research issues related to rickettsiae and rickettsial diseases in order to advance basic understanding and knowledge in this field. ESCAR also advises government health agencies, if necessary, on important aspects of these diseases. In our periodical meetings the scientists involved in the research on rickettsiae and rickettsial diseases exchange and share information as well as materials. ESCAR holds its annual meeting during ECCMID and organises an international meeting in conjunction with the American Society of Rickettsiology every 3 years in different European cities. The previous one was hosted in 2002 in Ljubljana (Slovenia) and the scientific contributions are published in a special number of the Annals of the New York Academy of Sciences (1). The next meeting will be 19–22 June 2005 in Logroño (Spain).
We also support a European Network for Surveillance of Tick-borne Diseases. The main objective of this network is to report on tick-borne diseases by collecting epidemiological, clinical and laboratory data from patients referred to us by the different members. The network involves either reference laboratories, which already cover most of the demand for diagnosis of tick-borne diseases, or some referral medical centres for tick-borne diseases that treat a large number of patients. The secondary objective is to set up a blood and tissue bank for future use to identify missed diagnoses in patients with a non-diagnosed disease.

ESCAR also supports and encourages the teaching of new scientists on matters of investigation on the above-mentioned diseases. Thus, in 2004-2005 we will run a “European training course on tick-borne disease” in Europe. Topics include the various tools used in diagnostics and for detecting different microorganisms in the vectors and the exchange of information about collected vectors and clinical experience between specialists.

Finally, in the immediate future the “Guidelines for the diagnosis of tick-borne bacterial diseases in Europe” will be published as a monographic supplement to our Society journal, Clinical Microbiology and Infection. The Guidelines aim at helping clinicians who encounter a suspected tick-transmitted disease to make the appropriate diagnosis as well as microbiologists to standardise diagnostic methods.

ESCAR has a website, which can be accessed from the ESCMID website (http://www.escmid.org, Study Groups or directly at http://euwog.free.fr). Here you can contact us, and find out about our current activities and future meetings. The statutes, list of members and other information can be also found on the website.

José A. Oteo
Chairman of ESCAR

REFERENCES


Mechanisms of Antimicrobial Resistance: A Practical Approach

28th ESCMID POSTGRADUATE EDUCATION COURSE
PALMA DE MALLORCA, SPAIN, JUNE 20–26, 2004

This course is organised in cooperation with the Spanish Society of Infectious Diseases and Clinical Microbiology, Spanish Society for Chemotherapy, and the Group for the Study of the Antimicrobial Action and Resistance. The objective is to provide participants with updated background information and a practical approach to the study of clinically relevant mechanisms of antimicrobial resistance. This 5th edition of the workshop will focus on Gram-negative bacteria expressing extended spectrum beta-lactamases, with altered outer membrane permeability, mutations in QRDR of gyrases, and expressing active efflux.

For further information please contact: Dr Sebastian Alberti, Phone +34 9711 73353, Email salberti@hsd.es or consult the ESCMID website (www.escmid.org), Courses & Workshops.
ESCMID Scholarships 2003

The individuals listed below were awarded an ESCMID attendance grant in 2003 for one of the following events:

13th ECCMID 2003 Glasgow (travel grants and/or free registration):

Alecu, Florian Silviu .......... Bucharest, Romania
Allice, Tiziano .......... Rovili, Italy
Avison, Matthew B. .......... Bristol, United Kingdom
Branger, Christine .......... Nantes, France
Brito, Daniela A. .......... Oeiras, Portugal
Costa-de-Oliveira, Sofia .......... Porto, Portugal
Dobay, Orsolya Eva .......... Edinburgh, United Kingdom
Docquier, Jean-Denis .......... Siena, Italy
Enne, Verve .......... Bristol, United Kingdom
Gerber, Joachim .......... Göttingen, Germany
Guinea Ortega, Jesús .......... Madrid, Spain
Hopkins, Conor .......... Birmingham, United Kingdom
Houhoula, Dimitra .......... Athens, Greece

Koprnova, Jana .......... Bratislava, Slovakia
Liptakova, Adriana .......... Kosice, Slovakia
McMullan, Ronan .......... Belfast, United Kingdom
Petrella, Stéphanie .......... Paris, France
Potrykus, Joanna .......... Gdansk, Poland
Rupnik, Maja .......... Ljubljana, Slovenia
Saeedi, Baharak .......... Linköping, Sweden
Schmidt, Holger .......... Göttingen, Germany
Sergeev, Alexey .......... Moscow, Russia
Templeton, Kate .......... Leiden, the Netherlands
Van den Berg, Renate .......... Leiden, the Netherlands
Van den Wijnjaert, Sigi .......... Brussels, Belgium
Yong, Dongeun .......... Seoul, Korea

Postgraduate Education Courses and ESCMID School of Clinical Microbiology & Infectious Diseases and other Conferences co-organised by ESCMID:

Bagrade, Linda .......... Riga, Latvia
Bazarov, Andrei .......... Moscow, Russia
Bedenkov, A.V .......... Smolensk, Russia
Bekker, Tenna .......... Copenhagen, Denmark
Benko, Ria .......... Szeged, Hungary
Bolisheva, Galina .......... Voronezh, Russia
Brati, Blerta .......... Tirana, Albania
Burillo, Almudena .......... Madrid, Spain
Carev, Merica .......... Split, Croatia
Celik, Selcen .......... Aydin, Turkey
De With, Katja .......... Freiburg, Germany
Dogan Celik, Aygul .......... Istanbul, Turkey
Dumpis, Uga .......... Riga, Latvia
El Ania, Mohamed Ibrahim .......... Doha, Qatar
Esen, Saban .......... Samsun, Turkey
Ferech, Matus .......... Wilrijk-Antwerp, Belgium
Filip, Roxana .......... Iasi, Romania
Giannitsioti, Efthymia .......... Athens, Greece
Guleri, Achyut .......... Glasgow, United Kingdom
Hosoglu, Salih .......... Diyarbakir, Turkey
Inal, Ayse Seza .......... Adana, Turkey
Jameson, Conor .......... Birmingham, United Kingdom
Jindrak, Vlastimil .......... Praha, Czech Republic
Jurna-Ellam, Marika .......... Tallin, Estonia
Kachanka, Alena .......... Minsk, Belorussia
Kandel, Karoline .......... Vienna, Austria
Kayguyuz, Sedat .......... Kirikkale, Turkey
Keuleyan, Emma .......... Sofia, Bulgaria
Kumarasamy, Yashoharan .......... Aberdeen, Scotland
Lawson, Wendy .......... London, United Kingdom
Lorent, Sophie .......... Anderlecht, Belgium

Lul, Raka .......... Kacanik, Kosovo
MacKenzie, Alexander .......... Aberdeen, Scotland
Markogiannakis, Antonios .......... Athens, Greece
Milic, Dada .......... Belgrade, Yugoslavia
Mitt, Piret .......... Tartu, Estonia
Nair, Sajan .......... Anand, India
Nchabeleng, Maphoshane .......... Pretoria, South Africa
Nekhaeva, Galina .......... Voronezh, Russia
Nys, Sita .......... Maastricht, Netherlands
Ogrinc, Patarina .......... Ljubljana, Slovenia
Onci, Serkan .......... Aydin, Turkey
Papadomichelakis, Evangelos .......... Athens, Greece
Pchenitchniaia Dr, Natalia .......... Rostov-on-Don, Russia
Raka, Lul .......... Kaçanik, Kosovo
Revath, Gunturu .......... Nairobi, Kenya
Rezaee, Abbas .......... Tehran, Iran
Rezaee, Abbas .......... Tehran, Iran
Singh, Meeta .......... Jaipur, India
Souredeau, Luc .......... Brussels, Belgium
Talapan, Daniela .......... Bucharest, Romania
Tansel, Özlem .......... Edirne, Turkey
Tavdova, Milada .......... Detva, Slovakia
Tavdovà, Milada .......... Zvolin, Slovakia
Tomic, Viktoria .......... Golnik, Slovenia
Van den Wijnjaert, Sigi .......... Brussels, Belgium
Vata, Andrei .......... Bucharest, Romania
Vlahovic-Palcevski, Vera .......... Rijeka, Croatia
Wechsler-Föröös, Agnes .......... Vienna, Austria
Wulf, Mireille .......... Nijmegen, the Netherlands
Yilmaz, Mesut .......... Istanbul, Turkey
Zarb, Peter .......... Gwardamangia, Malta
Affiliation of National Specialist Societies to ESCMID

The current affiliation scheme was a major agenda item at the European Council meeting on May 11, 2003 in Glasgow (see the Minutes on page 6). For the reasons given below the ongoing pilot programme has been terminated. In 2004 the member societies of the European Council will be invited to become “ESCMID affiliated” under a revised scheme. The rationale for this proposal is summarised below.

**Principle**

Affiliation is a process whereby national societies in microbiology, infectious diseases and related disciplines can become affiliated to ESCMID in order to promote the wider interests of both organisations in the scientific, educational and professional areas relevant to their respective memberships.

**Status**

Since 2001 three societies (British Infection Society, Swiss Society of Infectious Diseases and Association of Italian Clinical Microbiologists) were participating in a pilot affiliation scheme. For an annual price of EUR 5 per member it comprised the following benefits for affiliated societies or their members, respectively: ESCMID News, electronic mailings, annual postgraduate course supported by ESCMID, lower ECCMID registration fee (minus 25 EUR), promotional booth at ECCMID at cost price, business meeting at ECCMID with room rental paid by ECCMID and venue and programme announced in the Programme Book.

**Assessment**

The affiliation scheme has recently been assessed by the ESCMID Executive with the following results:
- professional cooperation of the infection societies across Europe must be strengthened – ESCMID is the natural platform for this.
- with the current pilot affiliation programme the benefits for affiliated members in comparison with regular ESCMID members are too attractive. ESCMID is therefore losing members.
- the current programme for EUR 5 per year has incurred a budget deficit for ESCMID which the Society cannot afford if it is to continue or even extend affiliation more broadly.

**Proposed action**

To put affiliation on a more firm basis the following measures will be initiated:
- seek feedback from the currently affiliated societies on the strengths/weaknesses of the pilot scheme
- develop new proposals that support and strengthen the general principles of affiliation
- ensure that the new scheme is at least cost neutral for ESCMID
- consult the European Council to determine whether the represented societies would wish to participate in the revised scheme.

For the ESCMID Executive

*Peter Schoch*, Managing Director

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ESCMID’s Homepage Needs Your Input

To keep the ESCMID membership database and online directory up-to-date please notify us of your address changes (names, titles, street address, telephone, email, etc) through the website at www.escmid.org, section Membership.

Furthermore, to fulfil our role as repository of European and national practice guidelines for the diagnosis and management of infectious diseases please send your contribution for publication on the ESCMID website to info@escmid.org.
The 2nd ESCMID School was held from June 28 – July 4, 2003 in Utrecht, the Netherlands, hosted by the Department of Acute Medicine & Infectious Diseases of the University Medical Centre in Utrecht. Thirty-one fellows and specialists attended the school from the following 13 countries: Portugal (4), Greece (2), Russia (2), the Netherlands (11), Italy (1), Belgium (2), Lithuania (2), Serbia (2), Germany (1), Sweden (1), Nicaragua (1), UK (1) and Slovenia (1). A 50% increase in the total number of participants compared to the first School demonstrates the enthusiasm and need for this initiative. After conclusion of the course, participants were requested to fill out an evaluation form as feedback to better meet the expectations at the next School.

On Saturday, June 28th the School was opened with two lectures on HIV followed by an Indonesian meal for participants, facilitators and the organising committee.

