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Dear Colleagues

As this issue of the News illustrates, the Society is vibrant with scientific, educational and health promotional activities. Echoes from the recent 15th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Copenhagen last April underline the important continuing educational role it plays as Europe’s premier international congress on diagnosis, therapy and prevention of infection. Attended by over 6000 participants, it featured over a hundred oral sessions, pre-congress educational workshops and more than 1700 scientific communications. According to the online opinion poll held about the event, the vast majority of attendees found the balance between basic science and practical issues adequate while the Programme largely met their expectations of getting the latest information in their field. Useful suggestions and criticism from pollsters will be taken onboard by the organisers and programme planners of the forthcoming ECCMIDs to strive for the best standards for scientific output.

The ESCMID Assembly of Members approved the Executive Committee’s annual report of activities (see Minutes, page 4) and the European Council met to discuss partnerships with national societies of Clinical Microbiology and Infectious Diseases. The many members of affiliated national societies now receive an electronic summary of the ESCMID News, thereby getting better acquainted with ESCMID’s programme of activities.

Whilst the current outbreak of H5N1 avian influenza expands and keeps the world on alert to react to the potential unfolding of the next influenza pandemic, it is comforting to note recent progress made toward better international response to communicable disease threats. The World Health Assembly adopted the new International Health Regulations on 23 May, following a decade of negotiations. New procedures enable the WHO to assess any disease report in terms of risk of global spread, declare emergencies requiring international action, and recommend quarantine or restriction of travel and trade. Event notification to WHO includes novel and unknown diseases as well as an expanded list of infectious diseases of potential serious public health impact. Governments are asked to critically review and improve their communicable disease surveillance and response systems.

These are challenging times that require enhanced cooperation between specialists in the infection disciplines, health policy makers and healthcare authorities. The mission and priorities for the newly launched EU agency, the European Centre for Disease Control and Prevention in Stockholm, is presented in this issue by its Director Ms S. Jakab who invites scientists and medical specialists across Europe to support and advise on the Centre’s activities. ESCMID will contribute to this effort through its representation in the ECDC Advisory Forum.

Marc Struelens
Past President
Chairman, Publication Committee

Front page:
The cover shows a scanning electron microscopic picture of Salmonella. This pathogen is a well-known cause of food-born gastroenteritis. As described in the feature article on page 31, Salmonella infections are also frequently contracted from pet reptiles.
Message from the President

With great anticipation I started my 2-year period as ESCMID President. Having followed the Society closely since the end of the 1990s it is striking how ESCMID has developed. Clearly, ESCMID is the leading organisation for those who are professionally active in Clinical Microbiology or Infectious Diseases. Several factors have contributed to this successful development. Most important are the persons who have been or are members of the Executive Board. They are well known experts in their fields and have been willing to contribute a considerable amount of their time to the Society. In particular my appreciation and thanks go to Roger Finch who left the Executive Board last April after having served 8 years as Member, President-elect, President and Past President. He has certainly been an outstanding representative of ESCMID within as well as outside of Europe.

Another person who has left the Executive Committee after many years of service is Claude Carbon whose contribution as Education Officer has resulted in several summer schools and web-based education. His initiative to start the ESCMID Summer School has resulted in four successful one-week courses. This year the Summer School moved to Hungary.

Another matter of importance discussed at the latest Executive Meeting was ESCMID’s engagement together with the European Respiratory Society (ERS) in a recently-approved large project financed by the directorate for research within the EU. It has been given the acronym GRACE (Genomics to Combat Resistance against Antibiotics in Community-acquired LRTI in Europe) and will implement a broad scientific approach to study and improve management of community-acquired lower respiratory tract infections. The task of translating the results of the many work packages into workshops, training courses, summer schools and web-based educational material will rest with ESCMID and ERS. We see this as an important step in the relation between the EU and a society such as ESCMID and, importantly, we are now clearly recognised as partners in improving science and medical practice in Europe.

For a long time there has been a tendency towards concentrating scientific affairs in Europe to the West European countries. ESCMID has tried to overcome this problem, e.g. by encouraging and facilitating attendance at ECCMID by young scientists from Central and Eastern Europe through travel grants. For several years we have also participated in meetings of the Interregional Association for Clinical Microbiology and Antimicrobial Chemotherapy, IACMAC. The latest meeting of this Russian society was held in May this year whereby several representatives of the Executive Committee contributed to the scientific programme. This cooperation with Eastern European countries will further expand with ESCMID participating in meetings in the Baltic countries, Georgia and the Ukraine under the leadership of the President-elect, Giuseppe Cornaglia. We see this as a first step towards improved scientific and educational cooperation within an expanded Europe.

Finally, ESCMID now has a European Council consisting of affiliated scientific societies from most European countries. The Council will be an essential forum for communication with and input from as many as possible of those involved in Infectious Diseases and Clinical Microbiology in Europe. The Council will meet annually during ECCMID. We also hope that this system of affiliation will result in an expansion of ESCMID’s regular membership.

Journal discounts

We are pleased to announce that in 2006, ESCMID members will be able to take advantage of a preferential subscription rate to:

- **INFECTION**
- **Reviews in Medical Microbiology.**

Details on these offers will be given in the next ESCMID News and on the membership renewal form to be sent out later this year.

The Publication Committee
Assembly of Members 2005

Minutes

The Assembly of Members in the year 2005 was held during the 15th ECCMID in Copenhagen on 3 April at 17:45 h

1 Welcome and President's report
Marc Struelens welcomed the 98 attending members to the 2005 Assembly. He observed that the minutes of last year's Assembly have been published in ESCMID News 2-2004 and that the invitation to and the agenda of the Assembly 2005 had been correctly sent out as stated in the Statutes.

From his report on the many activities during the past year only the key points shall be mentioned here:

Membership and Management
- geographically balanced and expanding membership
- healthy finances due to fiscal prudence
- renewed European Council based on a revised affiliation scheme of national societies
- reorganised Executive Office with additional manpower

Education
- several postgraduate education courses and pre-ECCMID workshops
- 3rd ESCMID School (Athens, Greece)

Science
- Memorandum of Cooperation with FEMS
- practice guidelines published by ESCAR and ESGARS on tick-borne bacterial diseases and antibiotic resistance surveillance, respectively
- formation of two new study groups on primary care and biofilms, respectively
- CM: increased impact factor and publication output
- ECCMID: rising attendance and quality of presentations

Professional Affairs
- Cooperation with UEMS in the field of CME accreditation, training curricula and recognition of ID and CM across Europe
- EUCAST: breakpoints published, cooperation with EU, EMEA and CLSI
- Consensus declaration of Leuven workshop on Meeting the Challenges in CM and ID published
- ARPAC consensus recommendations in press

European Affairs
- Participation in EU-funded projects IPSE and GRACE
- Position paper on the new Commission's public health policy published

At the Assembly 2005 two new members of the Executive Committee assumed office: Prof Javier Garau, Barcelona, as Education Officer, and Prof Robert Read, Sheffield, as Professional Affairs Officer for Infectious Diseases. They were elected by the membership as successors of Claude Carbon and Roger Finch, who reached the end of their terms according to our Statutes. Marc Struelens thanked the two departing officers once again for their many contributions to the Society.

2 Report of the Secretary General
According to figures presented by Giuseppe Cornaglia, ESCMID has currently 2874 members, 144 more than last year. The best-represented countries are the UK with 212 members, Italy (192), Germany (191) and the US (185).

Giuseppe Cornaglia then expressed his satisfaction about the positive response by the majority of the members of the previous European Council to renew their affiliation with ESCMID under a new scheme. This renewed institution will need to be consolidated in the near future. Its purpose is to serve as a platform for the exchange of information (which includes a.o. an electronic newsletter), discussion and negotiation. It convenes once during ECCMID and will develop its own agenda devoted to professional issues of common interest. In response to a question from the audience Giuseppe Cornaglia confirmed that all major national societies in the field of CM and ID across Europe will be invited in the near future to join the Council.

3 Presentation of the ESCMID Research Fellowships
The ESCMID Research Fellowships 2005 were presented by Roger Finch, Past President and Chairman of the Awards Committee, to:

- Adilia Warris, MD, PhD, born 1968, Radboud University, Nijmegen Medical Center, the Netherlands. She has also been selected to receive the joint ESCMID/FEMS Research Fellowship.
- Pedro Cravo, PhD, born 1970, Centre for Malaria Studies, Lisbon, Portugal.
- Ronan McMullan, MD, born 1975, Department of Medical Microbiology, Royal Group of Hospitals, Belfast, UK.

Roger Finch congratulated the recipients (applause) who were each given a cheque of EUR 5000.

4 Financial report of the Treasurer
Andreas Voss presented the detailed but still preliminary profit and loss accounts for the year 2004. While the expenses of EUR 996'322 corresponded to budget the revenues of EUR 1'785'177 were much larger than expected due to the financially very successful 14th ECCMID 2004 in Prague. This allows saving EUR 500'000 as a reserve for poorer years.

The balance sheet showed a profit carried forward as of 31 December 2005 of EUR 1'624'030.

5 Approval of the accounts (vote)
Marc Struelens asked for a hand vote of approval of the financial report. It was approved unanimously.

6 Report of the Education Officer
Claude Carbon introduced Javier Garau, Barcelona, as new Education Officer in the ESCMID Executive and referred to the new members of the Education Committee: Marek Gniadkowski, Warsaw, and Daniel Christmann, Strasbourg.

In 2004 the following educational activities were held:

i) 3rd ESCMID School, Athens, GR, 26 June – 3 July 2004 (organised by the ESCMID Education Committee, 36 students attended)

ii) Six Postgraduate Courses or Workshops were held under the auspices of and supported by ESCMID:
- Microbial typing technologies, Warsaw, Poland, 25–30 April 2004 (organised by ESGEM)
Mechanisms of antimicrobial resistance, Palma de Mallorca, Spain, 20–26 June 2004 (organised by UAB and SEICM)

Measuring, auditing and improving antimicrobial prescribing, Prague, Czech Republic, 29 April–1 May 2004 (organised by ESAGAP)

Evaluation and management of treatment failure in HIV-infected patients receiving antiretroviral therapy, Prague, Czech Republic, 30 April–1 May 2004

Training course in hospital epidemiology, Freiburg, Germany, 17–20 October 2004 (organised by SHEA and ESCMID)

Treatment of ICU infections, Sochi, Russia, 8–9 October 2004 (organised by ESGARS and IACMAC)

i) 14th ECCMID: 17 Meet-the-Expert sessions and 4 pre-ECCMID workshops in collaboration with ESCMID Study Groups.

Furthermore, in the reporting year, GRACE, a Network of Excellence proposed to DG Research, led by Prof Goossens, was revised and re-submitted. As partners of this network, ESCMID and ERS would be responsible for an educational platform on community-acquired lower respiratory tract infections. Also under preparation was an educational project of ESCMID called CAPTRAIN for submission to DG Research’s Marie Curie programme. CAPTRAIN would essentially consist of 30 workshops on antibiotic resistance in community-acquired infections to be held during 3 years for early-stage researchers across Europe.

7 Report of the Professional Affairs Officer, Clinical Microbiology

Elisabeth Nagy showed a map of Europe with all countries labelled green where Clinical Microbiology is recognised as an independent specialty. This is the case in the vast majority of countries, which strangely contrasts with the fact that Clinical Microbiology is still not an independent section in UEMS. She then referred to the ESCMID workshop held in Leuven in March 2004 on the Challenges in Clinical Microbiology and Infectious Diseases. The proceedings, which addressed many professional issues related to microbiological laboratories, were published as supplement to CMI in April 2005.

In the reporting period the European Board for the Accreditation of CME in Clinical Microbiology (EBACM) was set up as a joint venture between the Microbiology Commission of UEMS and ESCMID. For details Elisabeth Nagy referred to the ESCMID website.

Currently a questionnaire is being evaluated aimed at gathering information about recognition, admission, training, CME and medical practice in the fields of CM and ID across Europe. The results will be published in ESCMID News as soon as they are available. Currently there are still gaps that need to be filled in by obtaining feedback from national societies who have not yet received the questionnaire.

8 Report of the Professional Affairs Officer, Infectious Diseases

Among the countries represented in UEMS only 4 still do not recognise ID as a medical specialty in its full right as explained by Ragnar Norrby. This is encouraging and should facilitate further harmonisation of training, CME and practice of ID across Europe. The questionnaire referred to by Elisabeth Nagy will identify the major needs for action. Our goals will be to further cooperation between disciplines, mainly CM and ID. The establishment of ID as subspecialty of paediatrics should be encouraged.

9 Report of the Scientific Affairs Officer

Jordi Vila conducted a review among the 12 ESCMID Study Groups about their activities in the past year. Among the eight responders all communicated results on behalf of their Study Group at a scientific meeting, six published a paper or guidelines, five organised a scientific meeting, seven organised educational activities and four ran a research project. He congratulated the Study Groups for these activities, which are central to the mission of our Society.

He then referred to the first joint Conference on New Frontiers in Microbiology and Infection co-organised with FEMS on Lessons on Escherichia coli: from basic research to clinical aspects. It will take place from 4–8 September 2005 in Villars-sur-Ollon, Switzerland.

10 Report of the Chair of the Publication Committee

As chair of the Publication Committee Roger Finch reported on the key figures of CMI which developed so positively during the past year: increasing number of submissions (570 in 2004), shorter acceptance to publication time (5–6 months), increased impact factor (2.24), increased subscription rate (+10%), increased consortia online access (+58%). Financially we have almost broken even despite substantial costs for the purchase of additional pages to publish the inherited backlog of accepted papers.

An issue which has been repeatedly debated by the Publication Committee and the Publisher is the initiative for “open access” to scientific journals. In contrast to the current situation where subscribers pay for scientific information, this movement would reverse situation by charging the expenses for publication to authors. In the case of CMI this would be about EUR 2000–2500 per paper. “Hybrid” models were also discussed: authors can buy immediate and free online access for a certain fee on a voluntary basis. This might be an attractive approach to test the market and avoid an abrupt and risky transition of CMI from the current scheme to “open access”. The situation is being constantly reviewed but the decision as to which way to go is still pending.