From Sunday the 29th to Friday July 4th, the programme featured plenary lectures in the morning and group discussions in the afternoon. Renowned experts in the field from seven countries reviewed the key aspects in Microbiology and Infectious Diseases on:
- HIV and AIDS (immunity, HIV globally, pediatric HIV, resistance)
- Antimicrobial chemotherapy and immunization (vaccines against meningococci, new antiviral agents, new agents against fungi)
- Major clinical syndromes (SARS, meningococcal encephalitis, parasitic diseases, rickettsiosis, hemorrhagic fevers, bone and joint infections, low risk febrile neutropenia)
- Immunocompromised host (susceptibility factors to mycobacterial infections, diagnostic techniques for fungal infections)
- Epidemiology and public health (hospital epidemiology, optimal control of the usage of antimicrobial agents in the community).

The overall evaluation of the plenary lectures was very good. Forty percent of the participants even wanted to increase their number. Especially the plenary lectures by Prof JT van Dissel, University of Leiden, on SARS and by Dr SPM Geelen, University Medical Centre Utrecht, on paediatric HIV and prevention of mother to child transmission were highly appraised.

For the afternoon sessions the attendees were divided in four groups. Three groups discussed cases with facilitators (members of the ESCMID Education Committee [EDC] and staff members of the Department of Acute Medicine & ID) while the remaining group prepared the presentation of cases that were selected by two members of the EDC (Achim Schwenk & Luis Martinez-Martinez).

School participants highly rated the interactive style of most of the facilitators and even suggested shortening the lunch break to allow for longer group discussions. Case presentations took place during plenary sessions from 5 to 7 pm. Thereafter, all participants used their rental bikes to return to the hotel.

On Tuesday afternoon there was a canal tour through the centre of Utrecht and on Wednesday evening, the official course dinner sponsored by GSK, the Netherlands, was held. Overall the course closed with balanced accounts mainly due to grants from Abbott, Grunenthal, Pfizer, MSD, Gilead and BMS, all from the Netherlands. The organising committee would like to warmly thank the speakers who delivered fine talks, the facilitators who spent an entire week in Utrecht, our secretary Jeannette Westerbeek and the members of the ESCMID EDC who helped to shape not only the programme but also the complete course.

The 2nd School received very high evaluation marks from the participants and this is a stimulus for the ESCMID EDC, under the leadership of Claude Carbon, to even extend the 3rd School which will be held in Athens, from June 26 – July 2 and will be organised by Matthew Falagas.

Andy IM Hoepelman
Coordinator of the 2nd ESCMID School
ESCMID Workshop

Progress Toward Meeting the Challenges in Clinical Microbiology and Infectious Diseases

Leuven, Belgium, 17–19 March 2004

Organised jointly with the Belgian Society for Clinical Microbiology and Infectious Diseases (SBIMC-BVIKM) at the Catholic University of Leuven.

The objectives of the workshop are to: identify the public health challenges and medical needs arising from the evolution of infectious diseases in a changing Europe; determine which professional organisation models and communication networks allow the delivery of optimal management and prevention of infectious diseases and; review the current modalities and up-date plans for training and continuing professional development of medical specialists in the infection disciplines.

For more information, please contact:

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www.escmid.org,
Courses & Workshops.

Announcement

3rd ESCMID School of Clinical Microbiology and Infectious Diseases

Athens, Greece, June 26 – July 2, 2004

A one-week course dedicated to postgraduate and continuous medical education. The programme covers most of the relevant topics in clinical microbiology and infectious diseases, thus being of particular interest to young MD’s at the end of their specialty training as well as those wishing to broaden their professional knowledge. By providing short reviews and well-selected case studies, the ESCMID School helps the students to prepare for their examination.

For details see the ESCMID homepage spring 2004 at www.escmid.org, ESCMID School.

Organised by the ESCMID Education Committee   Under the auspices of the Henry Dunant Hospital in Athens
Dear colleagues

It is an honour and privilege to invite you on behalf of the Organising Committee to participate in the 14th ECCMID to be held in Prague, Czech Republic, May 1–4, 2004. A stimulating scientific programme and the fascinating historical and architectural heritage of Prague await you there. The annual ECCMID is one of the largest international meetings on infectious diseases and microbiology. With thousands of participants, including clinicians, clinical microbiologists, biomedical scientists, public health specialists and trainees from more than 80 countries, the ECCMID offers an interdisciplinary forum to share knowledge in a collegial atmosphere.

We plan to focus the attention on new developments in the treatment and diagnosis of established and emerging infectious diseases as well as on the need for international co-operation in solving the current global problems in these fields.

In addition to keynote lectures, symposia and meet-the-expert sessions we will again organise guided poster tours and a European Network Corner to facilitate contacts and interaction between the participants. The industry exhibition will be an integral part of the congress and inform you on the latest products and services available to meet your professional needs.

The ancient city of Prague with a centre dating back to the Middle Ages has been selected to host the ECCMID 2004 for a variety of reasons. Its natural beauties, history and outstanding tradition of music and fine art have made Prague one of the most delightful and charming cities in Europe.

We warmly invite you to share and enjoy with us and look forward to seeing you in Prague,

Prof. Jarmila Jelinkova
14th ECCMID President

Prof. Marc Struelens
ESCMID President
The Federation of European Microbiological Societies (FEMS) recently published a European Declaration for Microbiology on the occasion of the 1st FEMS Congress held in Ljubljana, Slovenia (29 June–3 July 2003). The 10 statements of this Declaration express the political concerns and objectives of FEMS and its constituent societies relevant to the development of microbiology and the benefit of society in general. In view of recent bioterrorist activities the importance of an ethical discussion about the role of microbiology and microbiologists in modern society is certainly warranted. ESCMID is pleased to publish and support this Declaration (see below).

However ESCMID regrets that it was not invited to contribute to this Declaration. ESCMID is not a member of FEMS nor are many other European national societies devoted to clinical microbiology and infectious diseases. The important perspectives which these societies bring to the issues surrounding human infectious disease and its diagnosis, treatment and prevention were thus not adequately represented. We feel that statements related to the particular focus of such societies would have strengthened this Declaration.

Issues such as the toll of one third of human deaths caused by infectious diseases, the pending medical crisis of antibiotic resistance, (re-)emerging infections like West Nile Virus and SARS, the increasing number of immuno-compromised patients and their vulnerability to opportunistic infections, the role of commensals in health and disease, the changing prevalence of infectious diseases consequent on global warming and the need for global surveillance are just a few aspects of human infection that deserve highlighting in the Declaration. Containing the human and economic impact of infectious diseases remains an important public health and societal need. It is to be met by more basic research in microbial physiology, better diagnostics, drug development and vaccine production.

Another concern that ESCMID has and which is not adequately dealt with in the Declaration is the need for better collaboration between basic, applied and clinical science and its role in supporting political decision making. Present and future challenges require optimal integration of and mutual understanding between those involved in medical science and practice, whether in academia, health care systems, industry or government agencies. Since professional and political issues often have complex determinants, multidisciplinary cooperation between individuals and professional organisations is mandatory if efficient solutions are to be found.

We agree with FEMS that the Declaration should be broadly discussed by the professional community. We encourage our readers to comment. Your opinion is important and welcome. We hope to publish a selection of these in a future issue of ESCMID News.

Peter Schoch and Jordi Vila on behalf of the ESCMID Executive

FEMS Declaration for Microbiology

FEMS intends with this declaration to specifically advance the following issues:

1. To ensure that Microbiology serves the welfare of mankind, allows sustainable development for all people, ensures the protection and preservation of nature and helps achieve world peace.

2. To enhance the public awareness of the benefits of microbes to the world and mankind, and the understanding that the dangers posed by microbes are few and vastly outweighed by their benefits.

3. To encourage the highest standards of safety in all microbiological processes, products and procedures. To ensure that technological advances arising from microbiological research are thoroughly tested before exploitation.

4. To support the understanding and preservation of microbial biodiversity, by research and the maintenance of a network of microbial culture collections.

5. To condemn the deliberate use of microbes to the disadvantage of humans (biological warfare and bioterrorism).

6. To ensure that the teaching of microbiology should be part of all European educational systems, and be fully integrated into scientific and social education, at all levels. To encourage microbiologists to communicate with the public about their work and the importance of microbes.

7. To encourage the highest standards of safety in all microbiological processes, products and procedures. To ensure that technological advances arising from microbiological research are thoroughly tested before exploitation.

8. To make certain that microbial genomic data are to be considered the heritage of all humanity and are available to all mankind.

9. To nurture European microbiology by increasing mobility of researchers within Europe, and retaining the best microbiologists in Europe, by providing frameworks to ensure that strong microbiological research takes place in Europe in universities, hospitals, government and industrial laboratories.

10. To support the potential growth areas of microbiology such as biotechnology, food microbiology, rapid diagnostics and environmental protection.

Published by the Federation of European Microbiological Societies at their first Congress in July 2003. The complete version is available at www.fems-microbiology.org. The Federation
Microbiology & Infectious Diseases: An Appeal for Two Autonomous but Complementary Specialties

A recent survey of the European Society for Clinical Microbiology and Infectious Diseases has revealed the geographical distribution of which European countries officially recognize Clinical Microbiology and Infectious Diseases as medical specialties (1). From time to time, a recapitulation of the links and differences between the responsibilities of microbiologists and infectious diseases specialists by the professionals working in the infection disciplines seems necessary. The general consensus is that clinical microbiologists and infectious disease physicians have essentially a single common goal: the diagnosis, therapy and prevention of illnesses caused by (or involving) microorganisms. The question that is reiterated year after year in different places is the same: why, if there is a common goal, should we have two different specialties? From the operative point of view, the distinction seems evident: the main object of Microbiology is the microorganism, and the main object of Infectious Diseases is the infected person. In the European and rationalistic Kantian way of thinking, the object of a science defines a science and hence a specialty, defined as an ensemble of knowledge applied to the whole understanding of a particular object. As a corollary, the ability to make progress in the understanding of its object is a particular feature of science. The fact that Microbiology is a science is beyond any discussion: its object is well defined. In many people’s minds, the issue is less clear for Infectious Diseases. How can progress be made in the understanding of Infectious Diseases without making progress in Microbiology, Immunology, or Pharmacology? As was once the case with the specialty of Internal Medicine, the confusion arises from the lack of distinction between first-order (to use the nomenclature of hierarchical structures) specialties, and secondary-order specialties. Microbiology is a first-order or basic specialty; Infectious Diseases, Internal Medicine or Biopathology are second-order specialties. Therefore, it is simultaneously true that Microbiology is focused on a part of the object of Infectious Diseases, but the object of Infectious Diseases is not the same object (as it is a higher hierarchical-level object) as Microbiology. In other words, because Infectious Diseases is a complex specialty, infectious diseases specialists cannot be reduced to microbiologists; and because Microbiology is a first-order specialty, microbiologists cannot step up to the complexity of Infectious Diseases. It has been a seminal mistake by some misled infectious disease specialists to consider Microbiology merely as a “specific technique” that infectious diseases specialists use (or own?) to appropriately diagnose their patients, in a similar way as electrocardiography is owned by cardiologists, or endoscopy by gastroenterologists. The original fear behind this misconception was that without any specific and specialty-owned technique, Infectious Diseases would be very difficult to separate from Internal Medicine. To convince the “subordinate” microbiologists to accept such a humiliating condition, something like a bribe has sometimes been proposed: under the umbrella of Infectious Diseases, Clinical Microbiology will be less exposed to be captured by another, but less prestigious, second-order specialty, Biopathology. Microbiology between Scylla and Charybdis. In reality, Microbiology and Infectious Diseases are different specialties; they are complementary and synergistic, but not the same. The proof of this principle is that synergy no longer occurs when both specialties are merged contra natura and forced to function as a single specialty. A person trained as microbiologist will devaluate the possibilities in Infectious Diseases when taking full responsibility for the direct care of infected patients. In the hands of a person trained in Infectious Diseases the possibilities for microbiology will be largely simplified and devaluated. In other words, it is simply impossible to become part time microbiologist and part time infectious disease physician. One part will dominate the other, preventing full expression of all possibilities for the recursive activity. Only as fully separate specialties can microbiologists acquire the essential knowledge of infectious diseases, and infectious disease specialists the essential knowledge of microbiology. An important level of mutual understanding is obviously needed to accomplish the required interpretation of infection problems from both points of view. Moreover, a clinical specialist in Infectious Diseases can (and probably should) do some research using microbiological technology, but only for precise and limited research subjects, in which full competence could be acquired under the guidance of a microbiologist. Eventually a medical specialist in Microbiology may specialise in a particular type of infected patient, using some clinical technology, but probably should maintain, even in this case, close collaboration with a clinician. These observations about the interaction of microbiologists and infectious diseases specialists should not be considered as pure speculation. They are the result of an observational or even experimental process that I started more than 25 years ago. Leading a large Microbiology Department, I decided that the requirements of a number of infected patients were neither adequately covered by the good will of clinical microbiologists alone, nor by the interaction of microbiologists in conjunction with other clinicians not professionally devoted to infectious diseases. Because of that, in 1977 I already offered a number of positions in the Microbiology Department to particularly brilliant young physicians trained (originally outside Spain) in Infectious Diseases. The resulting Section of Infectious Diseases rapidly differentiated its activities from those of Microbiology, and was immediately accepted as an essential
clinical activity of the hospital, resembling in prestige and volume of provided care other classic medical specialties, such as Cardiology, Nephrology or Gastroenterology. Excellent complementary and cooperative relations with microbiologists were maintained during that time. I tried to communicate the experimental success to the international microbiological community in a report on “Integrated Hospital Microbiology” published in 1988 in a broad coverage Journal, emphasising the need for recognition of both specialties under the principle “being-together-but-not-the-same” (2).

Few people know that this experience was very influential in the official change of denomination of the European Society of Clinical Microbiology into the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in March 1988. Many other prestigious infectious diseases groups have flourished in Spain during these years, most of them within Internal Medicine Departments. Year after year, we have been asking, supported by the successive presidents of the Spanish Society for Clinical Microbiology and Infectious Diseases, for the official recognition of Infectious Diseases as a separate specialty in Spain, the only way of assuring a controlled official training of future Infectious Disease specialists. Not only that, the specialty of infectious diseases is the only way to facilitate the acquisition of official levels of “particular competence in infectious diseases” to be offered to other clinical specialists (as an example: intensive care specialists who are interested in infection). Much time has passed and, despite the relevant development and international success of different groups of Spanish infectious disease specialists, the specialty of Infectious Diseases still remains officially unrecognized in Spain. In 1999, the number of physicians, local influence, scientific production, and prestige of the Section of Infectious Diseases of the Department of Microbiology at the Ramón y Cajal Hospital was so high that I decided it was time to create a Department of Infectious Diseases, fully independent (it was almost so in practice) from the father-Department of Microbiology. This Infectious Diseases Department was the first recognized as such in the Network of Hospitals belonging to the Spanish National Institute for Health (INSALUD). Nothing changed in reality. Both groups, microbiologists and infectious disease specialists, continued to cooperate in a quite productive way under the principle “being-together-but-not-the-same” (2).

We are certain that good microbiology promotes the prestige of infectious diseases, and good infectious disease creates constant opportunities for the development and prestige of microbiology. Indeed cooperation of microbiologists with infectious diseases specialists is a need for the future of microbiology (3). Both types of specialists could be eventually integrated in “Units for Infection” (4), with a federal structure (5), assuring mutual independence. Clinicians involved in well-developed infectious diseases groups have frequently asked microbiologists for support in the official recognition of Infectious Diseases as a specialty in Spain (5). I am certain that microbiologists have only to gain in the process: clinicians are accepted to become chimerical medical specialists in both Microbiology and Infectious Diseases, the clinical part of the activity will necessarily become dominant, and Microbiology will be reduced to a servant science for infectious disease physicians.

Microbiology and Infectious Diseases, contrary to previous expectations, are facing a new golden age in our rapidly changing world. Microbiology has been enriched in recent years with many new technological possibilities and many new and extremely promising interactions with neighbor basic sciences (as genetics, ecology, population biology, cell biology, or evolutionary biology). Many of these new techniques and conceptual frames will shape a new type of integrative microbiology (6), maintaining its classic principles (7), but with potentially explosive developments in research and human health (8). Only mediocrity and short-sighted attitudes can be considered as threats for Microbiology in particular places. In the future Microbiology will constantly fuel the activity of Infectious Disease specialists, who should be able to integrate the microbiological findings into the medical and clinical complexity of the infected or exposed patients and to make practical decisions to benefit the individual and the society. To reach such an interactive goal, the specialty of Infectious Diseases should be urgently recognised in all European countries, including Spain. Any help from the European Society of Clinical Microbiology and Infectious Diseases will be welcome.

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REFERENCES


Manuscript received on 2 September 2003
ESCMID Position Paper

European Centre for Disease Prevention and Control (ECDPC)

Proposal by the European Commission to the European Parliament and Council

OVERVIEW OF THE COMMISSION’S PROPOSAL

The following overview is based on the European Commission information document available at: http://europa.eu.int/comm/health/ph_overview/strategy/ecdc/ecdc_en.htm

Background of the proposal

Since 1999, the Commission has managed a communicable diseases network. This is currently based on ad hoc co-operation between the Member States within the legal framework of Council and Parliament Decision 2119/98/EC. However, substantial reinforcement of this system is needed if the European Union is to be in a position to control communicable diseases effectively. In 2002, following external reviews of the network achievements, the State Epidemiologists from the Member States gave their view on the future of the surveillance of communicable diseases at the European Union level and favoured the creation of an EU-level centre.

The present proposal aims at creating a European Centre, able to provide a structured and systematic approach to the control of communicable diseases and other serious health threats, which affect European Union citizens. The creation of a European Centre (for Disease Prevention and Control), an independent European agency, would mobilise and significantly reinforce the synergies between the existing national centres for disease control.

Art. 3 states that: “The mission of the Centre is to analyse and assess risks to human health from communicable diseases and other serious health threats affecting the European Community, to provide expert advice to the Commission and the Member States, and to enhance the capacity of the European Community and its Member States to protect human health through prevention and control measures on communicable diseases and other serious health threats”. The main tasks of the European Centre would include:

1. Epidemiological surveillance and networking of laboratories

The Centre would develop epidemiological surveillance at the European level. For this work, the Centre could either use its own staff, staff from the dedicated surveillance networks (DSN), or, in some instances, it could subcontract tasks to a national centre of excellence. The Centre could also identify and maintain networks of reference laboratories, and enhance the quality assurance schemes of microbiological laboratories.

2. Early warning and outbreak response

To be effective the early warning and response system (EWRS) requires “around the clock” availability of specialists in communicable diseases. Whilst the responsibility for action will remain with Member States and the Commission, technical operation of the EWRS would be undertaken by the Centre and its networks.

3. Scientific opinions to the Commission and Member States

Public health decisions must be based on independent scientific evidence. Scientific issues arising in the area of communicable diseases vary widely, ranging from questions of clinical medicine and epidemiology through to standardisation of laboratory procedures. Creating one permanent scientific committee to cover all these issues would not, therefore, be appropriate. The Centre would, instead, bring together scientific expertise in specific fields through its various EU-wide networks and via ad hoc scientific panels.

4. Technical assistance and communication

The Centre’s rapid-reaction area could cover more than the European Union itself, and include such areas as the EEA/EFTA, as well as candidate countries. When requested, it would send an EU-team to investigate an outbreak of an unknown human disease in a European country. The Centre should also have the ability to support, if necessary, those Commission services that give humanitarian aid or other types of assistance in response to disease outbreaks in third countries. Objective, reliable, and easily accessible information is essential for the general public and as well as for decision-makers in the Commission, Member States and international organisations. The Centre will report on its activities and results, and disseminate information tailored to meet the needs of its different audiences.

Organisation and financing

A Director appointed by the Management Board will manage the Centre. The Director will be responsible for daily administration of the Centre and preparation of the work programme. The Management Board will be composed of 15 members: 6 represent the Commission, 6 the national executives and 3 are nominated by the Commission, representing patients’ organisations, professional bodies and academia. It shall adopt the Centre’s programme of work and ensure that it carries out its mission as planned. An Advisory Forum shall be composed of senior scientific members of tech-
ESCMID comments on the European Commission proposal to establish the ECDPC

1. Scientific support of ESCMID
The European Society for Clinical Microbiology and Infectious Diseases (ESCMID) fully supports the Commission proposal to create a European Centre for Disease Prevention and Control (ECDPC), an independent European agency:

- “to analyse and assess risks to human health from communicable diseases and other serious health threats affecting the European Community,
- to provide expert advice to the Commission and the Member States, and
- to enhance the capacity of the European Community and its Member States to protect human health through prevention and control measures on communicable diseases and other serious health threats”. (Mission, Art. 3)

ESCMID holds the view that the establishment of the ECDPC in 2005 is an essential and timely step toward improved co-ordination of surveillance and control of communicable diseases in Europe and beyond. It is ESCMID’s opinion, however, that the means of the project do not match the goals.

ESCMID has identified four areas that require additional consideration:

- the scientific input and support to the Centre of learned professional societies such as ESCMID;
- the role of biomedical scientists and a central laboratory capacity;
- training needs in public health and infection disciplines; and
- the integration of enhanced research programmes with the ECDPC activities.

A first aspect that should be further developed is the range of expertise required to support the activities of the Centre. The pooling of expertise from state epidemiologists and other public health staff from national communicable disease control institutes, as foreseen in the present proposal, does not encompass the multidisciplinary scientific and medical expertise needed to optimally inform and support the work programme of the ECDPC.

ESCMID members have broad expertise and an international perspective in the field of laboratory diagnosis, clinical management, epidemiology and prevention of infectious diseases, particularly at healthcare facilities. To this end, ESCMID is of the opinion that European decision-makers should explore the possibility of an ESCMID delegate participating in the ECDPC Management Board, who would be well equipped to contribute to the Centre’s work programme as well as its execution. Moreover, since infectious disease study and management is the core of the ESCMID operations, the Society would also offer to provide nominees to the Centre for participation to ad hoc scientific panels and external review panels.

2. Role of biomedical scientists and the need for a central laboratory capacity

The control and prevention of communicable diseases require close cooperation between laboratory scientists, epidemiologists and public health practitioners. ESCMID holds the view that developing microbiology laboratory facilities at the level of the ECDPC would provide a much greater capacity to respond to emerging and re-emerging infectious diseases than depending entirely on external facilities, through complicated multinational co-operative arrangements with national reference laboratories. Of course duplication of existing facilities should be avoided. The establishment of new laboratories will require appropriation of a larger budget than that included in the current proposal. Development of this central laboratory would be more efficient if located in an existing institute with large laboratory facilities. The development of such central laboratory capacity could provide the necessary impetus for upgrading and strengthening national laboratories’ input and support to public health programmes. To date the extent of interaction between laboratories and public health programmes differ greatly between Member States. To this end, ESCMID believes that the marked heterogeneity among Member States in communicable disease surveillance and control systems argues for a strong central resource to complement and support the national systems where needed. This is particularly evident for smaller and lower-income countries where the financial and human resources are simply not available to develop a comprehensive reference laboratory system and a polyvalent response capacity to potential threats, including bio-terrorist attack with rare disease-causing agents.

Furthermore, establishing central European reference laboratories to support communicable disease surveillance would greatly facilitate the development of a co-operative spirit and sense of collective responsibility among professionals. It would also ensure the integration of biological scientists into the pool of expertise required for designing and updating communicable disease control policies and operations in a timely manner.