We have recently been able to negotiate with the owner of Reviews in Medical Microbiology and Infection preferential subscription rates for ESCMID members. With the 2006 membership renewal form these offers will be included.

11 Report of the President of the 15th ECCMID

Niels Hoiby thanked his colleagues from the Organising Committee for their support which made presidency of this congress an “easy job”. With 5326 delegates (plus 273 accompanying persons and 780 exhibitors), 129 scientific sessions, 1589 posters and 80 exhibiting companies this year’s ECCMID was another big success. He then wished Pierre Dellamonica all the best for his job in preparing the 16th ECCMID 2006 in Nice and handed over the “challenge cup” which is a silver plate with the engraved ESCMID logo and a list of all ECCMID venues since 1983.

12 Report of the Chair of the 15th ECCMID Programme Committee

After many years of responsibility for the scientific programme Patrick Francioli resigned from his office as Programme Director after the ECCMID in Copenhagen. In looking back he drew a positive balance:
if the attendance and number of abstracts submitted are indicators of quality and satisfaction the recent history of ECCMID proves that we have been successful. He not only thanked his colleagues in the Programme Committee but also the ESCMID Study Groups and the participating industry for their contribution to the quality of our Congress. Last but not least he acknowledged the ESCMID membership for the increasing trend to submit the best data to ECCMID and not to other meetings. Andreas Voss will follow him as chair of the Programme Committee. Patrick Francioli wished him success, satisfaction and all the best in his new job.

13 Release from responsibility of the Executive Committee
Marc Struelens asked for a hand vote about the exoneration of the Executive Committee. This was approved unanimously.

14 Any other business
No request to speak.

15 Inauguration of the new President
At the end of his term, Marc Struelens handed over the “gavel” to his successor for the next two years: Ragnar Norrby, Professor of Infectious Diseases, Stockholm, Sweden. Ragnar Norrby thanked Marc Struelens for 2 fantastic years of leadership. It was a pleasure to be member of “his” Executive which was a strong and unified group inspired by his enthusiasm. He also thanked Roger Finch and Claude Carbon for their many outstanding contributions during their long service for the Society. His last address was directed at the ESCMID membership: “We want to deliver to you. This is only possible with your help: please get involved with the Society, we need your input!”

AstraZeneca / ESCMID Research Grant 2005

Turning the Tide of Resistance

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and AstraZeneca are proud to announce the recipient of the EUR 40’000 research grant for research in the field of antibiotic resistance. The grant, sponsored by AstraZeneca, was announced under the logo Turning the Tide of Resistance during 14th ECCMID 2004 in Glasgow.

The ESCMID Awards Committee selected the project
Emergence of beta-Lactam Resistance in Gram-negative Bacteria during Therapy: Factors Important to the Emergence, Mechanisms of Resistance and Prevention
by Dr Irma Bakker-Woudenberg (principal investigator), Dr. W.H.F. Goessens from the Erasmus University Medical Centre Rotterdam and Dr J.W. Mouton, Canisius-Wilhelmina Hospital, Nijmegen, the Netherlands, for support.

We would like to express our congratulations on their success.

ESCMID Awards Committee

Dr Irma Bakker-Woudenberg being handed over the award by Dr Barry Mason, Global Product Director for Anti-infectives, AstraZeneca (left) and Prof Marc Struelens, ESCMID President, during 15th ECCMID 2005 in Copenhagen
The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and bioMérieux are proud to announce the recipient of the first Clinical Microbiology Award 2005. The award was announced to recognise excellence and/or major contributions to progress in Clinical Microbiology by a young scientist from Central or Eastern Europe.

The ESCMID Awards Committee selected Prof Dr Roman Koslov, Institute of Antimicrobial Chemotherapy, Smolensk State Medical Academy, Smolensk, Russia as the first recipient of this award in recognition of his excellent research achievements as well as of his educational and professional contributions to the field of clinical microbiology in his home country and beyond.

We would like to congratulate Roman Kozlov on this success.

ESCMID Awards Committee

Prof Roman Kozlov (centre) receiving his award from Dr Jean-Pierre Marcel, bioMérieux Medical Director (left) and Prof Marc Struelens, ESCMID President, during 15th ECCMID 2005 in Copenhagen

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

The award expresses the shared mission of ESCMID and bioMérieux to advance laboratory practice of clinical and diagnostic microbiology across Europe.

Application

Nominations of Central and Eastern European scientists born in 1965 or later are to be submitted in writing. They must contain a description of the nominee’s career, his/her postal and email address, place and date of birth, list of publications, research interests and major contributions to the development of Clinical Microbiology. Two supporting letters from outside the nominating institution must be included. Self-applications will not be considered. Seven copies of all materials, plus one colour photograph (on paper or electronic) must be sent to the ESCMID Awards Committee.

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

The deadline for submission is 1 October 2005. Applicants will be notified of the decision by 1 March 2006. The Award will be granted at 16th ECCMID 2006 in Nice.

Please send your application to:
ESCMID Executive Office, P.O. Box 6, Clarastrasse 57, CH-4005 Basel, Switzerland, Phone +41 61 686 77 99
15th ECCMID 2005 Photo Gallery

A participant explaining her poster during a poster walk

Albert Osterhaus making a point during his talk titled Avian flu and the threat of a pandemic

Welcome reception

Patrick Francioli, the outgoing ECCMID Programme Director, gave a short talk on the history of ECCMID during the Opening Ceremony

Elisabeth Nagy, Professional Affairs Officer for Clinical Microbiology, presenting the Young Investigator Award to Mihai Netea

Niels Hoiby, Congress President, opening the 15th ECCMID 2005 in Copenhagen
Results from the Opinion Poll

Over 5,300 participants attended the 15th ECCMID 2005 in Copenhagen. An opinion poll was conducted through the internet soon after the meeting. Approximately 2,200 delegates were asked by email to fill in a short online questionnaire about the Congress, 609 of which compiled.

The first four questions in the poll concerned the demography of participants (educational background, specialty training, and workplace). No major changes from previous years were noted: almost 60% of the ECCMID attendees are MDs, 40% are clinical microbiologists, 25% are ID physicians and 15% have a degree in both these specialties. More details from these and other questions/answers can be called up from the ESCMID website (www.escmid.org), Information & Opinions, Opinion Poll.

Most respondents (82%) found the balance between basic science and practical aspects of Clinical Microbiology and Infectious Diseases good with the remaining equally split between deeming it too practice oriented and having too much basic science. As the needs of the participants vary depending upon their professional activities the organizers strive to offer a broad spectrum from basic science to the latest results in a subspecialty.

As seen in Table 1, only 58% of the respondents found that the Programme met their expectations of getting the latest scientific information/results with 38% responding with “partially”. Clearly there is room for improvement in this area as some indicated at the end of the survey that not all data presented in the talks was new. This concern is taken seriously in planning future ECCMID’s. While in part depending on scientists and industry, we hope that the steady improvement and growth of ECCMID will convince scientists and industry to bring their latest results to our European meeting.

Table 1

<table>
<thead>
<tr>
<th>Did the scientific programme meet your expectations of getting the latest scientific information/results in your field?</th>
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<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Partially</td>
</tr>
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</table>

Table 2

<table>
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<tr>
<th>The quality of the poster sessions is a constant concern. Would you support to substantially increase the abstract rejection rate?</th>
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<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Slight increase only</td>
</tr>
</tbody>
</table>

At ECCMID we usually reserve a two-hour lunch break for poster sessions and guided poster walks without “competitive” activities scheduled in parallel. Two thirds of the respondents agreed that poster sessions deserve an exclusive time slot.

The quality of the poster sessions is a constant concern. One question therefore addressed the acceptance of increasing the rejection rate (Table 2). We will follow the advice and slightly increase the rejection rate compared to previous ECCMIDs. As a consequence, the “abstract for publication only” category will be kept. This is supported by the negligible number of withdrawals or cancellations of authors in this category. Furthermore, the category is necessary for some participants who would not be able to attend the meeting otherwise, according to their institutional rules.

At the 15th ECCMID in Copenhagen there were 21 oral sessions with 144 presentations. The vast majority found this number adequate. The Programme Committee is therefore planning for a similar number of oral sessions also next year.

This year the ECCMID abstract book reached a weight of close to 2 kg. This has prompted the question as to whether this paper cannot be saved and the abstract book be replaced by an electronic database. Two thirds supported this idea (Table 3). In 2006 we will therefore replace the abstract book by a CD-Rom. Despite our intention to provide additional workstations to screen the abstracts onsite, you may want to take advantage of the on-line meeting planner facility available before the meeting. For more flexibility in viewing abstracts, bringing your laptop to Nice next year would be advantageous.

This year we offered nine pre-ECCMID educational workshops. We recognise that there is an opportunity for improvement with regard to content, handouts as well as the logistics. Implemented changes will be based upon experience this year and feedback from the poll. Pre-registration and a modest tuition fee will still be required, and educational workshops will remain separate from ECCMID and only organisationally linked to the Congress. However ESCMID members shall in future profit from lower fees than non-members.

In Copenhagen, the Saturday afternoon on the opening day featured a few symposia and several scientific sessions and educational workshops organised by ESCMID study groups. According to the Poll this seems to be a generally accepted schedule. We thus do not foresee major changes next year.

We will do our best to further improve the ECCMIDs taking into consideration your many comments and suggestions, and hope very much to see you at the 16th ECCMID, 1–4 April 2006 in Nice.

Peter Schoch, ESCMID Managing Director

Among the respondents to the questionnaire three laser pointers were raffled. The lucky winners were: Jakrapun Pupaibool, Urszula Nawrot, Graham Atherton.

Table 3

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<th>What is your opinion about the proposal to abandon the regular abstract book and to make the abstracts available on the Congress website 10 days prior to ECCMID in a searchable way and onsite as CMI supplement on CD only (i.e. in citable form)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>I support this proposal</td>
</tr>
<tr>
<td>I am against this proposal and think that the usual printed abstract book should be maintained</td>
</tr>
</tbody>
</table>
Leonid Stratchounski, member of the ESCMID European Council and of the ESGARS Executive Committee, met a tragic and absurd death in Moscow on 7 June 2005.

A Corresponding Member of the Russian Academy of Medical Sciences, he was head of the Department of Clinical Pharmacology of Smolensk State Medical Academy, president of the Interregional Association for Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC), and head of the Scientific Center for Antimicrobial Monitoring at the Russian Ministry of Health.

His relentless energy and enthusiasm led to the creation of the Institute of Antimicrobial Chemotherapy (IAC), in Smolensk the first of its kind in Russia.

He aimed at placing Russia at the core of the ESCMID scientific and educational activities, and his efforts culminated in the visit to Moscow of an official ESCMID delegation to sign a Memorandum of Collaboration with the Russian Academy of Medical Sciences (2003), and in the joint organisation between ESCMID and IACMAC of the VII International Conference on Antimicrobial Therapy (May this year). He was also involved in organising several ESCMID postgraduate educational courses, conferences and meetings.

His main legacies will include the forging of a new class of fully-committed young Russian scientists and the creation of a new building and ultramodern facilities at the IAC, which he had been attending to with incredible energy over the last years without being able to see their completion. In the years to come IAC will be the hub of basic research in the antibiotic field and for educational activities for physicians from the vast territory of the Russian Federation, thus representing the best memorial to Leonid Stratchounski as its founder.

In accordance with Leonid’s own aspiration, the IAC is also likely to become a meeting point for scientists from both Eastern and Western European countries. ESCMID is fully committed to contribute to this legacy thus paying a fitting tribute to him as a son of Russia and a citizen of modern Europe.

Giuseppe Cornaglia
Ragnar Norrby

A Tribute to Leonid Stratchounski

Leonid Stratchounski
1952–2005

FEMS / ESCMID Research Fellowship 2005

Ida Kovács
Department of Medical Microbiology and Immunobiology
University of Szeged, Hungary

ESCIMID and FEMS have agreed on a joint initiative to foster outstanding research in microbiology by young Europeans. Every year each organisation selects one individual among their recipients of research fellowships to receive an additional amount of EUR 1000 from the other organisation. We are delighted to announce that the second combined FEMS/ESCMID fellow in 2005 is Ida Kovács from Szeged, Hungary.

Research Interests
Ida Kovács was awarded the FEMS-ESCMID Research Fellowship based upon her research topic titled: Association between the genotypes of human cytomegalovirus isolates and their ability to induce IL-8 production in syncytiotrophoblast cells. Her previous research projects focussed on postnatal diagnostic possibilities in congenital cytomegalovirus infection and mother-to-fetus transmission of cytomegalovirus.

John David Williams
1931–2005

On 11 July 2005 David Williams, one of the founders of ESCMID, passed away after a short and difficult illness with lymphoma. David Williams was Emeritus Goldsmith Professor of Microbiology at the London Hospital Medical College, member of the first ESCMID Executive Committee and President of the 2nd European Congress of Clinical Microbiology in Brighton, UK, in 1985. A tribute to his many achievements will follow in the next ESCMID News.
Protecting Europe from Communicable Diseases

Mission and Tasks of the European Centre for Disease Prevention and Control (ECDC)

Background

In the last ten years we have seen a number of new infectious threats to human health emerge around the globe and affect the public health systems also in Europe. West Nile virus, which has havoced the eastern part of North America, is also present in Europe. In 1998 it was shown beyond any doubt that avian influenza could indeed be transmitted to man, and the SARS epidemic of 2003 reminded us once again that infectious diseases travel the world at the same pace as modern jet planes. In the same period old threats, such as HIV/AIDS, other sexually transmitted infections, tuberculosis and food-borne infections were re-emerging or rapidly increasing in incidence in many parts of the European Union. After September 11 and the anthrax threats (true or hoaxes), it became evident that also Europe needs to be well prepared for the possibility of bioterrorism attacks.