Another important added value of this laboratory capacity at ECDPC level would be to offer an international work environment for microbiologists’ training programmes with the aim of harmonising and improving the quality of microbiological methods used at local and national levels in the Member States. Such harmonisation would become vital during an epidemic, in order to successfully manage and control a communicable disease outbreak.

3. Bridging the gap between public health agencies, general practitioners and clinical/academic specialists in microbiology/infectious diseases

To achieve Europe-wide preparedness to detect and manage communicable disease threats effectively, there is a need to reinforce significantly the response capacity of “front line” cli-
nicians, general practitioners as well as hospital specialists, and their local microbiology laboratories. This capacity will, in turn, depend on upgrading the training and continuing professional development of these healthcare professionals with a view to harmonisation of diagnostic, treatment and prevention methods.

Complementary to national training programmes, ESCMID has a long-standing track record in training at the international level, with the regular organisation of international postgraduate training courses that are attended by over 300 professionals each year. In addition, its advisory role to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) has been instrumental in harmonising guidelines and standards on drug susceptibility testing methods and interpretation criteria developed by national advisory committees across Europe. These common European standards are essential for providing a comparable approach to the surveillance of bacterial and fungal resistance to antimicrobial agents. Here also, training workshops will help integrate the guidelines into laboratory practice.

Therefore, ESCMID offers to play the role of facilitator in building a partnership between the ECDPC public health programme coordinators and practitioners in the field. The creation of a well-trained ECDPC epidemiological task force requires major educational efforts. We hold the opinion that the European Programme for Intervention Epidemiology Training (EPIET) should be reinforced to expand more rapidly the “field force” of interventional epidemiologists. In addition, ESCMID offers to develop intensive international training programmes in additional areas of expertise, complementary to the EPIET programme through co-operation with other learned societies and stakeholders. These areas include the clinical management of infection at primary-, secondary-, and tertiary-care levels, laboratory detection and characterisation of emerging and deliberately released pathogens, and control of healthcare-associated infections. ESCMID educational programmes should receive EU recognition. It should be recognised that these programmes will need financial support in addition to that foreseen in the Commission’s proposal for the epidemiologists’ training programmes.

4. The pressing need for more investment in research on communicable disease and of integration of biomedical research with surveillance/control activities

The paradigm for success epitomised by the US Centers for Disease Control and Prevention (CDC) is firmly rooted in its close integration of research and reference laboratories with disease surveillance and control programmes in a common organisation. This organisation allows for a daily interaction between laboratory scientists and epidemiologists, thereby enhancing intellectual cross-fertilisation between disciplines and cohesion in applying scientific advances in the field.

Commissioner Busquin has identified fragmentation of research, by country and by discipline, as a major handicap to be overcome in Europe. The 6th Framework Programme for Research and Technological Development has the laudable ambition to address this issue by the development of the European Research Area. There is a clear historical opportunity to boost this approach with regard to biomedical research in infectious diseases by physically linking the establishment of the ECDPC to that of new centres co-ordinating networks of excellence in this domain.

One particular research priority most suitable to initiate this process is the development of integrated molecular epidemiology of infection. This approach combines the study of human and microbial genomics, population genetics, ecology, epidemiology and sociology to analyse the determinants of evolution and epidemiologic success of pathogenic microbes. These biological advances are the keys to more predictive assessment of infectious disease risks and designing effective control programmes.

It is ESCMID’s strong belief that there are ample reasons to seek a much larger budget to fund these types of research programmes. Firstly, in an era of rising costs of healthcare fuelled by increasing risks of infection and drug resistance, investment in prevention has become an urgent priority. Secondly, this ambitious project would provide a valuable symbol of peaceful European co-operation and contribution to global health and security. Thirdly, it would strengthen European competitiveness in biomedicine, limit the brain drain of its best scientists and provide biotechnological leads in developing new vaccines, diagnostics and therapeutic agents.

Marc Struelens
ESCMID President

The Position Paper was approved by the ESCMID Executive Committee on 28 November 2003 and distributed to the European Commission, Members of European Parliament and National Permanent Representatives to the EU.
Meeting Report

European Conference on the Role of Research in Combating Antibiotic Resistance

The 4th European Conference on Antibiotic Resistance was organised by the Research Directorate-General of the European Commission and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) under the patronage of the Italian Ministries of Research and Health and the Istituto Superiore di Sanità during the Italian Presidency of the EU from November 28 - 30, 2003 in Rome.

SETTING THE STAGE
As pointed out by Marc Struelens, Brussels, ESCMID President, in his opening address, the Rome Conference reflects the increasing awareness that only a multidisciplinary approach involving all stakeholders - physicians, researchers, politicians and industry - is apt to overcome the problem of resistance. Anna Lönnoth from the DG Research emphasised the strong commitment on the part of the European Commission to the challenge of overcoming resistance. Based on the conviction that research will contribute to the solution, she announced that the research priorities formulated by this Conference will be reflected in the research agenda of the Commission in future years. To emphasize the importance of multidisciplinary networks involving the full range of research priorities, the industry was invited to participate in future calls for proposals.

Giuseppe Cornaglia, Verona, ESCMID Secretary General, who was greatly acclaimed for his contribution to the organisation of the Conference, stressed that sustainable solutions must also take into consideration the social and political diversity of Europe, thus adding another dimension to the complexity of the problem.

OBJECTIVES
The objective of the Conference was to develop recommendations in six topical fields of research directed at overcoming resistance. The Working Groups charged with developing these recommendations were organised around plenary lectures and introductory talks on the current state of technology available for detecting resistant strains and the present understanding of clonal selection and spreading of resistance in both hospital and community settings. The recommendations made by the six Working Groups, comprised of 20 to 30 participants each, will be summarised and published in a forthcoming issue of Clinical Microbiology and Infection. This short report simply touches upon the main conclusions from an individual perspective, without any claims of completeness.

To demonstrate the spectrum of opinions even among specialists, I provide one reminiscence: in one of the Working Groups the discussion started with a basic question about the need for new antibiotics in dealing with resistance. While most of the participants spontaneously agreed that there is an urgent need for new compounds, there was also a statement to the contrary, claiming that the problem of resistance is simply about good clinical practice. As proof, the proponent referred to the unequal geographical distribution of resistance prevalence(s) across Europe. If this assessment of the problem were indeed true and if fighting resistance were that simple, my suggestion would be to legally restrict the prescription of antibiotics, as in the case of drugs with a potential for abuse.

RESEARCH TOPICS: OPEN ISSUES AND MISSING TOOLS
An in-depth discussion of the problem and its solution indicated that, in addition to stricter prescribing policies, there are many other issues that need to be addressed to fully develop our weapons against resistance:

i) Bacterial physiology, clonal selection and spreading mechanisms, as well as the role and interactions with commensal microflora

ii) Reversibility of resistance, also in relation to prudent use of antibiotics
iii) role of “reservoirs” in livestock and poultry for resistance development
iv) tools to study the mechanisms and dynamics of clonal spread
v) rapid laboratory diagnostics and determination of resistance genes in the hospital and the community, thus allowing the prescription of more narrow spectrum antibiotics
vi) role of consumption, behaviour (patient and physician), infection control and type of antibiotic concerning causation of antibiotic resistance
vii) microbial genomics, bioinformatics and new technologies for antimicrobial drug discovery
viii) pharmacokinetic optimisation of drug combinations and “old” chemical structures
ix) identification of validated outcomes to support measurement of clinical and economic burden of resistance
x) improved studies linking resistance to interventions and outcomes
xi) comparison of clinical outcome in areas with low and high antibiotic consumption
xii) role of generics in driving resistance development
xiii) role of epidemiology in the implementation of target-specific control measures concerning usefulness, organisational aspects of data collection, laboratory methods and integrated databases and data mining systems
xiv) economical incentives for pharmaceutical companies to invest into the research and development of new anti-infectives, e.g. by eased registration requirements on the part of regulatory authorities, prolongation of patient lives, price concessions, etc
xv) lobbying for more support, e.g. by establishing and liaising with patient organisations of antibiotic resistance victims

As the emphasis now and in the future must be on overcoming resistance rather than on describing the problem, any progress with the above research agenda must involve its immediate translation into improved treatment regimens and/or the political measures necessary to make a measurable impact.

The single most important conclusion, which shall be highlighted again, was the need to raise the political awareness of antibiotic resistance as the extent of the problem is still not fully recognised by the wider public. Part of the reason for this might be the lack of actively-lobbying patient groups. To persuade the policy makers it will be of paramount importance to make an in-depth analysis and demonstrate the full economic costs resistance puts on society.

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REBECCA

An interesting proposal came from Fernando Baquero, Madrid: since most people outside the profession continue to downplay the urgency of taking measures, we should look for more persuasive arguments based on personal well-being, which is a concept most people do take seriously. He suggested a long-term longitudinal study with the acronym REBECCA: Risk Evaluation and Benefit Evaluation of Consumption of Chemotherapeutic Agents. By linking the consumption of antibiotics with individual health rather than with the emotionally remote frequency of genes and strains, public awareness of resistance might be raised, as well as the level of acceptance of restrictive measures. Risk and benefit would need to be broadly defined as relating to clinical outcome and to the adverse effects of antibiotic therapies, the recurrence and morbidity of infections and the prevalence of “unrelated” chronic diseases throughout a lifetime.

CONCERTED ACTIONS REQUIRED

Antibiotic resistance has much in common with global warming: in both cases basic observations are unequivocal (spread of resistance genes and increased emissions of greenhouse gases, respectively) while in both cases much of the evidence for their causation and consequences remains circumstantial or controversial. However, in view of the pending threat, the consensus in Rome was that measures to interfere with the spread of resistant strains are urgently needed. The most promising strategy is a mixed and well balanced bag of scientific, clinical and political measures. In addition to better scientific insights into microbiology and infectious disease mechanisms, a sustainable solution also requires the political will to take action appropriate in the face of a pending medical crisis. Providing advice and leadership in this process might be an important objective of the emerging European Centre for Disease Prevention and Control. But also for ESCMID, which provides diverse platforms for research cooperation, consulting and education, resistance remains a challenge.

Peter Schoch
ESCMID Managing Director
The Mother of All Plagues

New Findings Make Progress Possible in the Fight against Cholera

Each year when the monsoonal rainfalls hit the foothills of the Himalaya, Bangladesh's Brahmaputra River overflows its banks. Where it overflows, hundreds of villages become islands in a sea of muddy water. In conjunction, floods of water from the enormous river press into the sewers and infiltration pits and the untreated mixture then finds its way into the drinking water wells. After a couple of days the next catastrophe begins, which is probably just as old as monsoonal flooding: cholera. It starts out as a few scattered cases, and then the infectious enteritis takes shape as a mass epidemic.

How many humans contract cholera in the following weeks is unknown, since the minister of health in Dhaka has other concerns than to keep records on cholera cases. Experts estimate the attack rate to be two to four per 1000 persons. Of the approximately 125 million inhabitants 250,000 to 500,000 persons contract cholera per monsoon.

At least the death rate has drastically sunk, since oral rehydration has become part of the therapeutic repertoire even in the most remote primary health care centres. Every village health care worker masters this simple treatment measure. Until the mid 80’s every third cholera patient died as a consequence of the intense cholera-typical diarrhoea and vomiting, which leads to dehydration.

Yet the prospects are good that in the future the average Bangladeshi will no longer regard cholera as a natural phenomenon, against which he can protect himself just as little as against the flooding of the Brahmaputra. Numerous research results put *Vibrio cholerae* in a new epidemiological and pathophysiological light and open up prospects, until now unknown, for control measures. Particularly at the Centre for Diarrhoeal Research in Dhaka, the Maryland Marine Biotechnology Institute and the John Hopkins Bloomberg School of Public Medicine, the latter two in Baltimore, Maryland, groundbreaking international research is being conducted.

First of all the researchers at these institutions cleared up the paradigm, originating from the era of Robert Koch, discovering of the comma-shaped bacillus in an Egyptian patient that *Vibrio cholerae* (as it can still be found today in textbooks) is a very fragile pathogen able to survive outside the human intestine for only a few hours. The truth is actually the opposite. The cholera vibrio is a true survival artist. In the aquatic environment it adheres to the surface as well as the internal organs of tiny crustaceans, which constitute, en masse, the zooplankton. The small crustaceans not only guarantee its survival but also act as a perfect in vivo culture medium. They enable the cholera vibrio to reproduce in an aquatic setting and be transported long distances, for example by water or wind currents.

Depending upon the species and size, each small crustacean can harbor up to 10,000 cholera vibrios. In September and October when the zooplankton flourish in the Brahmaputran tributaries and in the gulf of Bengal, in no time a concentration of 10,000 to 100,000 pathogens per cubic millimeter water is reached, which is the minimum infection dose. Clearly less than a thimbleful of this water is sufficient to turn a healthy person into a cholera patient in a few hours.

The reason for the cholera vibrio’s extreme virulence is meanwhile being explained down to the molecular level. Once in the jejunum, the microorganisms begin producing their specific enterotoxin. This toxin causes the mucosa to excrete large quantities of water into the intestinal lumen. It consists of two subunits, which are encoded by a gene sequence, termed CTX.

However, the toxin molecule is not an invention of the cholera vibrio, but merely “borrowed”. The CTX gene sequence actually originates from a bacterial phage, which in the course of evolution has “specialised” on *V. cholerae*. All pathogenic variants of the cholera vibrio have a second virulence factor, the so-called toxin-coregulated pilus (TCP). TCP serves as a sort of “mooring anchor”. The bacteria use it to hook onto the surface of a mucosa cell. TCP’s genetic code is embedded into a complex DNA
World-wide three oral vaccines are presently available. The parenteral vaccine, until now approved in Germany, Austria and Switzerland, was recently taken off the market by the manufacturer. One oral vaccine (Dukoral®) contains inactivated 01-vibrios (equal parts of the Inaba classic strain, Inaba El Tor strain, Ogawa classic strain, and Ogawa strain) together with a recombinant B-subunit of the enterotoxin. Field studies in Bangladesh and Peru showed that this vaccine gives protection in 85–90%, however only for a period of six months. Subsequently, the protection rate decreases rapidly. A second vaccine contains only inactivated vibrios without the enterotoxin. This vaccine is only approved in Vietnam. The third vaccine is a live vaccine and consists of attenuated 01-vibrios. Population-based studies of its efficacy are not available. In volunteers a protection rate between 65 and 95% was reported. Presently the WHO does not foresee mass use of any of the available cholera vaccines in the endemic areas. In the context of travel medicine, indications are limited to travelers to high risk areas, where there are no sufficient options for exposure prophylaxis. The Dukoral® vaccine has an additional protective effect against traveler's diarrhea caused by E. coli (ETEC).

sequence, which is called a "TCP island". Interestingly enough, the TCP ligand serves as a receptor at the same time, through which the CTX bacteriophages enter the inside of a "pristine" vibrio. To complicate matters further, it turns out that one gene sequence in the TCP island called toxT codes for a transcription factor, which augments both expression of the TCP gene and the cholera toxin gene, if certain environmental conditions signal to the bacterial cell that it has arrived in the human small intestine. This is an astonishing example of evolutionary co-adaptation, in which a virus lends a virulence factor to a bacterium, uses an existing virulence factor as an entryway and finally alters the DNA of its host in such a way that the synthesis of both virulence factors is synchronized to optimize further spreading of *Vibrio cholerae*. The cholera patient's 15 to 20 diarrheal episodes per day ensure that the newly produced pathogens are dispersed far into the surroundings – be it through contaminated hands, toilet items, clothes or bed linens. Meanwhile another group of genes ensures that the vibrios arriving into the outside world are particularly contagious, so that even a small dose is sufficient to infect another person. These "hyperinfectious" pathogens are only found in human stool. If vibrios excreted by a patient are cultivated on a medium or passaged in laboratory animals, then their infectivity decreases rapidly: the pathogens from a cholera patient are 700 times more infectious than those after cultivation or animal passage.

In 1992 in Bengal a cholera-causing vibrio was first discovered, which did not belong to the "classic" family of the 01 serotype. This was not only a scientific sensation, but infection health professionals feared that a pathogen had emerged, against which the existing vaccine would be less efficacious. The new variant, 0139, one of the known 206 *Vibrio cholera* serotypes, has indeed the stuff to become a successful gladiator in the microbiological arena. Long-term investigations in Bangladesh have shown that 0139 and 01 fight with ferocity familiar to us in the business world, e.g. when a newcomer goes to all lengths to push an old-established company out of the market. At the beginning 0139 succeeded in displacing the classical cholera serotype in extensive parts of Bengal. Shortly thereafter 01 got the upper hand once again. Meanwhile dozens of variants of both strains have been discovered. These typically appear on the "epidemiological scene" for a short time, compete with one another and then disappear again. A still difficult-to-assess threat for persons in Bengal emerges as an unusual chance for bacteriologists to observe a natural experiment in a population of millions: the fast-motion evolution of competing disease-causing microorganisms.

In Bangladesh long-term studies showed that fighting cholera does not require complicated technology but can be accomplished by anyone with minimal investment. There, as in other developing countries, toilet paper is either in short supply or simply unheard of. In ignorance of basic hygiene, the left hand is usually used where we use sanitary articles. Soap for washing off the infectious material afterwards is not at hand under such living conditions. Thus hands are the transit site for microorganisms to find their way from the anus to the kitchen table.

Scientists at the International Centre for Diarrhoeal Disease Research in Dacca have now shown that the status quo can change. In a carefully carried-out study 115 women from several villages participated in an experiment, which was as convincing as simple. After using the restroom, the women were required to wash their hands with either soap and water, ash and water, or clay and water. A fourth group did not wash their hands, as is usual. Subsequently, fingertip swabs were taken and analyzed in vitro for *V. cholerae*. It turned out that washing with ash or clay reduced the number of microorganisms just as much as with soap, which is relatively expensive for Bangladeshis. Even the use of surface water in the monsoon season does not automatically lead to infection. Because cholera vibrios are mostly found in the small crustaceans in the zooplankton, it follows that filtration could remove the zooplankton and consequently the pathogen as well. Indeed recent investigations confirmed this. A nylon fabric with a mesh size of 150 micrometers filters out the zooplankton and thus about 99% of all cholera vibrios. A cloth, which is gratis and in sufficient quantity in southern Asia works even better: used sari fabric. By folding the material eight times, a filter with a mesh size of 20 micrometers on average is generated, fine enough to trap every tiny particle of that size. Old sari material is even more effective than new, because long use, in particular washing, frays fibers improving their capacity to filter small organisms.

Last year the rule was put to the test in 2212 households in rural Bangladesh, and the effectiveness of this appropriate technology was confirmed. The cholera incidence in families who regularly filtered their water through old sari fabric sank from 4 to 0.6 cases per 1000 inhabitants; compared to no significant change for households where things remained as before.

If the climate warms up bringing even more rain during the monsoon season in southern Asia, more surface water will be contaminated by zooplankton and cholera vibrios. Only simple technologies such as hand disinfection by ash and filtration of drinking water using old fabric can reliably protect the Bangladeshi population against the "mother of all plagues" since the efficacy of the current vaccines is still unsatisfactory.

Hermann Feldmeier
Conventional diagnostic imaging techniques such as X-rays, ultrasound, CT and MRI scans are usually the techniques of first resort for infection localisation, nuclear medicine techniques being reserved for instances where the former do not yield useful results. Increasingly, however, nuclear medicine imaging is being used as a first resort. This may be, at least partly, due to its higher sensitivity especially in the early stages of the infectious process before anatomical changes have taken place.

**CONCLUSIONS / THE FUTURE**

Advances in modern medical management have led to an increase in the number of immunocompromised patients with a heightened susceptibility to infection. This coupled with significant advances in nuclear medicine imaging means that the latter will play an increasingly important role in infection diagnosis in future.

Established nuclear medicine techniques such as radiolabelled leucocyte scans continue to play a useful diagnostic role while others such as Gallium-67 are fading. However, most of the current nuclear imaging techniques stumble on their inability to distinguish inflammation due to infection from that due to multiple other causes. Thus there is an increasing need for more sensitive and specific agents for infection imaging in the new millennium. Sensitivity implies the ability to detect the vast majority of infective lesions, including small ones. It is notable that the sensitivity of current methods is very poor in infective endocarditis. Specificity implies the detection of infective lesions to the exclusion of non-infective inflammatory ones. The ciproxin infecton is a positive step in that direction and is finding a useful niche in the diagnosis of orthopaedic infections. Several shortcomings, including false negatives due to current or recent antimicrobial therapy have meant that its initial promise has not been fully realised in practice. 99mTc-HNP-1 has a similar theoretical advantage as 99mTc-Ciproxin in that it targets bacteria rather than the inflammatory response. Unfavourable biodistribution kinetics and a less than encouraging performance in experimental mouse trials imply that much further development is needed before 99mTc-HNP-1 is deemed suitable for use in a clinical diagnostic setting.

It is hoped that future developments would overcome the drawbacks of earlier nuclear medicine imaging techniques. The latter include: inability to distinguish between bacterial and non-bacterial inflammatory processes, insensitivity at detecting small foci of infection, dependency upon a polymorphonuclear leucocyte response and inability to detect dead bacteria. The best hope for the future appears to lie in a marriage between two technologies, that of microbiology/immunology and nuclear medicine. Specific radiolabelled monoclonal antibodies or antibody fragments directed against bacteria, mycobacteria, fungi or viruses, theoretically offer not just accurate localisation of infection but also distinction between these various groups of infectious agents, i.e. a diag-

**Table 6: Systematic Imaging**

<table>
<thead>
<tr>
<th>A. Pyrexia of unknown origin (PUO)</th>
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<tbody>
<tr>
<td>✩ PUO is defined as fever of ≥37.8ºC, persisting for ≥ 3 weeks with no obvious cause despite investigation. Infection accounts for around half the cases, while tumours and connective tissue disorders collectively account for a further quarter. Leading infectious causes of PUO include TB, sepsis/pyogenic collection, bacterial endocarditis, imported diseases and zoonosis.</td>
</tr>
<tr>
<td>✩ Pyogenic collections or TB cavities can be detected equally well by conventional imaging as by Gallium-67 scanning.</td>
</tr>
<tr>
<td>✩ Vegetations associated with bacterial endocarditis can be too small (c. 0.5 cm), however, to be reliably detected by any of the available methods. Transthoracic ECHOs (TTEs) have a sensitivity of only around 60% while the more invasive trans-oesophageal (TOE) approach better 90%. Nuclear imaging is currently not sensitive enough to detect such small lesions and this must await the new more specific methods under development.</td>
</tr>
<tr>
<td>✩ The value of scintigraphy in PUO is unclear, largely due to scarce and conflicting data. However, Gallium-67 citrate and leucocyte scintigraphy are the most commonly used imaging techniques for this indication. Gallium-67 citrate scan is indicated in PUO of over 2 weeks duration as false negative results are common in PUO of under 2 weeks duration, vice-versa for Indium-111 leucocyte scans. Gallium-67 citrate is also unsuitable in suspected abdominal infection due to physiological cumulation in the bowel.</td>
</tr>
<tr>
<td>✩ Leucocyte scintigraphy is increasingly used as first line due to its superior image quality and lower radiation dose compared to Gallium-67 citrate and also in cases where Gallium-67 citrate scans are negative or are contraindicated. Indium-111 in-vitro leucocyte scintigraphy is generally preferred for this indication due to the longer half-life. Due to its high sensitivity, a negative leucocyte scan is believed by some to virtually exclude focal infection/inflammation as the cause of PUO.</td>
</tr>
<tr>
<td>✩ Due to its increased uptake in cells with a high glycolytic activity, common to both infections and neoplasms, FDG-PET may have a useful role in PUO. This is yet to be defined however. It is worthy of note that an abnormality demonstrated on scanning may not always be the cause of PUO and conversely a negative scan will not conclusively exclude infection as the cause. The imaging of other septic causes of PUO such as osteomyelitis and pyelonephritis are outlined below.</td>
</tr>
</tbody>
</table>
B. Vascular infection

- Synthetic graft infection of major blood vessels can have serious consequences and early diagnosis and treatment are therefore desirable. However, signs or symptoms can be absent or non-specific and X-rays are insensitive at detecting graft infection during the critical early months.