These scenarios were all part of the considerations when the European Commission proposed a new European Centre for Disease Prevention and Control in July 2003 to further strengthen the EU capacity of communicable disease control. In December the same year, it was decided that the new agency should be located in Sweden. After that the Centre was established at a record pace, and less than two years after the first proposal, the new ECDC was operational and officially inaugurated in Solna, just outside Stockholm in May this year.

Building on a strong tradition of European collaboration

The ECDC builds on a strong tradition of European collaboration against communicable diseases, dating back to the 1990s. In 1999, the then-loose collaboration was formalised through the Decision 2119/98/EC (and some subsequent daughter decisions), connecting surveillance institutes and competent authorities in the Member States with the European Commission in Networks for Surveillance of Specific Infections and a system for Early Warning and Response (EWRS) on health threats that could affect more than one Member State. The Designated Surveillance Networks (DSNs), now covering about 15 diseases, are often very well-functioning within their remits. These Networks are presently funded by the Commission under the Public Health Programme on 2- to 3-year contracts, which need to be regularly renegotiated based on an open call for proposals.

The Networks, with their hubs in the national institutes of the Member States, effectively bring key epidemiologists and microbiologists from all the Member States together, and provide some very useful information to the public health structures around Europe. However, they cover less than half of the more than 40 diseases to be covered under the 2119/98 and subsequent decisions, their actions are uncoordinated, and their funding is not sustainable. Furthermore, the events described in the introduction of this article, clearly show that, although good, the EU-level preparedness against new health threats is yet not optimal. With 10 new Member States, coordination of EU-level public health actions is even more crucial.

The tasks and responsibilities of the ECDC are spelled out in detail in the Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004, establishing the ECDC as a strong and independent agency. This regulation gives the Centre a very broad mandate in most aspects of EU-level disease control. The mandate, however, does not confer any regulatory powers on the Centre, and the Commission will retain the leading role in any new legislation in this area.

Governance

The Centre is led by Director Zsuzsanna Jakab, with a long background from various positions at the WHO Regional Office for Europe and as the highest civil servant in the Hungarian Ministry of Health. Assisting the Director is an Advisory Forum, with scientifically-recognised representatives from the technical competent bodies of all Member States, the European Commission and three non-voting members from non-governmental organisations (with ESCMID as one of the alternate members). The Director is appointed by a Management Board, representing the Member States, the Commission and the European Parliament. Besides appointing the Director, the Management Board adopts the financial and internal rules, the work programmes, and oversees the work of the Director and the Centre.

The Director is completely independent in the performance of her duties. She is the legal representative of the Centre. She is also responsible for the day-to-day management: drawing up and implementing its Programme; preparing the Management Board meetings and implementing its decisions; providing appropriate scientific and technical support; ensuring the scientific excellence and independence of activities and opinions of the Centre, and preparing and executing the budget and dealing with staff issues. She also directs the work on policy issues, partnerships, country support and other horizontal tasks. The Director is supported by her adviser in her tasks.

Zsuzsanna Jakab, ECDC Director, answering questions at the ECCMID press conference in April 2005 in Copenhagen
The two first years of ECDC will be devoted to moving forward from the empty office we moved into in March 2005, to becoming a strong European agency that makes a difference. In order to do this we now have an internal organisation in place with an Executive Management Committee and four units built around our main tasks; a Unit for Scientific Advice (headed by Johan Giesecke), a Unit for Surveillance and Communication (headed by Andrea Ammon), a Unit for Preparedness and Response (headed by Denis Coulombier), and an Administrative Unit (headed by Jef Maes). The Director and the unit heads, together with the Strategic Adviser to the Director (Karl Ekdahl), make up the Executive Management Committee.

Unit will set up six scientific panels in the areas of: 1) air-borne diseases (including influenza); 2) vaccine-preventable diseases; 3) sexually transmitted infections and blood-borne viral diseases; 4) food- and water-borne diseases, diseases of environmental origin and zoonoses; 5) antimicrobial resistance and nosocomial infections; and 6) serious imported diseases and other travel-related health issues. The experts on these panels will be recruited from the widest possible base in an open and fully transparent process, starting with a wide call for interest. From this roster of experts, the Advisory Forum will select the members (11 in each panel). Those not appointed to sit on a panel will remain in an expert database from which the Centre could choose for specific issues in urgent situations. The Chief Scientist (head of unit) will decide who processes individual questions posed to the Centre (in-house, the Advisory Forum, a scientific panel, a dedicated surveillance network, or other experts from the roster).

To be able to give the best scientific advice possible, the panels need to include the most suited experts in Europe. To recruit these people we will need the assistance of ESCMID and other learned societies to enlist the most suited experts in Europe. To recruit these people we will need the assistance of ESCMID and other learned societies to encourage their best minds to apply.

The Unit will also develop technical guidelines “on good practice and on protective measures to be taken in response to human health threats…” (Regulation Article 9:2). These guidelines will cover broad issues and be complementary to other guidelines produced by the WHO, US CDC and the Member States. They need to take the specific European situation into account, balance the responsibilities of the Member States and the

Commission under the subsidiarity principle, and facilitate a coordinated approach across Europe on key issues. Each guideline will be developed by a specific expert working group and approved by the Advisory Forum before being put on the ECDC web page.

Advisory Forum

The Advisory Forum supports the ECDC Director in ensuring the scientific excellence and independence of activities and opinions of the Centre. It is composed of experts representing the Member States as well as three members representing interested parties at the European level, which have been nominated by the European Commission. These three members of the Advisory Forum will be complemented by alternates, which shall also contribute to the workings of the Forum. We are pleased that ESCMID is an alternate member of the Advisory Forum in this latter category through the appointment of

Prof Elisabeth Nagy, Szeged, Hungary
ESCMID Professional Affairs Officer for Clinical Microbiology.

ESCMID is thus in a good position to act as link between the ECDC and the scientific community in the infection field.

Unit for Surveillance and Communication

The task of the Unit for Surveillance and Communication is to set up the European-level surveillance in a way that it provides the basis for action, for outbreak detection and for generating hypotheses for further studies. In 2005 and 2006, this work will mainly focus on having a smooth transition from surveillance focused on specific diseases within the DSNs to a more coordinated approach under the ECDC, as the present contracts of the Networks run out and the funding is taken over by the ECDC. To guide this transition, a document on the future surveillance strategies is presently being developed, based on a very wide consultation process with all key actors in the Member States and the Commission. A formal evaluation of the DSNs will take place in 2006 and 2007, starting with the Network contracts ending next year.

The foundation of future surveillance at the European level will be the Basic Surveillance Network aiming at collection of a minimal dataset on all diseases under Decision 2119/98. This will be supplemented by more in-depth disease-specific data collected by the DSNs. Even though the hubs of some of the Networks may remain in the Member States, eventually all the databases will be located in Stockholm.

Unit for Scientific Advice

The mandate of the Unit for Scientific Advice is to:

• secure a scientific basis of all work performed at the Centre and guiding direction of activities;
• answer “official” questions from the European Parliament, the Commission and the Member States;
• set up structures for cooperation with national surveillance institutes and with academia;
• set up a knowledge base;
• indicate areas where more research is needed and initiate studies;
• produce guidelines/tool kits;
• be pro-active in suggesting Member States action to fight communicable diseases.

For the processing of “official” scientific questions, which according to Regulations is a rather elaborate procedure, the
Review of the 4th ESCMID School 2005 in Szeged, Hungary

The 4th ESCMID Summer School was held from 25 June to 1 July 2005 in Szeged, Hungary. It was organised by the ESCMID Educational Committee and hosted by the Institute of Clinical Microbiology, Faculty of Medicine, University of Szeged. Venues of the School alternate each year between Northern, Southern, Western and Eastern Europe in order to allow members and trainees from all countries equal access. The venue was the Novotel hotel on the Tisza riverside, which provided excellent teaching facilities with internet connection. Szeged University, the second largest in Central Europe with 30,000 students and a 150-year tradition, has 11 faculties including Medicine. The faculty of the ESCMID School came from 9 European countries: Germany, Italy, UK, Spain, France, Switzerland, Portugal, Slovenia, and Hungary. The 27 participants came from 10 countries: the Netherlands, UK, Romania, Hungary, Portugal, Turkey, Sweden, United Arab Emirates, Ghana, and South Africa. Five students were supported by a €750 ESCMID scholarship. The academic staff of the Institute of Clinical Mi-

Building strong partnerships

The many tasks ahead of us cannot be accomplished without the strong support of all key actors in Europe, and without building on strong partnerships. In the first few months, we have already built very good and close collaboration with the European Commission, Member States and the WHO. As we are moving forward with our scientific agenda, we will now need to build equally strong links with the European scientific community and with the professional societies within our area of responsibility. We are therefore looking forward to a fruitful collaboration with ESCMID in the years to come.

Zsuzsanna Jakab
Director European Centre for Disease Prevention and Control (ECDC)
crobiology provided technical support and several main lectures. The relatively small number of students allowed very intense discussions, especially during the afternoon sessions.

The morning programme consisted of state-of-the-art lectures covering core topics in the fields of Clinical Microbiology and Infectious Diseases such as:
- emerging antibiotic resistance, development in vaccines,
- micro-organisms and infection pathogenesis,
- major clinical syndromes: diagnostics and management strategies,
- epidemiology, infection control, and public health.

During the afternoon sessions each participant gave a 10-minute presentation discussing a case from his or her own experience. A small group tutorial with the presenters was dedicated to improving their presentation skills. In four other group tutorials, selected cases were discussed with the students. Tutors for the afternoon sessions were Geoff Scott (UK), Achim Schwenk (UK), Luisa Peixe (Portugal), Elisabeth Nagy and Zita Borbenyi (Hungary).

The morning presentations were rated very highly by participants (average 4.4 for content, 4.1 for style and 4.1 for relevance on a rating scale of 0 = poor to 5 = excellent). Likewise the afternoon group sessions were highly appreciated (4.7, 4.5 and 4.6 for content, style and relevance). The mixture between clinical infectious disease and microbiology topics was well received. Students liked the stimulating and gregarious atmosphere of the School, the opportunity to meet new international friends and to exchange views between countries with widely different disease spectra and health care settings. They suggested advertising the School better in the future. The course price (€ 1000 for early, € 1500 for late application including full board accommodation and learning materials), albeit seen as commensurate to the service provided, was seen as too high for many trainees.

A half-day excursion was organised to Opuszta, a memorial to Hungarian history. The farewell party took place in a traditional Hungarian fish restaurant on the Tisza riverside. Several companies supported the school: Abbott Laboratories, Astra Zeneca, Bayer, Becton Dickinson Eastern Europe, Biomedica, bioMérieux, Bio-Rad, Colabor, Cordinat, Diagnosticum Ltd, Diagon Ltd, Gilead (US), Izinta, Frank Diagnosztika, MSD, Roche, and Wyeth. We would like to thank them for their generous support.

In its fourth consecutive year, the ESCMID School has established itself as a unique training course for aspiring young specialists in clinical Infectious Diseases and Microbiology from all parts of Europe. The combination of state-of-the-art morning lectures by experts and small group interactive teaching in the afternoon provides an ideal learning experience. The challenge ahead will be to attract more trainees from all over Europe who may use it as introduction, revision before examinations, or all-round refresher. Senior ESCMID members are invited to send their trainees to future ESCMID Schools.

Elisabeth Nagy
Coordinator of the 4th ESCMID School
ESCMID Professional Affairs Officer, Clinical Microbiology

Javier Garau
ESCMID Education Officer

ESCMID Awards and Fellowships 2006

The application deadline for the 2006 ESCMID awards and fellowships is 1 October 2005. We look forward to receiving your nominations and applications for the following:

- ESCMID Young Investigator Awards for Research in Clinical Microbiology and Infectious Diseases
- ESCMID Award for Excellence in Clinical Microbiology and Infectious Diseases
- ESCMID Research Fellowships
- ESCMID / bioMérieux Award for Advances in Clinical Microbiology.

Details on applying can either be found in ESCMID News 1-2005 or on the ESCMID website.

ESCMID Awards Committee
The 32nd ESCMID Postgraduate Education Course, Clinical Challenges in Diagnosis and Management of Atypical Pneumonia was held in Riga, Latvia, on 20–21 June. The Course was locally organised by Dr Arta Balode from the Paula Stradina Clinical University Hospital in Riga, and it was jointly supported by ESCMID and the European Respiratory Society (ERS).

The importance of the cooperation between the two Societies was stressed by Prof Giuseppe Cornaglia, ESCMID President-elect, and by Prof Francesco Blasi, Lead-elect of the ERS Assembly for Respiratory Infections. Prof Javier Garau, ESCMID Education Officer, remarked that the present course was the first educational event organised by ESCMID in a Baltic country, and expressed the Society’s wish that Eastern Europe be the venue of many future events of this type.

Altogether 27 participants from Latvia, Estonia, Slovenia, Switzerland, and the United Kingdom attended the course. They included microbiologists, physicians, allergologists, mycologists, and pulmonologists.

The Course Programme included different aspects of the diagnosis and treatment of atypical pathogens in respiratory diseases, which affect both children and adults, as well as the importance of appropriate diagnostic methods and antimicrobial therapies.

The atypical bacteria involved in respiratory diseases were reviewed by Giuseppe Cornaglia (Verona, Italy) and the diagnostic role of both conventional and new molecular microbiological techniques were discussed by Margareta Ieven (Antwerp, Belgium).

The clinical aspects of atypical pneumonia and the role of Mycoplasma and Chlamydia in the natural history of COPD were discussed by Alvis Krams (Riga, Latvia) and Francesco Blasi (Milan, Italy), respectively.

As regards the paediatric setting, atypical pneumonia in children was talked about by Dace Gardovska (Latvia) and Nicola Principi (Milan, Italy), whilst intriguing data about the role of atypical bacteria in the genesis of asthma were presented by Attilio Boner (Verona, Italy).