- Indium-111 in-vitro leucocyte scintigraphy is the technique of choice. It is more sensitive than 99mTc-WBC (94% vs. 55%). This is due to the fact that 111In-WBC is more rapidly cleared from the circulation than 99mTc-WBC and is thus associated with less spurious activity. However, false positive results amount to c. 13%, mainly in the groin area. Thus positive results in the groin area 4-8 months post-operatively should be interpreted with caution. Indium-111 in-vitro leucocyte scintigraphy can detect graft infections as early as one week post-operatively and positive scans can be obtained from three hours post leucocyte re-injection.

- CT scans are useful for pinpointing fluid collections, haemorrhages and thrombi. CT combined with Indium-111 leucocyte scintigraphy is believed to have such high sensitivity that a negative result would virtually exclude graft infection.

C. Bone infection

- Early diagnosis is critical in the successful treatment of osteomyelitis. Radiological diagnosis, however, lags at least two weeks behind bone damage, hence making bone scintigraphic techniques important. Indeed nuclear medicine is considered comparatively better at the diagnosis of skeletal infections than those of any other body system. Nearly 80% of cases of acute osteomyelitis occur in children and more commonly affect long bones than the axial skeleton.

- Technetium-99m phosphate, e.g. 99mTc-MDP, has usually been the most common used radiopharmaceutical for the diagnosis of acute osteomyelitis (Figure 2) except in infants (<6 months) where false negatives are common. Technetium-99m MDP or Technetium-99m HMPAO in-vitro leucocyte labelling have very high sensitivity in both adult chronic and acute childhood osteomyelitis.

- The Technetium-99m labelled murine anti-leucocyte fragment – Leucoscan® – is also licensed and in use for imaging of bone infection. None, however, can claim a high degree of specificity to infection. The specificity of 99mTc-MDP can be enhanced by 3 phase bone scanning, where the first phase is taken immediately post-injection, the second is taken five minutes post-injection with the third (conventional) image several hours later. The first and second phases visualise the blood supply and the vascular pool; infection is associated with “hot spots” on all three, while in metastases hot spots are usually seen in the third phase only.

- Technetium-99m ciprofloxacin has proven more sensitive than 99mTc-HMPAO-WBC in the imaging of acute osteomyelitis since the latter can display “cold spots” at sites of dead bone (involutrum). Additionally, 99mTc-ciprofloxacin has a higher sensitivity than Gallium-67 in chronic osteomyelitis including prosthetic joint infection. Technetium-99m ciprofloxacin has the additional advantage of lack of requirement for leucocyte harvesting and independence of leucocyte count. Technetium-99m ciprofloxacin is thus emerging as somewhat of a leader in orthopaedic imaging. Due to the variety of micro-organisms involved in chronic osteomyelitis (usually in immunocompromised patients), biopsy is nearly always required. Bone scans can also be used to delineate potential sites for biopsy.

- Technetium-99m MDP planar bone scans are usually sufficient in imaging of most cases of osteomyelitis. However, and where available, 99mTc-MDP-SPECT scintigraphy may provide more detailed information in acute osteomyelitis of the axial skeleton in both adults and children.

- Technetium-99m ciprofloxacin, FDG, HIG and anti-E-selectin antibodies have the advantage over both labelled leucocytes and Gallium-67 of lack of accumulation in bone marrow resulting in less background radioactivity.
D. Brain infection

- MRI is the technique of first choice for HSV encephalitis.
- In cases where MRI is negative, Technetium-99m HMPAO (stand-alone radiopharmaceutical, i.e. not associated with leucocytes) combined with SPECT scintigraphy may show enhanced brain uptake in HSV encephalitis 4–13 days after symptom onset. The mechanism for this is unclear but may be due to disruption of the blood-brain barrier. Cerebral toxoplasmosis is often, but not exclusively associated with AIDS. Diagnosis using conventional imaging can be difficult.
- Gallium-67 scans show enhanced uptake in toxoplasmosis space-occupying lesions. FDG-PET scans may show diffuse cortical lesions in AIDS-dementia complex. This technique is also useful in differentiating cerebral toxoplasmosis from tumours; e.g. hypometabolic “cold spots” are observed in cerebral toxoplasmosis and hypermetabolic “hot spots” in lymphoma.

E. Pulmonary infection

- Morphologic imaging such as chest X-rays (CXR) and especially CT and MRI scans, are effective tools for revealing pulmonary anatomical abnormalities, US scans being of limited use in the chest. However, gross functional defects can exist in the absence of discernible anatomical changes and may be revealed using nuclear medicine techniques. This is especially true in immunocompromised patients whose inflammatory response is attenuated. Suspected bacterial pneumonias in non-immunocompromised patients seldom call for such examination. However, when needed, and if available, FDG-PET scans are more sensitive than leucocyte scintigraphy. Paradoxically FDG produces excellent visualisation of lobar pneumonia but poor visualisation of bronchiectatic lesions and infection in cystic fibrosis patients which are well visualised by leucocyte scans (Figure 3).

E1. Pulmonary infection in AIDS

- Nuclear medicine imaging techniques have proven most useful in AIDS-related pneumonia. *Pneumocystis carinii* accounts for over 80% of pneumonias in AIDS patients and radiology is negative in up to 40% of subsequently proven cases.
- Gallium-67 has the theoretical advantage over leucocyte scans in that it is not dependent on a “normal” immune response. Thus Gallium-67 scans are often positive in AIDS associated *Pneumocystis carinii* pneumonia (PCP) where conventional radiography is negative. It is recommended that Gallium-67 scans are interpreted alongside a current CXR. Negative results on both investigations are said to exclude infection with a high degree of certainty. On the other hand, heterogeneous and intense pulmonary uptake on Gallium-67 scanning, accompanied by a normal CXR is strongly suggestive of PCP.
- A 99mTc labelled monoclonal antibody to *Pneumocystis carinii* has been trialled in 16 HIV positive patients with a clinical diagnosis of PCP pneumonia (19). The best images were obtained at 24 hours and the quoted sensitivity and specificity was 85.7% and 86.7% respectively.

E2. Pulmonary infection in febrile neutropenic patients

- Febrile neutropenic patients at high risk of severe infectious complications include allogenic bone marrow transplant recipients and those with prolonged and profound neutropenia (usually acute leukaemia patients). Pneumonia affects around a fifth of high risk febrile neutropenic patients and carries a mortality as high as 40%. This mortality is doubled in invasive pulmonary aspergillosis (IPA). The treatment for this condition involves a prolonged course of an Amphotericin B preparation which is significantly nephrotoxic. Early diagnosis is therefore very desirable in this group of patients.
- Conventional chest radiography has very poor sensitivity compared to CT scans, especially in the early stages. Early CT scans should thus be considered for high-risk febrile neutropenic patients who do not respond to antibacterial antibiotics by 72–96 hours and for whom no alternative credible explanation has been found for the continued pyrexia. Signs that are suggestive of IPA by CT (approximate incidence in parenthesis) include the “halo sign” (96% on day 1) and the “air-crescent sign” (28% and 63% on day 7 and 14 respectively). The halo sign represents an area of haemorrhage surrounding a necrotising lesion. None of these signs are pathognomonic for IPA, however, and they may occur in other types of pneumonia. Other non-specific signs on CT scanning include nodular lesions and ground glass opacities. These can be seen in wide variety of inflammatory, neoplastic, granulomatous and other disorders. CT scan findings may also be used to guide invasive diagnostic procedures such as percutaneous needle aspiration, bronchoscopy/lavage and open lung biopsy.
- MRI scanning may reveal a “reverse target sign” consisting of a hypointense rim sandwiched between the hyperintense necrotic and inflammatory areas. This sign is said to have a high specificity in diagnosis of early IPA.
- Gallium-67 is generally unsuitable for use in patients with haematological malignancy due to the defective inflammatory response as well as “physiological” cumulation in bone marrow. Leucocyte scintigraphy is also clearly unsuitable for infection localisation in neutropenic patients.
F. Abdominal infection

- The abdomen is often the site of pyogenic sepsis in PUO. For localisation, US and CT scans are usually performed initially, but are often negative in small, subdiaphragmatic or retroperitoneal collections or when spontaneous drainage or “decompression” occurs.

- Leucocyte scans using 111In-tropolonate can be helpful since it has no “physiological” bowel cumulation (see “in-vitro leucocyte labelling”, above). The, not infrequent, communication between abdominal abscesses and bowel lumen, often missed on US and CT scans can be readily visualised by 111In-WBC (Figure 4). 111In-WBC is also used to localise HIV associated oesophageal candidiasis.

- Technetium-99m HMPAO labelled leucocytes, on the other hand, exhibit “normal” pooling in bowel and gall bladder and this technique is therefore less useful for imaging of infections in these locations. Sequential and late scanning (e.g. at 1, 3 and 24 hours) using 111In-WBC is usually recommended if liver or gall bladder sepsis is suspected. In liver sepsis, images acquired at 24 hours usually reveal additional radiopharmaceutical uptake not detected at 3 hours. In the case of abscesses within the bowel lumen, activity increases steadily after 4 hours post re-injection while liver and splenic activity declines or remains constant (respectively) up to 24 hours.

G. Renal infection

- Acute pyelonephritis can have serious consequences, especially in children (renal scarring, chronic pyelonephritis and renal failure) and pregnant women (premature labour, septicaemia). Hence early and accurate diagnosis is important.

- Renal US and IVU are often performed initially but suffer from poor sensitivity. Renal US would be the preferred investigation for pregnant women.

- Technetium-99m dimercaptosuccinic acid (99mTc-DMSA) is highly concentrated in the renal tubules rendering it particularly suitable for morphological imaging, especially of the renal cortex. 99mTc-DMSA is well established in the imaging of renal scarring in children and non-pregnant adults as well as measuring relative renal function. Renal US and IVU are said to detect less than half and a quarter respectively of acute pyelonephritis cases detected by 99mTc-DMSA. It is considered the “gold standard” in early pyelonephritis imaging due to its higher resolution and lower gonadal radiation exposure. The latter is due to the fact that less DMSA accumulates in the bladder, compared to the alternatives.

- Technetium-99m pentetate (99mTc-DTPA) is mostly excreted by glomerular filtration and is thus useful in assessing renal perfusion and excretion. It is also used as a bladder instillation in the imaging of reflux nephropathy e.g. in children. Reflux nephropathy may be visualised using gamma camera micturating radionuclide cystography techniques, either directly, following instillation of a Tc-99m radiopharmaceutical (e.g. 99mTc-DTPA) into the bladder, or indirectly as an adjunct to renography when most of the radiopharmaceutical has drained to the bladder.

- Technetium-99m mercaptoacetyltriglycine (99mTc-MAG3) mostly undergoes renal tubular secretion and is thus especially useful in the imaging of reflux nephropathy as well as assessing renal tubular function. Where radiolabelled leucocyte imaging is deemed necessary, in-vivo labelling using 99mTc-anti-granulocyte antibodies may be preferable to 111In leucocyte scintigraphy in children as it obviates the need for leucocyte harvesting and delivers a lower radiation dose.