Antimicrobial therapy of community-acquired respiratory infections, with special reference to when and how to cover atypical pathogens, was reviewed by Uga Dumpis (Riga, Latvia), and Javier Garau (Barcelona, Spain) reported about the most recent data on antimicrobial resistance among atypicals and its clinical implications.

The Course was closed by a lecture on Modern trends and challenges in laboratory diagnostics and resistance detection of mycobacteria, delivered by Girts Škenders, head of the microbiology laboratory at the Latvian Centre for Tuberculosis and Pulmonology in Riga.

All the lectures generated lively discussions and the participants expressed the opinion that the course was not only highly beneficial as an educational event, but it also represented a great opportunity to meet an international panel of field specialists, to build links and to establish useful collaborative contacts. In addition to the highly productive scientific programme, participants also had an opportunity to visit the Old Town of Riga and enjoy its unique atmosphere.

Linda Bagrade, MD
Institute of Child Life and Health
Bristol, UK
ESCMID News 2·2005

Scientific

Project Presentation

European Antimicrobial Resistance Surveillance System (EARSS)

EARSS over the years

The European Antimicrobial Resistance Surveillance System (EARSS) was founded in 1998 and conceived as a network of national networks. Since then, this initiative has received funding as a dedicated surveillance network from the European Commission and the Dutch Ministry of Health, Welfare and Sports. Even though continued existence of the Network was initially received with skepticism, EARSS has become the most comprehensive public health effort that describes and analyses geographic and secular trends in antimicrobial resistance (AMR) in Europe.

Since its beginning, EARSS has steadily drawn in new participants from all over Europe. Starting with 14 countries in 1999, the current number of countries participating in EARSS has doubled. Not only have the number of countries increased, but also the number of laboratories contributing data within each country grew over the years, with a total of almost 800 laboratories serving over 1200 hospitals in 30 countries by December 2004 (Figure 1). Together, they provided health care services for an estimated population of more than 100 million European citizens. On the basis of its continuously growing database, EARSS has been able to report trends with increasing validity. Presently, the EARSS database contains AMR data for approximately 266,000 invasive isolates of five pathogens (Streptococcus pneumoniae, Staphylococcus aureus, Escherichia coli, Enterococcus faecalis, and Enterococcus faecium), providing comparable and validated data on the prevalence and spread of major invasive bacteria with clinically and epidemiologically relevant AMR in Europe. Since last year, it has also become possible to submit data on serogroups and serotypes of S. pneumoniae isolates, which will be linked to their respective resistance pattern already in the EARSS database. Finally, this year EARSS will expand its surveillance to include two new pathogens, Klebsiella pneumoniae and Pseudomonas aeruginosa.

Comparing antibiotic resistance proportions in Europe

Results are accessible through an interactive website at www.earss.rivm.nl and can be displayed in various downloadable formats such as maps, tables etc. The maps display resistance proportions for entire countries, simplifying the local distribution of antimicrobial resistance in Europe. Antibiotic resistance in European countries differs widely, which may be due to various reasons. European countries have different health care-, administration-, and reimbursement systems that influence prescription and antimicrobial consumption patterns as well as infection control policies in various ways. Also, the selection of hospitals varies between participating national networks, as does the number of laboratories. Furthermore, differences exist in antimicrobial susceptibility testing methodology and antimicrobial breakpoints between countries and laboratories, affecting the consistency with which resistance is ascertained. Finally, differences in diagnostic habits (hospitals that perform microbiological investigations only after the initial empirical treatment are bound to report higher resistance rates than institutions that conventionally sample patients before administration of antibiotics) can influence the AMR results as well.

Despite these differences between and within countries, a credible overall picture emerges. The sheer number of participating laboratories illustrates the broad coverage of EARSS and the fact that the number of countries and laboratories continue to increase adds to the value of EARSS. Protocols have been developed with professional help of ESCMID, the European Committee of Antimicrobial Susceptibility Testing (EUCAST), WHONET and the EARSS Advisory Board, to standardise data collection between countries. Over 90% of all laboratories repeatedly participated in the EARSS programmes for external quality assessment (EQA) carried out in collaboration with the United Kingdom National External Quality Assessment Scheme (UK-NEQAS). This continuous commitment to quality indisputably improves the accuracy and usefulness of the EARSS database. The EQA results show that there is still room for improvement, but at the
same time illustrates that routine AST results reported to EARSS in most instances have sufficient accuracy to provide good estimates of overall resistance prevalences. Especially trend analyses for a stable and representative set of laboratories within each country provide a reliable indication for resistance developments since diagnostic habits, methods and standards usually remain unchanged.

**EARSS-ibis: a rapid communication tool**

One of the new initiatives of EARSS is the development of the EARSS internet-based information system (Ibis), which enables rapid communication between laboratories about strains with unexpected antimicrobial resistance, virulence or transmissibility. EARSS-ibis provides an awareness system for unusual events, such as the occurrence/emergence and spread of pathogens of potential public health importance. Sharing information about the isolation of a specific bacterial pathogen will increase the awareness and diagnostic accuracy. This will be of immediate benefit to the treatment of patients and will also strengthen the ability of the entire network to assess the risk imposed by potentially harmful bacterial pathogens to populations. Microbiological laboratories that provide diagnostic services to hospitals and the community can participate. More information about the system and how to participate can be found at www.earss.rivm.nl. You can also contact your national EARSS representative or the EARSS management team (info.earss@rivm.nl).

**Staphylococcus aureus typing initiatives**

EARSS is trying to promote a unified typing strategy for all European Reference Centers for the strain identification of *S. aureus*. Therefore a “hands-on” typing workshop will be held in Münster, Germany from 12–14 October 2005. On this occasion, participants from national reference centers are introduced to Spa-sequence typing, MLST, and 16S ribosomal sequencing for species identification. Based on an expert meeting held in June 2004, a communication on the current situation of *S. aureus* typing in Europe will be published, including the results of a questionnaire on typing methods and national policies for *S. aureus*, already completed by 28 countries. These efforts should help develop a European expertise towards the exchange of typing as well as epidemiological information between National Reference Centers.

**Collaboration**

The EARSS Management Team is grateful to all laboratories, data managers and national representatives who continuously provide their routine susceptibility data to the EARSS network. EARSS has encouraged and helped sustain national surveillance efforts and the Network is the perfect basis for an integrated public health approach for AMR containment in Europe. To this end, EARSS operates in close collaboration with other EU-financed projects: European Surveillance of Antimicrobial Consumption (ESAC), Improving Patient Safety in Europe (IPSE), and Antibiotic Resistance Surveillance and Control in the Mediterranean region (ARMed). There is also a close partnership with ESCMID and two of the society’s sub-committees: EUCAST and the ESCMID Study Group for Antimicrobial Resistance Surveillance (ESGARS).

**Conclusions**

EARSS has become the most comprehensive public health effort that describes and analyses geographic and secular trends in antimicrobial resistance in Europe. Even though several factors can influence the proportion of resistance in a country, a large number of countries and laboratories, professionally devised protocols to standardise data collection, collected service characteristics of laboratories and hospitals, and the yearly quality assessment exercises, provides us with an overall credible picture of the situation of antimicrobial resistance in Europe.

For an update on results, the EARSS annual report 2004 will be available from the EARSS website in November 2005 (www.earss.rivm.nl).

**EARSS Management Team**

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**Footnote**

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- D. Monnet, R. Skov (Denmark); K. Kermes (Estonia); O. Lytylkainen, A. Nissinen (Finland); B. Loignon, V. Jarlier (France);
- W. Witte, K. Heckenbach (Germany);
- A. Tsakris, G. Vatopoulos (Greece); M. Fuzi (Hungary); K. Kristinsson (Iceland);
- D. Igoe, O. Murphy (Ireland); R. Raz (Israel); A. Pantosti, P. D’Ancona (Italy);
- A. Balode (Latvia); J. Miculeviciene (Lithuania);
- R. Hemmer (Luxembourg);
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- A. Johnson, R. Hill (England & Wales);
- H. Hughes (Northern Ireland);
- M. Coyne (Scotland (UK))

Other parties represented by:

- G. Cornaglia (ESCMID),
- F. Baquero (ESGARS),
- G. Kahlmeter (EUCAST),
- P. Jenkins (WHO),
- J. Stelling (WHONET),
- C. Walton (UK-NEQAS)

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A New ESCMID Educational Initiative

Europe Watching New and Emerging Resistance – EWNER

Why EWNER?
Identifying antibiotic resistance patterns at the bench has become increasingly difficult for microbiologists due to the huge number of new mechanisms of resistance described during the past 15 years. The interpretation of drug susceptibility tests is even further complicated by cross-resistance to antibiotics from different classes by permeability decrease or efflux, as well as mobile elements carrying transferable resistance traits to several classes of antibiotics, nowadays including quinolones. For these reasons, training clinical microbiologists in European labs to recognise the circulating resistance patterns represents an existing and challenging educational task for our Society. Moreover, providing microbiologists with a simple process for exchanging information and questions on puzzling resistance patterns with other microbiologists would be also of great help in the early spotting of unusual patterns.

For this purpose, ESCMID through the ESCMID Study Group for Antibiotic Resistance Surveillance (ESGARS), will launch a new educational initiative called Europe Watching New and Emerging Resistance (EWNER). The main target group of EWNER will be our youngest colleagues across Europe.

The two parts of EWNER
The first part, Resistance views, is strictly educational and will offer a comprehensive description of circulating patterns of resistance among the major bacterial pathogens as well as relevant information on these patterns. The second part, Watch and alert, will include a more operational tool to facilitate the identification of resistance patterns. Resistance views will be a comprehensive picture library of classical, recent and emerging bacterial resistance patterns. The library will be available through the ESCMID website. Some important pictures (“the pattern of the month”) would also be published in ESCMID News or another journal.

The educational material will include:
- photographs of disk diffusion plates,
- name of bacterial species, place, date and circumstances of isolation,
- list of tested antibiotics, inoculums used for testing and results: zone size diameters, corresponding MICs, particular features of the pattern of resistance (e.g. level of resistance, antagonism or synergy between antibiotics),
- further identification techniques (e.g. specific tests) when relevant,
- details on the mechanisms of resistance involved.

Authorship will be strictly respected and will include the name and address of the bacteriologist and institution providing the “view”, referred to as the “author”. Training sessions using the picture library as an educational tool will be organised by ESCMID.

Watch and alert will be a simple way for European microbiologists to warn other microbiologists when facing an apparently unusual or undescribed resistance pattern. Communication between the microbiologist facing the event and a pool of experts from the Society will allow exchange of technical aspects and expertise.

The process will be carried out using the ESCMID website. An electronic and confidential message (request) will be sent by the microbiologist initiating the process referred to as the “finder”. The request will include a picture of the susceptibility test plates and information on strain identification and circumstances of isolation. A pool of experts from the Society, with particular interest in medical microbiology, susceptibility tests and mechanisms of resistance, will receive the request sent by the “finder” who initiated the process, inviting them to answer. The exchanges between experts and “finder” will be confidential and will follow a strict ethical process in order to warrant the rights of the “finder”.

The experts will help further identify the pattern of resistance by providing technical advice. The “finder” will retain his/her status as the discoverer and initiator should a new geographical extension of an already described resistance pattern or an unusual or undescribed resistance pattern be identified and/or described.

ESCMID has many resources, including specialists on mechanisms of resistance and the required means of communication including publications, website and training programmes for making EWNER a success. We believe that EWNER will contribute to federate microbiologists working in European and nearby countries.

Vincent Jarlier, MD, PhD
On behalf of ESGARS
Dear Colleagues and Friends

On behalf of the Organising Committee, we have the honour and pleasure to invite you to the 16th ECCMID to be held on April 1–4, 2006 in Nice, France.

In a world of increasingly mobile populations, whether for leisure or through necessity, international cooperation in all aspects of health is proving essential to control the spread of infectious diseases. Coordinated efforts in prevention and control, standardised diagnostic procedures and management, global surveillance and timely information sharing should provide the necessary tools to prevent or contain future epidemics. Examples such as the recent outbreaks of SARS or of avian influenza are there to warn us of the potential for new pandemics to arise, while re-emergence of diphtheria and whooping cough are a reminder that sustained prevention remains mandatory.

In such a context the 16th ECCMID will provide an opportunity to bring together participants involved in all aspects of infectious diseases to share their expertise and describe new developments in biomedical research, diagnostic procedures, vaccines, anti-infective agents and public health issues. 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 over 80 countries, the ECCMID offers an interdisciplinary forum to share knowledge in a collegial atmosphere.

We are pleased that Nice has been selected to host the ECCMID 2006. Located on the French Riviera, in its spectacular setting between the Mediterranean shore and the Southern Alps, the city offers the unique combination of a French atmosphere with the Italian influence reflected in its architecture and traditional cuisine.

We warmly invite you to share and enjoy with us a stimulating scientific programme and the beauty of the “Côte d’Azur”!

Prof. Pierre Dellamonica
President of the 16th ECCMID

Visit the 16th ECCMID website featuring:
- Continuously updated scientific programme
- Online abstract submission (deadline 17 November 2005)
- Online registration as well as hotel & tours reservations
- Option to compose your personal congress programme
- Details about the industrial exhibition
- Information on the congress venue and the city of Nice

For further information please contact:

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CMI came into existence in 1995 with the aim of addressing the needs of a community of professionals seeking information relevant to but extending beyond the direct scope of their own research. Successful in that mission, CMI has subsequently been recognised as being among “four of the leading specialist journals in the antimicrobial area” (JAC, 2006 56:915-816).

J. Crane, CMI Managing Editor
Clinical microbiology & Infection 1995-2005

Not all research falls neatly into categories: CMI exists to tie these different aspects together by also including authors of specialist work in the same field, and this breadth helps to keep even the generalists in touch with new developments. No one has time to read everything!