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Figure 4. Female, 69 years, presenting with PUO and negative blood cultures. Anterior abdominal/pelvic 111In leucocyte scan at 24 hours shows extensive intra-abdominal inflammation/sepsis and possible communication with the bowel.
being costly. However, the rewards in terms of achieving the necessary leap forwards in infection imaging will, no doubt, make it worthwhile.

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ACKNOWLEDGEMENTS

The author is grateful to Dr. Linda Smith, consultant nuclear medicine physician at the Royal Liverpool Hospital for kindly supplying the imaging photographs (Figures 2–4) in this article and for reviewing the manuscript. Special thanks are also due to Dr. Hugh Wilkins, consultant physicist at the West Cumberland Hospital, Whitehaven for his critical review of the manuscript.

REFERENCES


Fontilles – the Last and Only Leprosy Hospital in Europe

What began as a vacation trip to sites of pre-historic paintings in the hilly up-lands of Alicante, Spain, ended as a very professionally rewarding visit of the last and only leprosy hospital in Europe. The first thing that attracted our attention when driving through the hilly hinterland of the Costa Blanca was a wall built from natural stones running up- and downhill almost like the Great Wall in China (Figure 1). From some-
body familiar with the local area we learned that this wall encloses a leprosy clinic comprised of several buildings. It carries the name of the small village nearby: Fontilles. We drove into the area and were taken in by the beautiful groves and well-kept buildings dispersed between large trees in this dry Mediterranean landscape. The first person we approached was a gentleman who turned out to be José Luis Beneyto, a Jesuit Father who, together with 4 fellow members of this order, runs the administrative directorate of Fontilles. He arranged a meeting with Dr Pedro Torres, pharmacist at Fontilles. Associated with the clinic for many years and responsible for the pharmacy and the laboratory, he was the right person to provide fascinating and surprising insight into an important institution that deserves to be better known.

The leprosy hospital in Fontilles was built in the early 20th century by the Jesuit Father Carlos Ferris (Figure 2) and inaugurated in 1909 as Sanatorio de San Francisco de Borja. At this time leprosy was still a widespread disease in this area as elsewhere in Europe. Previously leprosy patients were living in caves and primitive shelters not far from the location of the clinic today. Relatives deposited food, rang a bell and disappeared before the patients came down the hills to pick it up. Carlos Ferris found this situation unacceptable and decided to build a hospital for these unfortunate people. For political reasons he was looking for a property in a remote area and was lucky to receive the donation from a private individual of a large lot in the vicinity of Fontilles far away from civilisation. Yet the political opposition from the surrounding communities was so fierce that the price was building a wall, a “wall of shame” according to Pedro Torres, to contain the patients. In 1947 Fontilles began to reach out by organising educational courses for medical doctors and nurses in Spain and abroad. In 1968 the outpatient clinic was opened. In 1969 Fontilles became a member of ILEP, the International Federation of Anti-Leprosy Associations.

In Fontilles there are currently some 100 patients living in two wards, one for individual patients and one for couples (Figure 3). Most of these patients are cured but sadly enough, with their scars and disabilities they are stigmatised by others and prefer to live in Fontilles. Most of them are old and handicapped. For them the institution is rather an elderly home than a hospital. However the disease is still not eradicated in Europe. In 2002 there were 14 new cases in Spain, many of them Romas, some immigrants. The incidence in Europe is slowly decreasing with fewer patients admitted every year.

Treatment lasts 1 or 2 years and consists of a combination of rifampicine, clofazimine and dapsone. In addition to the in-patients Fontilles personnel look after 150 out-patients from all over Spain. Former patients have occasional relapses. Cured patients are thus called in once or twice a year for a check-up for the rest of their lives. Fortunately, leprosy is, contrary to general belief, not very contagious. Relatives of patients suffering from a relapse are given preventive treatment with rifampicine, ofloxacin and minocycline.

According to another myth leprosy is a tropical disease. This is not true as the disease can occur at all latitudes and is mainly related to poverty. In the 19th century the main leprosy country in Europe was Norway as described by Hermann Feldmeier in ESCMID News 1-2001. At present the annual incidence of leprosy worldwide is still about 580 000 with India and Brazil being the countries most afflicted. The goal of WHO is to eliminate the disease by the year 2005, with elimination being defined as a prevalence of < 1/10,000. Currently meeting this goal seems unrealistic.

Five years ago Fontilles considerably broadened its scope and went international by dropping Spanish from its Statutes. It offers educational programmes on diagnosis, treatment and rehabilitation of leprosy patients all over the world and cooperates with foreign research institutes for the development of new diagnostic methods, serological and PCR, for difficult-to-diagnose cases. Fontilles actively supports projects in India, Brazil, China and Nicaragua and contributes to the programmes which are conducted under the auspices of ILEP. The resources needed to run these activities are from charity and official organisations. Interestingly, funding from the latter is secured by a deal with the government to also run an Alzheimer clinic on the Fontilles premises in a building that became available due to decreasing numbers of leprosy patients.

At present the medical personnel of Fontilles is comprised of 3 physicians, 1 pharmacist and 10 Franciscan sisters as nurses. It nearly goes without saying that Fontilles publishes a journal on leprosy, Revista de Leprología, with three Spanish-language issues per year.

A holiday trip east of Alicante ended with a lesson about a disease which I thought would have disappeared from Europe. It also left the impression that Fontilles is an effective and much needed institution with a clear mission dedicated members of a catholic order and the medical community.
News in Brief

Infectious Diseases and Outbreaks

LEGIONNAIRE’S DISEASE IN UK
In an outbreak of Legionnaire’s disease in Hereford, UK, 12 cases have been confirmed, one of whom, a 76 year old man, has died. The source of the outbreak has not yet been traced.

CDR Weekly 2003; 13: 46

INFLUENZA OUTBREAK IN DUBLIN SCHOOL
An outbreak of influenza involving 81 cases has occurred in a secondary school in Dublin in September. The first case had just returned from a visit to Asia. Influenza A (H3N2) has been identified in four of nine throat swabs tested. This is the first influenza outbreak to be reported in the 2003-2004 season. Subsequent reports in November note a low incidence of influenza in Europe.

Eurosurveillance Weekly 2003; 7: 40, 8:45

NOROVIRUS INFECTION ON CRUISE LINER IN THE MEDITERRANEAN
Over 500 people out of 2,600 on board a cruise liner which set sail from Southampton, UK, in October contracted a gastrointestinal illness of short duration. The medical team on board confirmed the presence of Norovirus in patient specimens. The first cases occurred 2 days after leaving Southampton, with the numbers peaking at 6 days.

Eurosurveillance Weekly 2003; 7: 45

Viral Infections

SARS
Workers in The Netherlands have shown that cats and ferrets are susceptible to the SARS virus. The aim was to find a species other than non-human primates suitable for testing potential drugs and vaccines against SARS. Ferrets develop a disease with similarities to that seen in humans but cats, although shedding virus, are asymptomatic.

Martina et al. Nature 2003; 425: 915

A number of drugs with activity against either influenza or HIV are being tested for their activity against the SARS virus in vitro. Pfizer has submitted over 300 test compounds originally developed for activity against the common cold, many of which are protease inhibitors. The combination protease inhibitor Kaletra (ritonavir and lopinavir) is undergoing clinical trials and has shown some promise.

Vastag, JAMA 2003; 290: 1695

WEST NILE VIRUS (WNV)
Details have been published demonstrating the transmission of WNV through blood transfusion in the US. A total of 23 patients were found to have contracted WNV through transfusions of red cells, platelets or fresh-frozen plasma. The 16 donors linked with these infections were all negative for WNV-specific IgM antibody at the time of donation but nine reported viral symptoms.

Pealer et al. NEJM 2003; 349: 1236

As a consequence of the confirmation of the risk of transmitting WNV by blood donation, various European countries have issued guidelines and those who travelled to the US and Canada between June and November are barred from donating blood for 28 days after their return. Countries adopting this policy include France, Ireland, Malta, Norway, Switzerland and the UK. Several other countries are considering the situation.

Eurosurveillance Weekly 2003; 7: 34

A more rapid diagnostic test for WNV has been approved by the FDA. The test has been developed by PanBio, an Australian firm, and is an IgM capture ELISA assay which takes only two hours to complete. It cannot, however, distinguish between other closely related viruses.


A new test has been developed which can distinguish between WNV and the closely related flaviviruses Dengue and St Louis encephalitis. It is an immunoassay based on the presence of a non-structural protein (NS5).

Wong et al. J. Clin Microbiol 2003; 41: 4217

WNV cases have doubled in 2003 in the US, with the virus now established in many states. The total number of human cases in 2003 (as at November 12) is 8,393 in 45 states with an approximately equal distribution between the sexes. There have been 184 deaths. In addition, there have been over 11,000 dead birds infected with WNV recorded from 42 states, and a total of 4,084 horses, 26 dogs, 17 squirrels and 1 cat infected in 41 states.

MMWR Weekly 2003; 52: 1105

WNV infection has been found in two humans (one confirmed, one presumed) and in three horses (one confirmed, two presumed) in south-eastern France, near the Camargue. WNV has been documented before in horses in the Camargue, but these are the first cases for some years.

Eurosurveillance Weekly 2003; 7: 43

The structure of the WNV has been determined by a team of workers at Purdue University, US, using cryo-electron microscopy and imaging techniques. The orientation of the major surface proteins has been revealed, indicating how they interact with one another.

Kuhn et al. Purdue University News Release

A clinical trial to determine the effect of immunoglobulin containing antibodies to WNV has been launched by the National Institute of Allergy and Infectious Diseases in the US. The aim is to compare this therapy with standard immunoglobulin.

JAMA 2003; 290: 2117

Monitoring for WNV in Mexico and Jamaica has revealed that the virus is now widespread in horses in Mexico and in birds in Mexico and Jamaica but no human cases have yet been identified.


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Vaccines

SMALL POX VACCINE MAY HAVE ACTIVITY AGAINST HIV
Workers in the US examined blood from subjects vaccinated against smallpox using the Acambis vaccine. They claim that blood from vaccinated people was able to prevent or reduce the growth of HIV in culture. Further work is planned. The method of announcing these uncorroborated results, via a press release, has antagonised a number of workers in the field since the results have not been formally published. They have pointed out that many vaccinations can cause a temporary boost in immunity.

AVENTIS PASTEUR MSD GRANTED CONTRACT IN UK FOR SMALLPOX VACCINE
A £45.2 million contract has been awarded by the UK government to Aventis Pasteur MSD for providing smallpox vaccine.

NEW DUAL ACTION ANTHRAX VACCINE
A new anthrax vaccine has been developed that protects against both the bacillus and the toxin. This has been achieved by conjugating the capsular poly-D-glutamic acid (PGA) to the protective antigen (PA). This conjugation had a synergistic effect, enhancing the immunogenicity of PGA and the humoral response to PA. The vaccine was shown to be effective in mice.

DIFFERENT APPROACH TO MALARIA VACCINE
A worker from the US claims that progress is too slow in the development of a vaccine against malaria using the current approaches. He is investigating a modification of a method first suggested in 1967, namely the use of irradiated sporozoites. The sporozoites retain the ability to infect the liver but not to subsequently infect red blood cells and thus cannot cause a progressive disease. This is an imaginative approach with many technical difficulties but which could be highly effective.

WORK TO ERADICATE POLIO CONTINUES
The WHO has set, as a priority, the eradication of polio by 2005. The disease has been eradicated from all but seven countries but the last stages of eradication may prove difficult. Just one case can lead to a resurgence of disease. The widely used oral vaccine contains an attenuated strain which has the ability to mutate to a virulent strain. The Salk vaccine contains an inactivated strain but requires injection, and is thus less suitable for use in developing countries.