C. J. Madeley
CMI Editor

The European Commission endorsed CMI in 1995, when it stated, "It is a means to facilitate PC goals, among them the avoid terminal medicine."

A. E. Bacall, EC

CMI, at the forefront of European journals in the field, with an impact factor that nearly doubled last year and continues to rise, is swiftly catching up with the ASM sponsored journals.

A. van Belkum
CMI Editor
Getting It Right First Time

Writing Hospital Antimicrobial Guidelines

The following article has been commissioned by the Editors to support our readers involved in writing or revising hospital guidelines on the use of antibiotics. It describes the conceptual approach in developing antimicrobial guidelines as well as their scope and is illustrated with examples from the UK. For obvious reasons any new guidelines would need to take into consideration and be adapted to the specific situation of the country or region concerned.

The Editors

Summary and introduction
Formulating hospital antimicrobial guidelines is a complex process and should be approached in a multidisciplinary manner to encourage ownership by users. Microbiologists, pharmacists and clinicians should all be involved. They should be based on national guidelines where available, and take local antimicrobial sensitivity patterns into account. If and when antibiotics are indicated, the philosophy is now based on attempting to get it right first time based on likely pathogens and local sensitivity patterns, to avoid repeat visits and prescriptions. This is true for both community- and hospital-acquired infections. However, prescribers should be advised to change to a narrower spectrum antibiotic once the organism is known to be sensitive, in order to minimise the development of resistance. Readers should be advised to contact the local Public Health Medicine Consultant (HPA consultant or CCDC in the UK) in cases of suspected communicable diseases such as meningococcal meningitis, E. coli 0157 gastroenteritis, etc., even when cases are believed to be sporadic. The guidelines should be ratified by the hospital Drugs and Therapeutics Committee where any feedback or comments from the users should be invited. Contact details for microbiologists and pharmacists within and outside of standard working hours should be provided to enable round-the-clock advice regarding antimicrobial prescribing and monitoring. Guidelines should be continually updated and reference given to the internet/intranet address for the latest update.

Aims
The aim of the guidelines should be to encourage rational prescribing based on the best available evidence, and hence improve patient care by:

- optimising the treatment of infection
- reducing the risks of drug toxicity and secondary infections
- limiting the emergence of resistant strains
- reducing unnecessary costs.

Limitations
Guidelines are not intended to be comprehensive. Doctors are advised to consult the local formulary, e.g. British National Formulary (BNF), and the manufacturers’ Summary of Product Characteristics (SPC) for additional information. This is especially relevant for side effects, contra-indications, interactions with other drugs and the use of antimicrobials during pregnancy.

More detailed guidelines may be made available for certain more specialised groups of patients, e.g. febrile neutropenia, CAPD peritonitis, etc.

Scope
It is suggested that the guidelines should cover the following main areas:

- Aims and limitations
- General principles of antimicrobial therapy

Guidelines should cover the following main areas:

1. When to prescribe and when not to
   The decision to start antimicrobial therapy must be based on clinical evidence of infection. This evidence may be:
   - localised, e.g. cellulitis or pus for soft-tissue infections, frequency and dysuria for cystitis
   - systemic, e.g. pyrexia, rigors, tachycardia or hypotension.
   - Isolation of an organism without signs or symptoms of infection usually represents colonisation rather than infection and does not require treatment, i.e. no symptoms, no treatment.

Two common situations where antimicrobials are not indicated are:

- isolation of potential pathogens (e.g. Staphylococcus aureus, MRSA, Group A streptococci) from leg ulcers, pressure sores or other superficial sites, without local inflammation or systemic symptoms (e.g. pyrexia)
- bacteruria in patients with urinary catheters who have no systemic signs of infection.

2. First steps before prescribing antimicrobial agents
   - Make a provisional clinical diagnosis, noting the probable site and severity of the infection.
   - Send relevant specimens to the laboratory before starting therapy. As a minimum, every febrile patient seen in an Accident & Emergency Department or Medical Admissions Unit should have urine and blood culture specimens taken as well as any other relevant specimens depending on presentation (e.g. wound swabs, sputum, etc.). It is more difficult to isolate the underlying pathogen after antimicrobial therapy has been started.

3. Choice of antimicrobial agent
   - If and when antibiotics are indicated, the philosophy is now based on attempting to get it right first time based on likely pathogens and local sensitivity patterns, to avoid repeat
visits and prescriptions. However, change to a narrower spectrum antibiotic should be made once the organism is known to be sensitive.

To choose antimicrobial(s) for initial empirical therapy before microbiological results are available, see the empirical therapy by system section of these guidelines. These are based on the most likely infective organisms and on local sensitivity patterns and costs (see Appendices) of antimicrobial agents. Once laboratory results are available, review initial therapy. Wherever possible, use a narrow spectrum agent in preference to one with a broad spectrum, as the latter is more likely to cause side effects and encourage resistance.

- Refer to First choice antimicrobials and Restricted antimicrobials (Appendices).
- For dosage and other information, consult your local formulary, e.g. BNF.

N.B.: the antimicrobial section of this may be condensed and tailored to the needs of your hospital and enclosed as a separate section of your guidelines.

- For modification of dosage in cases of renal impairment, consult the ward pharmacist.

- Always check the formulary and SPC for possible contra-indications, drug interactions, adverse effects or toxicity, especially with regard to renal and hepatic function and pregnancy.

- Check whether the antimicrobial will achieve adequate concentrations at the target site.

- Find out whether the patient has a history of allergy to any antibiotics.

- Always consider prior therapy: patients who have not responded to a certain antimicrobial should receive an alternative from a different class.

- Wherever possible, avoid giving cephalosporins or co-amoxiclav to elderly patients because of the risk of C. difficile diarrhoea.

4. Allergy to beta-lactam antibiotics (penicillins and cephalosporins)

Patients with a history of:
- anaphylaxis
- urticaria
- rash occurring immediately after penicillin therapy are at increased risk of immediate hypersensitivity reactions and should not be given beta-lactam antibiotics (penicillins and cephalosporins). Alternatives for these patients should be given in the guidelines. Other symptoms show either no, or extremely weak associations with subsequent allergic reactions.

5. Routes of administration

- oral: preferred route for treatment of most infections
- intravenous: for initial treatment of severe* or deep-seated infections, e.g. septicaemia, endocarditis, meningitis, osteomyelitis (*associated with systemic symptoms such as fever, rigors, tachycardia, tachypnoea, shock)
- topical

6. When to change from iv to oral

Patients on iv antimicrobials must be reviewed daily with a view to changing to oral therapy as soon as possible, provided that:

- the patient does not suffer from endocarditis, meningitis, osteomyelitis, septic arthritis, immunosuppression, or any other contra-indication to oral therapy
- the signs and symptoms of infection are improving, e.g. temperature 36–38°C for at least 24 hours, WBC: 4–10 x 10⁹/L, heart rate: <100 beats/min for at least 12 hours, respiratory rate: <24 breaths/min
- the patient can take oral medication and there is no evidence of impaired absorption
- a suitable oral agent is available as per guidelines or microbiological results.

If all of the above apply, change iv antibiotic to oral equivalent and state stop date. Document it in the patient’s notes. (You may insert list of oral alternatives to iv antibiotics in Appendices).

7. What if a patient does not respond to initial treatment

Lack of response to antimicrobials may be due to:

- infection being caused by microorganisms that are resistant to initial therapy
- the presence of an abscess or collection of pus, which requires surgical drainage
- the presence of an infected foreign body, e.g. prosthetic joint or central venous catheter.

8. Length of treatment (when to stop antimicrobials)

Prolonged courses of antimicrobials increase the risk of adverse effects, secondary infections and emergence of resistance, besides being costly. A maximum of 5–7 days should be prescribed for most infections. (See Table below for some notable exceptions.) Always put a stop date (or review date) on the drug chart when the antimicrobial is prescribed.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Length of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>simple cystitis in women</td>
<td>3 days</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td>10–14 days</td>
</tr>
<tr>
<td>C. difficile colitis</td>
<td>10 days</td>
</tr>
<tr>
<td>endocarditis</td>
<td>4–6 weeks</td>
</tr>
<tr>
<td>osteomyelitis</td>
<td>6 weeks</td>
</tr>
</tbody>
</table>

9. Monitoring levels

- It is a legal requirement to monitor levels of aminoglycosides (e.g. gentamicin) and vancomycin if given for more than 48 hours (see prescribing guidelines for details).

- Refer to Appendices for gentamicin and vancomycin dosage and monitoring.

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**Empirical therapy by system**

**Important notes concerning the therapeutic regimens described in Tables 1 and 2:**

Antimicrobial therapy examples for common urinary and lower respiratory-tract infections are given here. Your guidelines, however, should be as comprehensive as possible without being too lengthy and complicated for the reader.

1. Dose only given where it differs from that in the BNF or equivalent.
2. Route only given where both oral and iv formulations are available.
3. Duration only given where it varies from the 5–7 day norm.
4. Alternative antimicrobials are for penicillin allergic patients only and are given in brackets.
Table 1

### Lower respiratory-tract infections

#### General principles
- Collect sputum and blood cultures (in pneumonia).
- Consult chest physician and/or microbiologist and refer to local, e.g. British Thoracic Society (BTS) ([www.brit-thoracic.org.uk/docs/cap.pdf](http://www.brit-thoracic.org.uk/docs/cap.pdf)) guidelines.
- Always consider prior therapy: patients who have not responded to a certain antimicrobial should receive an alternative from a different class.
- Change to oral therapy 48 hours after resolution of fever and satisfactory clinical response.

#### Local pathogen / sensitivity data:
It is very important to provide this for the users of your guidelines as a rationale for your recommendations. The following is an example from the north of England:
- Of the three primary LRTI pathogens locally, 2/3 are *Haemophilus influenzae* and 1/3 are *Streptococcus pneumoniae* and *Moraxella catarrhalis* combined.
- Resistance to penicillins locally (beta-lactamase positive) is 20% for *Haemophilus influenzae*, 5% for *Streptococcus pneumoniae* and 90% for *Moraxella catarrhalis*.
- The macrolides (erythromycin and clarithromycin) have very poor activity against *Haemophilus influenzae*.
- The tetracyclines (e.g. doxycycline), 3rd generation cephalosporins (e.g. cefixime) and newer quinolones (e.g. levofloxacin) are the most consistently effective against all three primary pathogens.

<table>
<thead>
<tr>
<th>Infection</th>
<th>Likely Pathogens</th>
<th>Antimicrobial Agent</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>infectious exacerbation of chronic obstructive pulmonary disease (COPD)</td>
<td>50% infections are viral, bacteria include: <em>Streptococcus pneumoniae</em></td>
<td>doxycycline po or levofloxacin po</td>
<td>BTS guidelines recommend oral antimicrobials wherever possible.</td>
</tr>
<tr>
<td></td>
<td><em>Haemophilus influenzae</em></td>
<td>Give iv cefuroxime (levofloxacin) in severe cases (febrile, high peripheral WBC count, ICU admission, etc.)</td>
<td></td>
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<tr>
<td></td>
<td><em>Moraxella catarrhalis</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mild community-acquired pneumonia (CAP)</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>amoxicillin and clarithromycin po</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Haemophilus influenzae</em></td>
<td>Give iv initially only in the more severe cases (levofloxacin monotherapy in penicillin allergy)</td>
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</tr>
<tr>
<td></td>
<td>atypical organisms, e.g. <em>Mycoplasma pneumoniae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Chlamydia pneumoniae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Chlamydia psittaci</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>severe community-acquired pneumonia (CAP)</td>
<td>as above including <em>Legionella pneumophila</em> <em>Staphylococcus aureus</em> **</td>
<td>&gt;70 years: amoxicillin + clarithromycin iv</td>
<td>CAP is defined as severe if 2 of the following are present:</td>
</tr>
<tr>
<td></td>
<td>(post influenza infection)</td>
<td>&lt;70 years or ≥ 70 and unsatisfactory response at 48 hours; cefuroxime and clarithromycin iv (levofloxacin and clarithromycin iv if penicillin allergy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>* If confirmed <em>Legionella</em> infection, use iv clarithromycin or levofloxacin.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>**If confirmed staphylococcal pneumonia, use flucloxacinil 2 g iv 6hrly + gentamicin.</td>
<td></td>
</tr>
<tr>
<td>mild to moderate hospital acquired or aspiration pneumonia</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>mild: co-amoxiclav + ciprofloxacin po, or cefixime + metronidazole po moderate: ceftriaxone + metronidazole iv (levofloxacin + metronidazole po or iv, if penicillin allergy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus aureus</em> coliforms and anaerobes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>severe hospital-acquired, ventilator-associated or aspiration pneumonia</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>tazocin +/- gentamicin (vancomycin + gentamicin + metronidazole, if penicillin allergy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Staphylococcus aureus</em> incl. MRSA coliforms and anaerobes</td>
<td></td>
<td>Though some recommend tazocin monotherapy, gentamicin should be added where resistance is prevalent or in severe or mixed infections.</td>
</tr>
<tr>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Urinary tract infections

General principles
- Use urine dipstick to exclude UTI; negative nitrite and leucocyte has 95% negative predictive value.
- If child, pregnant, man >65, send MSU/CSU before starting antibiotics and if systemically unwell/febrile, take blood cultures as well.
- In pregnancy penicillins and cephalosporins are the drugs of choice but short-term trimethoprim (theoretical risk in first trimester in patients with poor diet, as folate antagonist) or nitrofurantoin (at term, theoretical risk of neonatal haemolysis) are unlikely to cause problems to the foetus.
- Modify treatment according to culture result.
- Refer children under five years with any of these conditions to the paediatrician for investigation.

Local pathogen / sensitivity data:
It is very important to provide this information for the users of your guidelines as a rationale for your recommendations. The following is an example from the north of England:
- Over 50% of urinary coliforms are resistant to amoxicillin, 30% are resistant to trimethoprim.
- The threshold for use of an antimicrobial in empirical therapy of UTI is generally acknowledged to be no more than 20% resistance.
- Enterococci are now the second most common cause of UTI after coliforms. They are more common in elderly and catheterised patients and are intrinsically resistant to many antibiotics including the cephalosporins and aminoglycosides.