PROMISING NEW VACCINE AGAINST EBOLA
Immunity to Ebola can develop in as little as four weeks in macaque monkeys following a single dose of a new vaccine. If such a vaccine proves safe and effective in humans, this could limit dramatically the spread of outbreaks of Ebola. The vaccine has been developed from an adenovirus, which provokes an aggressive immune response, containing part of the genome of the Ebola virus.

PRIONS

PREVENTING THE PROGRESSION OF PRION DISEASES
Workers at the Institute of Neurology, UK, have shown that depletion of normal host prions (PrPc) in mice infected with scrapie prions prevented the progression of the disease. Depletion of the normal host prion in non-infected mice was without any apparent harmful effect. This study indicates that it is the conversion of normal prion protein to abnormal prion protein that causes the neuronal damage rather than the accumulation of the abnormal protein.

A SECOND PATIENT WITH VARIANT CJD IS TO RECEIVE EXPERIMENTAL TREATMENT
The experimental drug, pentosan polysulphate injected directly into the brain, was approved for use on a young patient with vCJD in Belfast, UK late in 2002. This patient is still alive and there are some indications of neurological improvement. Approval has now been given for another young patient in the UK to receive the same treatment. This patient is 18 years of age.
age and the disease has not advanced as far as it had with the first patient.

BMJ 2003; 327: 886

CHRONIC WASTING DISEASE (CWD) SPREADING RAPIDLY IN US
The latest studies in the US have revealed that the prion disease, CWD, in deer has the ability to spread with greater ease than was previously thought to be the case. The disease affects white-tailed deer, mule deer and elk and has spread into at least 12 states. The indications are that the disease can spread between animals as well as being passed from mother to unborn fawn. Stringent measures will be required to prevent further escalation of this disease.

Miller & Williams. Nature 2003; 425: 35

NEW STRAINS OF BSE PRIONS FOUND IN ITALY AND JAPAN
Routine sampling of cattle in abattoirs in Italy and Japan has revealed the presence of different strains of prions. These were detected using a conventional Western blot technique of brain tissue. To date all BSE prions analysed have been identical although there are different types of scrapie and variant CJD prions.


PRION PROTEIN CONVERSION TO ABNORMAL TYPE REQUIRE RNA
A paper published in Nature has shown that the conversion of normal to abnormal prion was stimulated in the presence of host-encoded nucleic acid. Single stranded RNA appeared to be necessary for the conversion. This was species-specific with no effect being seen in the presence of invertebrate RNA. They suggest that this may help in improving the sensitivity of diagnostic techniques.

Deleault et al. Nature 2003; 425; 717

HIV and AIDS

LACTOBACILLI CAN PROTECT AGAINST HIV
Lactobacillus jensenii is a commensal in the healthy human vagina and can help protect against a range of pathogenic organisms. It has been modified to secrete CD4, a protein normally present on immune cells; it is this protein to which HIV binds. The modified Lactobacillus binds HIV-1 and when incubated with cultured human cells, prevents their infection. It is hoped that it may provide a method of protecting women from sexually transmitted HIV.

Chang et al. Proc Natl Acad Sci 2003; 100: 11672

SURPRISING RESULTS ON EFFECTS OF NON-ADHERENCE TO DRUG REGIMEN AND RESISTANCE
A recent study published in the journal AIDS reveals that non-adherence to anti-HIV drug regimens does not lead to a greater risk of the development of resistance, rather the reverse. Pressure from antiviral medication seems to be required for resistance to develop. Good compliance leads to more resistance than occasional or inconsistent pill-taking. These surprising results indicate that the relationship between taking all the drugs prescribed and the development of resistance is more complex than had been thought.

Bangsberg et al. AIDS 2003; 17: 1925

New Chemotherapeutic Agents

NEW APPROACH TO TREATING RESPIRATORY VIRUSES
A group at Imperial College, London, UK, has tested fusion proteins that modify the cytokine response in mice and shown them to have a marked therapeutic effect against an experimental influenza infection. The protein binds to a receptor and reduces the influx of T-cells and thus the inflammatory response. The drug was administered intranasally and the authors suggest that this approach could prove of value for other respiratory conditions where an excess inflammatory response occurs, such as in SARS or asthma.


RNA POLYMERASE INHIBITORS SHOW PROMISE
A group of synthetic inhibitors of bacterial RNA polymerase has been shown to inhibit the addition of nucleotides in E. coli. These compounds (CBR703 series) appear to be selective for bacteria and do not affect RNA polymerase in human cells.

Artsimovitch et al. Science 2003; 302: 650

Industry and Drugs

EMTRIVA APPROVED BY EMEA
Gilead’s emtricitabine (Emtriva®) was approved for marketing in all member states of the EU on July 24th by the EMEA. It was also approved by the FDA the same month. (Emtriva®) is a nucleoside reverse transcriptase inhibitor available as capsules for adults and an oral solution for children, dosed once daily in combination with other agents for the treatment of HIV.

PROTEASE INHIBITOR LEVIXA APPROVED BY FDA
The protease inhibitor, fosamprenavir calcium (Levixar®), developed jointly by Glaxo SmithKline and Vertex, has won approval from the FDA. The drug has been tested in combination with ritonavir (Abbot) and will be dosed either once or twice daily.

KETEK STILL NOT APPROVED BY FDA
The Aventis ketolide, telithromycin (Ketek®) has still not won approval from the FDA for marketing in the US. This is in spite of the firm submitting a considerable amount of new data on safety in over 20,000 patients. The FDA did not, however, request more studies, but asked for additional analysis of the current data; this has now been submitted. There have been questions over liver toxicity, heart abnormalities and blurred vision. The company remains confident that approval will be given early in 2004. Ketek is already market-ed in Europe and in Latin America.

TAKEDA GIVE PENINSULA RIGHTS TO NEW CEPHALOSPORIN
The US company Peninsula has been granted the rights to develop a novel
cephalosporin, TAK 599, by Takeda. Clinical studies are scheduled to start in 2004. Takeda retains the marketing rights for Japan.

CUBIST AND CHIRON MAKE AN AGREEMENT OVER DAPTOMYCIN
The new antibacterial, daptomycin, was developed by Cubist who recently obtained marketing approval by the FDA. Cubist has entered into an agreement with Chiron who will commercialise the product.

NEW LABEL FOR PEG-INTRON APPROVED BY EMEA
Schering Plough's drug for hepatitis C, Peg-Intron, has had new labelling approved dispensing with the requirement for a live biopsy. This is in line with its competitor, Roche's product, Pegasys.

ROCHE BUYS RIGHTS TO SANKYO'S NEW CARBAPENEM
The new parenteral carbapenem, CS 023, developed by Sankyo, will be developed and marketed by Roche in the US and Europe. Sankyo retains the rights for Asia and parts of the Middle East. The compound is currently in Phase II studies.

LINEZOLID AND SEROTONIN TOXICITY
There have been suggestions that linezolid may cause serotonin toxicity when administered with certain other drugs. A letter in *Clinical Infectious Diseases* discusses this possibility and the author explains that if linezolid is a monoamine oxidase inhibitor (MAOI), then toxicity may be expected if it is co-administered with serotonin reuptake inhibitors or dual action antidepressants.


**European Matters**

DUTCH TO MAKE CUTS IN HEALTH SPENDING
Holland is currently one of the top three European countries in healthcare spending, but the government has just announced great cuts in the money allocated to health care. Charges will be introduced for many services that are currently free and many treatments will be removed from public health insurance. These plans have not met with approval from the Royal Dutch Medical Association.

*Sheldon BMJ 2003; 327: 641*

SPAIN INTRODUCES NEW PRICING SYSTEM FOR PHARMACEUTICALS
The pharmaceutical market in Spain is the seventh largest in the world ($8.56 billion in 2002) but the government has been trying to reduce the expenditure, with little success to date. It has now introduced a new reference price system and has listed 68 compounds that will be affected by this. It also intends to restrict the promotional activities of pharmaceutical sales representatives. A constraint on the prescription of high-priced drugs has already had an effect and this effect may increase.

*IMS Health online. October 26, 2003*

EMEA WARNS AGAINST NEW HIV DRUG COMBINATION
A triple combination of anti-HIV drugs proved disappointing in clinical trials carried out by Glaxo SmithKline (GSK), although all three agents have shown efficacy in other combinations. The EMEA has warned doctors not to use this new combination and to monitor those already on it very carefully. The combination consists of two GSK compounds, abacavir and lamivudine, both of which have been on the market for some years, and Gilead's tenofovir, which was launched in 2002.

CHANGES PLANNED TO EMEA
Currently regulatory approval for medicines in Europe is twofold with both the EMEA and a mutual recognition system being used. This dual system is seen as being inefficient but there has not been agreement as to the best way forward. There is now recognition that Europe needs to improve in order to compete with the US and a final draft of the desired reforms has emerged from the European Parliament Health Committee. These involve a phased change to a completely centralised system.

*www.pharmafocus.com November 6, 2003*

**EUROPEAN RESEARCH COUNCIL**
An interim report released by a group of national experts at the end of September outlined suggestions for a European Research Council (ERC). A major point made is that this should only be established if additional funds were provided for it and these did not come from existing projects.

*Watson. BMJ 2003; 327: 768*
Forthcoming Events

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**

17–19 March 2004
ESCMID Workshop on Progress Toward Meeting the Challenges in Clinical Microbiology and Infectious Diseases
Place: Leuven, Belgium
Contact: Prof Marc Struelens
Email: marc.struelens@ulb.ac.be

25 – 29 April 2004
24th ESCMID Postgraduate Education Course: 5-Day Workshop on Microbial Typing Technologies
Place: Warsaw, Poland
Contact: Dr Joanna Empel
Phone: +48 22 841 3367
Email: jempel@il.waw.pl

1 May 2004
Pre-ECCMID Teaching Courses (Please see ECCMID website for more information)

1 April 2004
Pediatric and Obstetric Aspects of HIV-Infection
Place: Basel, Switzerland
Contact: Prof Christoph Rudin
Email: christoph.rudin@unibas.ch
Phone: +41 61 685 65 65

5–7 May 2004
1st International Clostridium difficile Symposium
Place: Gozd Martuljek, Slovenia
Contact: Dr. Maja Rupnik
Email: mrupnik1@gwdg.de
Internet: http://rcul.uni-lj.si/~bfbcdiff/lcids/

15–18 May 2004
19th Annual Meeting of the European Working Group on Legionella Infections
Place: Chamonix, France
Email: jetienne@univ-lyon1.fr
Internet: http://www.invs.sante.fr/agenda/ewgli_2004/

22–24 September 2004
17th International Workshop on Gastrointestinal Pathology and Helicobacter
Place: Vienna, Austria
Contact: Vienna Medical Academy
Email: ehs2004@medacad.org
Internet: www.helicobacter.org

Supported by ESCMID

30–31 January 2004
9th International Conference on Infections in the Critically Ill Patient
Place: Rome, Italy
Contact: McCann Meetings
Phone: +34 93 206 46 46
Email: infections2004@mccann.es
Internet: www.infections-online.com/

1 April 2004
1 April 2004
Pediatric and Obstetric Aspects of HIV-Infection
Place: Basel, Switzerland
Contact: Prof Christoph Rudin
Email: christoph.rudin@unibas.ch
Phone: +41 61 685 65 65

5–7 May 2004
1st International Clostridium difficile Symposium
Place: Gozd Martuljek, Slovenia
Contact: Dr. Maja Rupnik
Email: mrupnik1@gwdg.de
Internet: http://rcul.uni-lj.si/~bfbcdiff/lcids/

14th European Congress of Clinical Microbiology and Infectious Diseases

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www.escmid.org/eccmid2004

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