<table>
<thead>
<tr>
<th>Infection</th>
<th>Likely Pathogens</th>
<th>Antimicrobial Agent</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>asymptomatic bacteriuria</td>
<td>coliforms (e.g. E. coli, Proteus, Klebsiella spp.) enterococci staphylococci</td>
<td>no treatment required except in pregnancy, childhood, or urinary tract abnormality/obstruction</td>
<td>In the elderly (&gt; 65 years) asymptomatic bacteriuria occurs in 25% of women and 10% of men and is not associated with increased morbidity.</td>
</tr>
<tr>
<td>uncomplicated cystitis non-pregnant</td>
<td></td>
<td>cefalexin po for 3 days, or co-amoxiclav po for 3 days, or nitrofurantoin po for 5–7 days use ciprofloxacin or cefixime only if resistant or recurrent</td>
<td>dysuria of varying frequency but no loin pain, fever or rigors significant bacteriuria (usually accompanied by pyuria &gt; 10–100 WBC/mm³)</td>
</tr>
<tr>
<td>acute pyelonephritis systemically well / afebrile non-pregnant</td>
<td>cefixime po or trimethoprim po (if susceptible, and not penicillin-allergic, change to amoxicillin) total course 10–14 days</td>
<td>significant bacteriuria (usually accompanied by gross pyuria &gt; 100–500 WBC/mm³) Loin pain, dysuria and frequency may or may not be present.</td>
<td></td>
</tr>
<tr>
<td>acute pyelonephritis (pyelitis) of pregnancy systemically well / afebrile</td>
<td>cefixime po or trimethoprim po (if susceptible, and not penicillin-allergic, change to amoxicillin) total course 10–14 days</td>
<td>Suggest MSU for susceptibility testing. Significant bacteriuria (usually accompanied by pyuria &gt; 100 WBC/mm³) should be treated, even if asymptomatic.</td>
<td></td>
</tr>
<tr>
<td>acute pyelonephritis systemically unwell / febrile including febrile pregnant patients</td>
<td>amoxicillin iv (trimethoprim po, if pen allergic and non-pregnant) + gentamicin (change to po drug – depending on sensitivity – once apyrexial and better for &gt; 48 hours) total course 10–14 days</td>
<td>Diabetics require an extended course for 3 weeks. Contact microbiologist, if pregnant and penicillin allergic.</td>
<td></td>
</tr>
<tr>
<td>bacteriuria in catheterised asymptomatic patients</td>
<td>coliforms enterococci Pseudomonas spp.</td>
<td>no treatment required</td>
<td>Smelly urine and catheter blockage are not indications for antibiotics.</td>
</tr>
<tr>
<td>complicated UTI including: – febrile catheterised patients – those with obstruction / stones</td>
<td>amoxicillin iv (trimethoprim po) + gentamicin (change to po drug – depending on sensitivity – once apyrexial and better for &gt; 48 hours) total course 7–10 days</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Antimicrobial prophylaxis

Only examples of medical and surgical antimicrobial prophylaxis are given here. Your guidelines, however, should be as comprehensive as possible without being too lengthy and complicated for the reader.

## Table 3

### General medicine

- Refer to national formulary or similar

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antimicrobial</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>prevention of secondary cases of meningococcal infection amongst household / kissing contacts, people in schools or institutions and healthcare workers exposed to droplet infection</td>
<td>rifampicin po q12h for 2 days (4 doses)</td>
<td>Public health medicine consultant (HPA consultant or CCDC in UK) will advise as to who requires prophylaxis. Refer to Hospital Infection Control Guidelines for Health Care Workers exposed to meningococcal infection. Prophylaxis should be given to contacts as soon as the diagnosis is made. Prophylaxis should be given to index case before discharge to prevent secondary cases (not necessary if cefotaxime or ceftriaxone were given for treatment, as these achieve adequate levels in saliva). rifampicin: need to warn patient that urine, saliva and other bodily fluids will be coloured orange/red and soft contact lenses may become discoloured. Patients on oral contraceptives should use additional means of contraception for at least 4 weeks (see BNF Part 7.3.1 for further information). Avoid rifampicin in pregnancy. Check for drug interactions.</td>
</tr>
<tr>
<td></td>
<td>adult: 600mg child: 10 mg/kg child &lt;1year: 5 mg/kg or ciprofloxacin* 500 mg po single dose or (in pregnancy) ceftriaxone* 250 mg im/iv single dose child &lt;12 years: 125 mg single dose</td>
<td></td>
</tr>
<tr>
<td>prevention of pneumococcal and other infections in asplenic or hyposplenic patients</td>
<td>phenoxymethylpenicillin po 250-500mg 6-12 yrs: 250 mg 1-5 yrs: 125 mg &lt;1 yr: 62.5 mg all q12h for life if penicillin-allergic, use: erythromycin po 250–500mg 2–8 yrs 250 mg &lt; 2 yrs 125 mg all q12h for life</td>
<td>Pneumococcal, <em>Haemophilus influenzae</em> type b and meningococcal vaccines are also required. Yearly influenza vaccine vaccines have also been recently recommended. Refer to guidelines (including update) for the prevention and treatment of infection in patients with absent or dysfunctional spleen. Full details also available from microbiological lab or pharmacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>prevention of endocarditis in patients with heart valve lesions, congenital heart valve lesions or prosthetic heart valves</td>
<td>dental, local anaesthetic: amoxicillin 3g po 1 hr before procedure (clindamycin 600 mg) dental/upper respiratory, general anaesthetic: amoxicillin 1g iv at induction (clindamycin 300 mg iv over 10 min then 150 mg 6 hrs later) dental/genitourinary, general anaesthetic, prosthetic valve or previous endocarditis: amoxicillin 1g iv + gentamicin 2 mg/kg at induction (teicoplanin 400 mg + gentamicin 2 mg/kg at induction)</td>
<td>For details, including children’s doses see Part 5.1, Table 2 in the current edition of the BNF. Advice is also available from the Consultant Microbiologist. Alternatives for penicillin-allergic patients are given in brackets. Patients who have received more than one dose of penicillin over the previous month are at increased risk of harbouring resistant organisms and should receive the alternative antimicrobial (in brackets).</td>
</tr>
<tr>
<td>recurrent UTI (women of childbearing age)</td>
<td>trimethoprim 100 mg or nitrofurantoin 50 mg immediately post coital or once daily at night</td>
<td>Post-coital prophylaxis is as effective as prophylaxis taken nightly.</td>
</tr>
</tbody>
</table>
Important principles of surgical prophylaxis

- Antibiotics used must cover the common pathogens. Refer to surgical prophylaxis guidelines at www.sign.co.uk.
- The shift from cephalosporin use is necessitated by the rise in incidence of MRSA as well as the importance of MRSE (methicillin-resistant Staphylococcus epidermidis) in surgical and especially prosthetic infections. Both are, by definition, resistant to the cephalosporins.
- All drugs are given iv as a single dose at induction (roughly 1/2 hour before operation, 1 hour if im) unless otherwise stated. This should achieve maximum tissue concentrations at time of operation.
- A single dose is sufficient in most cases unless there is blood loss of up to 1500 ml during surgery, haemodilution of up to 15 ml/kg or when surgery lasts for over 4 hours. Further doses are also needed in cases of contamination of site during surgery. Consult Microbiologist.
- Prophylaxis should be recorded in the single dose part of the drug chart in most cases.
- Recommendations are based on national guidelines (where available) and local antimicrobial sensitivity patterns.
- An important aim of these guidelines is the reduction in the use of cephalosporins as part of the control of MRSA and C. difficile infection in hospital.
- Contact the Microbiologist for clarification/alternatives, contact the Pharmacist for advice regarding drug interactions, side effects, etc.
- Drug levels, e.g. gentamicin, need not be measured when given for less than 48 hours (e.g. single dose).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antimicrobial</th>
<th>Notes</th>
</tr>
</thead>
</table>
| standard surgical regime | standard surgical regime: co-amoxiclav 1.2 g + gentamicin 160 mg (240 mg if weight > 80 kg) | All single doses iv at induction except in situations outlined at top, including contamination at operation where therapeutic (non-prophylactic doses are given for usually 48 hours).
| | if penicillin allergic or known to be MRSA colonised: clindamycin 600 mg + gentamicin 160 mg (240 mg if weight > 80 kg) | Bowel flora causing post-operative sepsis includes: coliforms (e.g. E. coli), anaerobes (e.g. Bacteroides spp.), enterococci (previously known as faecal streptococci) and Pseudomonas spp.
| | | Post-operative wound infection is most commonly caused by Staph. aureus (including MRSA), beta haemolytic streptococci as well as a mixture of the above «faecal flora».
| | | Gentamicin may interfere with some muscle relaxants such as suxamethonium. If giving these is unavoidable, please discuss alternatives with the Microbiologist. |
| upper GI including: oesophago-gastrectomy | standard surgical regime | Prophylaxis is not given routinely. If obstruction or malignancy is present, then prophylaxis is given, as the upper GI tract may become heavily colonised with bacteria under these circumstances. |
| appendicectomy, colo-rectal surgery, exploratory laparotomy | standard surgical regime | Prophylaxis is given to all patients. |
| vascular surgery (Refer to informative article in Drugs & Therapeutics Bulletin, Vol 42, No 6, June 2004) | standard surgical regime | Prophylaxis is given for patients undergoing amputations, vascular implants and arterial grafts. High-risk patients, e.g. diabetics, may be given a further dose at 24 hours. |
| | | Pre-operative screening and eradication of Staph. aureus / MRSA carriage (as per Infection Control Protocol) desirable. |
| | | Audit of early and late postoperative infections pre- and post-introduction of this regime is desirable. |
| prosthetic joint replacements (arthroplasties: THR, TKR) | standard surgical regime | Main infecting organisms are staphylococci (Staph. epidermidis, Staph. aureus and MRSA). |
| internal fixation of fractures with pins, screws, etc. around pelvic area (e.g. fracture neck of femur) | standard surgical regime | Pre-operative screening and eradication of Staph. aureus / MRSA carriage in nose using mupirocin is desirable. |
| | | If a tourniquet is used (e.g. for total knee replacement) then antibiotic prophylaxis must be given 10 to 15 minutes before the tourniquet is applied. |
| | | Prophylaxis does not prevent the haematogenous infection of prosthetic joints and antibiotics should be administered prior to bacteraemia-inducing procedures such as catheterisation. |
| | | Audit of early and late post-operative infections pre- and post-introduction of this regime is desirable. |
Appendices

1. **First choice (default) antimicrobials:** these would tend to be the narrower spectrum, less toxic and less costly drugs, e.g. penicillin V and G.

2. **Restricted antimicrobials** (consultant prescription or microbiologist advice only): conversely, these would tend to be the broader spectrum, more toxic or costly drugs, e.g. meropenem and amikacin.

3. **Switch from iv to oral:** list of oral alternatives to iv drugs. Refer to discussion under General principles.

4. **Gentamicin and vancomycin iv dosing and monitoring:** this should include: cautions and contraindications, dose, how to collect levels, when first levels and subsequent levels taken, pre-dose and post-dose timing, therapeutic pre-dose and post-dose levels.

5. **Comparative cost of iv and oral antibiotics over 7 days:** this is best given in graph form to encourage cost-consciousness amongst prescribers, all other considerations being relatively equal.

**General references**

- The importance of using the most appropriate empiric antibiotic early to treat nosocomial infections – getting it right first time. This article reviews the evidence for using appropriate empiric antibiotics early in the treatment of patients with nosocomial infections to improve clinical outcomes. Download from: www.infectionacademy.org/downloads/Empiric_antibiotics_%20right_first_time.doc

- british pharmacist, BMA and British Pharmaceutical Society; Vol. 44, September, 2002


- Manufacturers’ Summary of Product Characteristics


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**European Surveillance of Antimicrobial Consumption (ESAC)**

**Introduction**

Several antibiotic resistance surveillance programmes are operational in Europe, yet a publicly available programme for the collection of antibiotic use data was lacking. At the European Conference on Antibiotic Use in Europe (Brussels, Belgium, 15–17 November 2001), during the Belgian EU Presidency, the European Surveillance of Antimicrobial Consumption (ESAC) project was launched as an international network of surveillance systems. ESAC, funded by DG SANCO of the European Commission, collects information on antibiotic use in EU member states and several other European countries in a standardised manner, and makes this information available free of charge.

During the first phase of the ESAC project (November 2001-January 2004), actions were taken to harmonise the collection of antimicrobial consumption data in all participating countries [1] and valid data on outpatient antibiotic use were analysed [2].

During the second phase of the ESAC project (February 2004–January 2007) the methodology will be consolidated, quality indicators of antibiotic prescribing will be developed, and the more detailed antimicrobial use data, including antifungals and antivirals, will be collected.

In 2005, 34 countries are participating in the ESAC project, including all 25 EU countries, 4 applicant countries (Bulgaria, Croatia, Romania and Turkey), 2 of the 3 EFTA-EEA countries (Iceland and Norway, not Liechtenstein), Israel, Russia and Switzerland.

**Methods**

Use data of systemic antibiotics for ambulatory and hospital care from 1997 to present were collected retrospectively, in accordance with the ATC classification and Defined Daily Dose (DDD) measurement unit [1]. Detailed information on the sources of antibiotic use data can be found at the ESAC website (www.ua.ac.be/ESAC) or in our recently published paper [1]. The validity of the data collection process was evaluated by assessing: coverage bias in census data; sampling bias in sample data; bias by unaccounted OTC sales, parallel trade or inadequate registration of non-reimbursed antibiotics; and finally bias by shifts in the mix of consumption between ambulatory and hospital care. Use data were expressed in DDD per 1000 inhabitants per day (DID).
Ambulatory care use of antibiotics in Europe

Antibiotic prescribing in primary care in Europe varied greatly; the highest was in France and the lowest in the Netherlands (resp. 32.2 and 10.0 DID in 2002) [2]. A shift from the old narrow-spectrum to the new broad-spectrum antibiotics was observed. Striking seasonal fluctuations were observed in some countries with higher winter peaks of antibiotic use in countries with high annual levels. We found that differences in selection pressure account for geographic variation of resistance. Countries in Southern and Eastern Europe generally consume more antibiotics than countries in northern Europe and higher rates of antibiotic resistance exist in those high-consuming countries [2]. Although the volume of outpatient antibiotic use in DID rose in most European countries between 1997 and 2003, this trend was reversed in Belgium and France. A significant and sustainable annual reduction of outpatient antibiotic use was recorded in Belgium after 2001 and a drop of antibiotic use by 7.8% was observed in France in 2003. These changes are probably due to the nationwide campaigns to improve antibiotic use in Belgium (started in 2000) and France (started in 2002), which are the only countries in Europe that have undertaken such national campaigns.

Hospital care use of antibiotics in Europe

With valid data sets from 15 countries, the data collection from the ESAC project was not as successful in hospital care as in ambulatory care. The median of the aggregated national hospital consumption of antibiotics was 2.1 DDD/1000 inhabitants/day in Europe in 2002, ranging from 3.9 in Finland and France to 1.3 in Norway and Sweden (manuscript in preparation). Countries with high hospital care use generally also have high outpatient use of antibiotics. Substantial white spots for hospital data remain on the European map and considerable efforts will be needed to start, extend and complete data collection in many European countries. Because hospital consumption is only a tenth to a twentieth of total antibiotic consumption in a country, the validity of the hospital data is much more vulnerable to biases in ambulatory/hospital case mix. Bias is potentially more important in hospital care as consumption patterns may differ substantially among hospitals. We were forced to express the aggregated national antibiotic consumption data as a function of the population of the country and not as a function of the number of bed-days. Indeed, we discovered that timely and reliable national data on the number of hospital bed-days were not available for most European countries.

As in ambulatory care, substantial variation in the level of exposure of the population to antibiotics in hospital care was observed in Europe, which may be considered as a clear indication that in some European countries there is inappropriate use of antibiotics.

Conclusions and future

For the first time, a credible alternative to industry sources has been established on the collection of internationally comparable data on antibiotic consumption in Europe. However, the antibiotic use data collected in ESAC must be still interpreted with caution as more efforts are needed to consolidate and enhance the quality of the surveillance of antibiotic consumption. An enhanced protocol to collect data on antibiotic use linked to patient age and gender, the indication, the prescriber, and nursing homes, as well as point prevalence and cross sectional studies on hospital care use, will be deployed in 2006. Additionally, information on the regimen (dosage and length of treatment) will be collected to perform sensitivity analysis of the ESAC methodology performance, considering various units of measurement.

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References

Antibiotic Resistance in Anaerobic Pathogens

Detection of differently sized IS elements upstream of cfiA genes in B. fragilis strains from Sweden and the United Kingdom. 1–9: B. fragilis An494, KSB-R, SWE94, B16078, GBR32, 76Ba, O:21, 16997 (positive control with no IS), 638R (negative control). M: 100 bp ladder

In 2003 I was awarded an ESCMID Research Fellowship and was invited by Professors Carl Erik Nord and Ekkehard Collatz to pursue research at their laboratories at the Division of Clinical Bacteriology in Stockholm and at the Molecular Research Laboratory for Antibiotics at the Paris University, respectively. My original research goals were to examine the molecular background of a newly-discovered metronidazole resistance gene, nimE, of Bacteroides species, and to further investigate the carbapenem resistance of the same genus.

These important antibiotic resistances of Bacteroides spp. are based on the production of an inactivating enzyme, a metallo-ß-lactamase, for carbapenems and a nitroimidazole reductase for 5-nitroimidazoles, the coding genes of which are termed cfiA and nim, respectively. Interestingly, these genes are usually not sufficient to cause resistance. An activation mechanism should operate, which is a promoter supplied by insertion sequence (IS) elements known to be involved in certain resistance mechanisms of some aerobic species. Without the insertion of suitable IS elements into the upstream region of these resistance genes, they usually remain “silent”, and, consequently, the strains that carry them remain phenotypically susceptible. This case is very common for the cfiA gene-bearing strains, but rare for the nim genes. The cfiA genes are restricted to a genotypically separate group of B. fragilis, as has been demonstrated by molecular typing methods. The nim genes, nimA-G, which exhibit ca 70% DNA homology among themselves, however, are widespread in all species of Bacteroides, and harbour on small mobilisable plasmids or a mobilisable chromosomal element.

Additionally, Bacteroides have a unique promoter structure. Hence, to search for the mechanism of transcriptional activation of their resistance genes, we must find this promoter structure too.

The group of Ekkehard Collatz, which I visited first, has recently characterised some novel IS elements (IS1187 and IS1188) and their promoters participating in the activation of cfiA. My work was to determine the transcriptional initiation sites and the corresponding promoter structures in some interesting B. fragilis strains. The method applied was the rapid amplification of cDNA ends (RACE) in which mRNA is transcribed into cDNA. cDNA is tailed at its 5’-end, which corresponds to the mRNA 5’-end. With suitably chosen primers, this construct is amplified by PCR and the resulting fragment is sequenced. The examined strains had novel cfiA-activating IS elements (IS943, IS614B and IS614C), the latter two are frequent in clinical isolates from the USA and the UK, and are probably mosaic elements of IS612 and IS614 from Japan. Among Hungarian imipenem-resistant B. fragilis strains, we found one that had an imipenem MIC of 16 µg/ml. It did not harbour any IS element upstream of the cfiA gene, but had a promoter-like sequence in this region, illustrating another type of cfiA gene activation in this genus. The PCR amplification results confirmed our suspicions and the fragments are currently being sequenced.

In Stockholm, working with Maria Hedberg, we analysed a collection of Bacteroides strains from a European resistance surveillance study involving 1284 isolates by PCR methods. Among 64 strains not fully susceptible to imipenem (MICs ≥ 1 µg/ml), we found 24 cfiA-positive strains. We also detected the activating IS elements IS613, IS614B and IS1186, causing a high level of resistance to imipenem (MICs > 128 µg/ml) in circa 0.4% among all 1248 isolates. Interestingly, we again encountered strains (about 1%) which did not harbour IS elements in the close (300 nt) upstream regions of the cfiA genes, but which had considerably high resistance (MICs > 8 µg/ml). The cfiA activation mechanisms in these strains are now being further studied in our laboratory in Szeged, Hungary. The carbapenem MICs of imipenem and meropenem were repeatedly determined by controlled agar-dilution measurements.

We were not only interested in the “geographical distribution” of imipenem-resistant strains, but we also studied the temporal occurrence of such strains, examining the imipenem-resistant B. fragilis strains from Sweden. Altogether 8 strains were collected, all cfiA-positive, for which imipenem MICs > 128 µg/ml were determined and which harboured IS elements (3 IS614B, 3 IS1186, 1 IS1187 and 1 IS942) upstream of cfiA. There was a shift in the temporal occurrence of the activating IS elements from IS1186 to IS614B. This latter finding was reported at the 15th ECCMID 2005 in Copenhagen. We
have also been preparing manuscripts for publication in the near future on the promoter and cfiA-mediated carbapenem resistance studies.

In my home laboratory in Szeged, I completed the analysis of the novel metronidazole resistance nimE gene of Bacteroides spp. By Southern hybridization and conjugation studies, it was localised on a 8.3 kb plasmid. Upstream of this gene, an IS element, termed IS86, was found with possible Bacteroides promoter motifs. These results with my previous findings on nim gene-carrying genetic elements of Bacteroides have led to a manuscript being submitted to the Journal of Antimicrobial Chemotherapy. Additionally, during a European resistance surveillance study, my friends and colleagues in Stockholm recently found a new nim gene, nimF, that originated from Hungary. The B. vulgatus strain harbouring this nimF gene is currently being analysed similarly to the nimE strains.

Beyond the benefits from working in leading laboratories on antibiotic resistance mechanisms of anaerobic pathogens in Europe, I took the opportunity to visit the most interesting cultural sights while being in these most wonderful and fascinating historic capitals of Stockholm and Paris. Finally, I am very grateful and wish to express my thanks to the ESCMID Awards Committee for choosing me as one of the recipients of a ESCMID Research Fellowship. I also thank my hosts, Ekkehard Collatz and Isabelle Podglajen in Paris, and Carl Erik Nord and Maria Hedberg in Stockholm, for receiving me as their co-worker.

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Zoonoses: an Underestimated Health Risk

In 1989, 34 cynomolgus macaques died in an animal unit in Reston, Virginia from an infection with Ebola virus. A further one hundred monkeys were killed, since it was unclear whether they were also infected. The animals had been imported some weeks before from the Philippines to be sold to private monkey aficionados. How the monkeys became infected with the filovirus, which occurs only in the tropical Africa, could not be found out, because the animal dealer in the Philippines had in the meantime disappeared. However, it is certain that persons in Virginia had just barely escaped disaster: in three cases the pathogen had been passed to animal caretakers, but caused no illness. A small difference in the gene sequences coding for virulence probably made the Reston variant of the Ebola virus less dangerous to humans than the strains from Sudan and the Congo.

Ten years later in Queens in New York City 56 persons contracted West Nile fever, which is caused by a virus originating in the West Nile province of Uganda. Once in the USA, the virus infected the local bird population. Migratory birds have meanwhile spread the virus into all states in the continental US (with the exception of Washington) and over wide areas of Canada and Mexico. Since the pathogen is transferred by different culicidae species, it is probable that the virus will continue to spread north- and southwards in the next years. The costs of keeping mortality and morbidity of West Nile illness at bay (8912 cases in 2003 and 2470 in 2004) are gigantic. There is convincing evidence that the pathogen was brought to North America through illegally-imported birds.

In 2000 the English Ministry of Health first warned of Enterobacteriaceae spread by reptiles. A toddler died from Salmonella meningitis. The classification indicated extremely rare serotypes. It was no wonder. The one child was infected through his grandmother’s iguana and the other by a Chinese water dragon, which was kept as a family pet.

On 15 May 2003 a three-year-old girl in Newton, Massachusetts, was infected through her mother’s pet Chinese water dragon and died in an animal unit in Reston, Virginia.

In autumn of that very year a new coronavirus in Eastern Asia provided for a scare. Altogether 8098 persons got sick with severe acute respiratory syndrome (SARS). Travelers brought the virus to Toronto, among other places, where a satellite epidemic developed. Epidemiological and virologic investigations showed that the coronavirus originated from a civet (Viverra zibetha), an animal native to China. The civet is one of 54 wild species that is on the bill of fare at Chinese restaurants. It is sold live at public markets and there are hints that an infected animal dealer was the source of the epidemic.

It may be merely coincidence that the time span between important epidemics of
zoonotic origin have continuously shortened over the past 16 years. Clearly, changed animal husbandry practice (commercially and leisure-related) has increased the risk of infection with zoonotic pathogens together with changes in the way of life and the creation of new peri-urban habitats for native wild animals and imported exotics. Animals live with us, are playmates, sometimes eat with us at a table, and sleep with us in bed. This type of cohabitation causes an evolutionary conundrum in connection with the emergence of new, or already-forgotten infectious diseases.

In 2004 Spanish veterinarians carried out a systematic survey of dogs. It revealed that between four and ten percent of the animals had visceral leishmaniasis depending on region. On the Balear Islands, a typical vacation spot, to which travellers often bring their pets, the prevalence was six percent. These figures indicate a significant exposure risk for animals brought to Spain. A study by the Liverpool School of Tropical Medicine confirmed this: in 2002 there were 17 imported or travelling dogs diagnosed with leishmaniasis; in 2003, 37 animals. Similar figures can be found in the US. There animals became infected through visits to Central America. Since *Phlebotomus* species suitable for leishmaniasis parasites are not only restricted to southern Europe, transmission of the pathogen from the pet to humans may occur also in Central Europe. Importing stray dogs from Mediterranean areas out of sympathy is therefore urgently advised against.

The fact that the most common domestic pets represent a health danger is easily forgotten. Who remembers when purchasing a budgie that parakeets can cause psittacosis? And who keeps in mind when building a sandbox for a grandchild that dogs and cats like to use sand as a spot in which to defecate, hence increasing the risk of toxocariasis?

An illness, known about for a long time, but only recently known to be a true zoonosis, is cat scratch disease, caused by *Bartonella henselae*. The bacteria are directly transferred via blood or saliva of infected animals or indirectly, when cat fleas suck blood from a cat owner. In Austria 33% of all cats have antibodies against *Bartonella henselae*, and in the USA each year approximately 24,000 cases of cat scratch disease are documented. The majority of the patients are children and adolescents. This indicates that close contact with cats – stroking, playing, teasing – is characteristic of children, carries a particularly high risk.

With human granulocytic ehrlichiosis, cats and dogs as well as humans are victims of ticks. Different species of ticks transfer the recently-identified pathogen, *Anaplasma phagocytophilum*. The anaplasmas are transmitted by ticks that fall from animals and attach to humans. In Germany approximately two percent of healthy blood donors have antibodies against *Anaplasma phagocytophilum*, in Austria four percent and in Slovenia even 16%. The differences reflect approximately the frequency of dog and cat tick infestation in the three countries.

Even without having a pet, one is not protected from zoonoses associated with domestic animals, as shown by the Q fever example. *Coxiella burnetii* is also found in dogs and cats, but it very frequently infects animals with cloven hooves such as goats and sheep. *Coxiella* are present in the excreta and are virtually always present. If females become pregnant, the organisms proliferate in the placenta and in the amniotic fluids. During delivery *Coxiella* are shed into the environment. They are still infectious even months after the birth residues are completely dried out. Typically the *Coxiella* are whirled up with dust and inhaled by humans. Hence Q fever frequently begins like classical pneumonia, gradually accompanied by other symptoms.

Since meanwhile sheep and goats are also kept within cities, Q fever can also hit persons who have never had direct animal contact. In the Dortmund district of Asseln, 97 persons came down with it. The explanation: animal lovers were keeping a small herd of sheep on the edge of the suburb, which on winter evenings was regularly driven into a stable in the town centre. That winter was markedly dry and windy, so that the animal

### Box 1

**Tracing a monkeypox outbreak: a case history**

How difficult it is to trace unknown pathogens when brought in by exotic animals, is exemplified by the monkeypox epidemic in the US in May 2003. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared. On 9 April an animal wholesale dealer in Texas received a shipment of 762 rodents from Ghana, including different species from ground squirrel, porcupine, Barbary striped mouse to Gambian giant pouched rat. 584 animals found their way to pet stores in six states. 178 animals disappeared.

In the course of the next weeks the prairie dogs were sold to various pet stores in Wisconsin, Illinois, Indiana, Missouri, Kansas and Ohio or sent directly to customers in these states. Between 15 May and 20 June, 71 persons came down with monkeypox. All had had contact with prairie dogs or had been in kennels, which had been inhabited by the rodents. Since the illnesses started with single cases within a wide geographical range, the onset of the epidemic was not recognisable to the physicians. Only when CDC became involved due to suspicion of an attack with smallpox virus, was the mysterious pathogen identified. How seriously the US authorities took the illnesses is evident by the fact that as an emergency measure, 30 persons were inoculated for smallpox. In any case the vaccine did not protect persons already infected with monkeypox.

### Box 2

**Travelling with pets**

This year British veterinarians anticipate that from Great Britain alone about 150,000 pets will be taken on a trip. Most owners are unaware of the potential dangers, to which they expose their pet and possibly themselves. Considering the health risk connected with the travel of pets, the EU issued new guidelines valid from 1 October 2004. Consequently dogs, cats, and ferrets must:

- have a European Union animal passport
- have effective vaccination protection against rabies
- be identified by a microchip or a tattoo
excrement quickly dried and was blown as infectious dust into the local neighbourhoods.

Similar epidemics are well-known from other non-European countries. Moreover, a study from Algeria showed that blood culture-negative endocarditis is frequently caused by Coxiella burnetii, Brucella melitensis, and Bartonella quintana, likewise typical pathogens from sheep and goats. Children have a particularly high risk, since they have close contact with goats and sheep and ignore hygienic precautionary measures.

A particularly high infection risk is associated with keeping small exotic animals. African hedgehogs are frequently infected with Mycobacterium marinum, different Salmonella species, Yersinia pseudotuberculosis, also occasionally with Yersinia pestis, Toxoplasma gondii, Cryptosporidium and different pathogenic viruses and fungi. Dwarf hamsters and prairie dogs can get sick with tularaemia, and at the least the latter can transfer Francisella tularensis to humans. Also known are infections with E. coli O157 from reptiles and with Salmonella from reptiles.

In fact, about 90% of all exotic reptiles continuously shed Salmonella. The CDC in Atlanta estimates 90,000 cases of reptile-transmitted Salmonella infection each year in the USA alone. The infection occurs either via contact with the animal (e.g. petting) or contact with surfaces contaminated with excrement. In addition, the cages or terrariums are frequently washed in the household bathtub, in which young children later bathe.

In Sweden, 339 reptile-associated Salmonella cases were registered from 1990 and 2000. After the import restrictions for reptiles were waived in 1996, in the context of conforming to EU regulations, the incidence rose from 0.15/100,000 to 0.79/100,000 per year. Children were more affected (incidence 1.3/100,000). After a country-wide information campaign the incidence decreased to 0.46/100,000. These figures show that the reptile owners were not conscious of the health risks to themselves and family members.

Canadian geese are frequently infected with Salmonella, E. coli and Campylobacter species. If numerous animals cohabit in lakes or ponds, the bodies of water and potential drinking water reserves, become contaminated with Enterobacteriaceae. A recent study in Georgia indicated that Canadian geese should be regarded as vectors for resistant genes of E. coli.

In summary, when animals are shipped from their original habitat into another biotope, they do not come alone. They carry viruses, bacteria, fungi, or parasites quasi by piggyback. Not only potential health risks are an argument against the sale and keeping of exotic animals, but also respect for animals calls for preventing trade with exotics for purely economic reasons. There is no doubt about it: prairie dogs are no substitute for dwarf rabbits and Gambian giant pocketed rats should not compete with Guinea pigs in the pet stores. Chameleons belong in the trees of tropical regions. Civets and other four-legged supposed delicacies have to be banned from the menu.

**What’s New in Microbiology and Infectious Diseases?**

**Emerging Infectious Diseases**

**Human metapneumovirus (hMPV)**

Human metapneumovirus (hMPV) is an emerging respiratory pathogen first discovered in 2001. The illness is similar to that produced by respiratory syncytial virus (RSV); it can produce disease both in the upper and lower respiratory tract and can cause life-threatening illness in vulnerable patients. Diagnosis is by reverse transcription PCR or rising antibody titers but commercial tests are not yet available. Bosis et al. collected nasopharyngeal swabs from 1,505 children for the detection of hMPV, RSV, and influenza virus RNA by reverse-transcriptase polymerase chain reaction (RT-PCR). hMPV was detected in 42 children (2.8%); RSV in 143 (9.5%); P < 0.0001 vs. hMPV, and influenza viruses in 230 (15.3%); P < 0.0001 vs. hMPV. The co-infection rate was 16.7%. The households of the hMPV- and the influenza-positive children had significantly more illnesses, needed significantly more medical visits, received more antipyretics, and missed significantly more work or school days than those of the RSV-positive children. Thus hMPV may have a significant clinical and socio-economic impact on children and their families. Considerable genetic and antigenic diversity was observed for hMPV, but the implication of this diversity for vaccine development and virus epidemiology requires further study.


**Human coronaviruses (HCoVs)**

The SARS outbreak affected 26 countries during 2002/2003, causing 774 deaths out of 8098 clinical cases. It was caused by a previously unknown coronavirus SARS-CoV that probably originated from an animal reservoir. Two previously unrecognised human coronaviruses were discovered in 2004 in the Netherlands (HCoV-NL, related to group-1 coronaviruses) and Hong Kong (HCoV-HKU1, related to group-2 coronaviruses). Symptoms ranged from mild respiratory tract infection to severe pneumonia. The clinical impact and epidemiology of HCoVs are largely unknown and warrant further investigation.

**Influenza A virus (IAV) / avian influenza**

Several subtypes of this virus causing avian influenza were transmitted from birds to humans, and these continue to constitute a pandemic threat. The H5N1 IAV causing outbreaks in Southeast Asia since 1997 have mostly homogenous HA and NA genes, while their descendants causing infection in 2003/2004 are more genetically diverse, and have increased virulence for animals and possibly for hu-
mans. The clinical symptoms associated with these zoonotic transmissions range from mild respiratory illnesses and conjunctivitis to pneumonia and acute respiratory distress syndrome, sometimes resulting in death. Of 44 confirmed cases in Vietnam and Thailand, 32 were fatal. Overall, it is a potentially alarming situation. A further outbreak of the highly pathogenic avian IAV occurred in the Netherlands during 2003, with 89 human cases and one fatality. More basic research into virus ecology and evolution and development of effective vaccines and antiviral strategies are required to limit the impact of influenza A virus zoonoses and the threat of an influenza pandemic.


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**Chandipura virus / encephalitis**

Rao et al. report on an outbreak of acute encephalitis of high case fatality (183 of 329 cases) in children from Andhra Pradesh state in southern India during 2003. Clinical samples tested negative for IgM antibodies to known encephalitic viruses. A virus was isolated from six patients with encephalitis and was identified as Chandipura virus by electron microscopy, complement fixation, and neutralisation tests. Chandipura virus RNA was detected in clinical samples from nine patients. Sequencing of five of these RNA samples showed 96.7-97.5% identity with the reference strain of 1965.


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**Monkeypox**

Ligon reviewed the emergence of this zoonosis in the USA when a mysterious disease was reported on 24 May 2003 in a 3-year-old girl who had been hospitalised in central Wisconsin with cellulitis and fever after being bitten by a prairie dog on 13 May. By 30 July 2003, 72 confirmed or suspected cases of monkeypox had been reported in Wisconsin, Illinois, and Indiana and represented a large outbreak. Traceback investigations from the child and other patients followed the route of introduction of monkeypox into Wisconsin to a distributor in Illinois, who had received a shipment of exotic animals imported into the United States through Texas from Ghana, West Africa. No further cases of illness have been reported in humans since 22 June 2003.


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**Viruses and schizophrenia**

Evidence for an infectious cause includes the increased risk among those born in the winter and spring months, and at times when other infections (measles, varicella, poliomyelitis) show increased activity. Herpes simplex virus (HSV) has been implicated in schizophrenia as it has a tropism for the nervous system and is capable of replication in the brain. A recent, nested, case-control study evaluated pregnant women between 1959 and 1966 and identified 27 surviving offspring who were later diagnosed with schizophrenia. Analysis of stored blood samples showed an association between high levels of maternal antibody to HSV-2 and subsequent development of adult psychosis. No association was found between HSV-1 infection and psychosis. There is also evidence that human endogenous retroviruses (HERVs) may play a role in schizophrenia, as antibodies to these agents have been found at a greater frequency in the sera of affected individuals compared with controls. This is supported by the presence of reverse transcriptase at levels four times higher in the cerebrospinal fluid of people with recent onset schizophrenia compared with controls, and by its elevated presence in long-term schizophrenic patients. Yolken et al. detail the above and conclude that further research to investigate the relationship between virus infection and schizophrenia is warranted.

Yolken R. Viruses and schizophrenia: a focus on herpes simplex virus. Herpes 2004;11 Suppl 2:83A–88A

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**Entericaggregative Escherichia coli diarrhoea (EAEC)**

Huang et al. recently reviewed the epidemiology, pathogenesis, and host susceptibility factors of this important emerging pathogen that causes enteric and food-borne infectious diseases. Children throughout the world appear to be susceptible to EAEC infection. EAEC pathogenesis involves the following three stages: 1) adherence to the intestinal mucosa; 2) increased production and deposition of a mucus biofilm; and 3) mucosal toxicity due to inflammation and cytokine release. The HEp-2 cell adherent assay allows identification of EAECs characteristic aggregative or «stacked brick» adherence pattern. Azithromycin and rifaximin have been shown to shorten the course of EAEC diarrhea in adults and probably represent the recommended antimicrobials of choice for children with severe or persistent illness.


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**Intracellular bacterial infections**

Human infections by intracellular bacteria have been recognised for many years, but much of what we know about the pathogenesis of these diseases and their etiologic organisms has emerged within the past few years as a result of improved molecular-based means for their detection and classification. Katz et al. related new insights concerning the epidemiology and pathogenesis of intracellular bacterial infections and methods for the detection of Chlamydia pneumoniae, Ehrlichia chaf-
feensis, Anaplasma phagocytophilum, and Rickettsia species. Emerging evidence suggesting a possible intracellular existence for another organism, Mycoplasma pneumoniae, may explain how this organism interacts with the host to induce chronic inflammatory conditions of the respiratory tract. 

**Rhinosporidiosis**

Arsuculeratne reviewed the significant advances in knowledge on rhinosporidiosis and Rhinosporidium seeberi made from 1999 to 2004. R. seeberi, the pathogen that causes rhinosporidiosis, has been definitively classified using molecular biological tools in a new clade - the Mesomyctezotoza, along with 10 parasitic and saprobic microbes. The controversial spherical bodies of the endospores have been shown to comprise both lipid / protein nutritive bodies and other spherical bodies that are metabolising units that reduce MTT (3-[4,5-dimethyl-2-thiazolyl]-2,5-diphenyl-2H-tetrazolium bromide). This indicates the viability of these spherical bodies, provisionally identified as the electron dense bodies that have also been shown to contain nucleic acids. MTT reduction as an indicator of viability has been used to determine the sensitivity of rhinosporidial endospores to biocides, antimicrobial drugs, and to specific antibodies. Genetic heterogeneity has been identified in strains from humans and animals. Cell-mediated and humoral immune responses have been demonstrated in human patients and in mice. Several mechanisms of immune evasion by R. seeberi have been identified.


**Human immunodeficiency virus (HIV)**

Highly active antiretroviral therapy (HAART) dramatically changed the course of HIV infection. Barbaro et al. recently reviewed the current state of the art. HAART involves the use of agents from at least two distinct classes of antivirals: a protease inhibitor (PI) in combination with two nucleoside/nucleotide reverse transcriptase inhibitors (N(t)RTIs), or a non-nucleoside reverse transcriptase inhibitor (NNRTI) in combination with N(t)RTIs. Recently, the third family of antivirals started to be used clinically, with the advent of enfuvirtide, the first fusion inhibitor (FI). Other drugs in advanced clinical evaluation or recently approved include tenofovir, an N(t)RTI; atazanavir and tipranavir (both PIs) mainly against drug-resistant viruses. Other compounds undergoing trial include those inhibiting HIV integrase, the third enzyme of HIV (L-731, 988 and S-1360) and those that target the ejection of zinc ions from critical zinc finger viral proteins resulting in inhibition of viral replication.

**New Antiviral Agents**

**Hepatitis B and C (HBV, HCV)**

Thomson and Main recently reviewed the literature on this subject. The key findings concern the value of prolonging treatment in patients with genotype 1 hepatitis C infection, the use of pegylated interferon in chronic hepatitis B infection and the emergence of new treatments such as adefovir for resistant HBV infection. Certain subgroups of patients such as those co-infected with HCV and HIV, those who have had liver transplantation or who are immunosuppressed are also discussed.

Entecavir is a guanosine nucleoside analogue, currently undergoing phase III trials. In a recent double blind randomised trial in HBV infected patients with (n=121) and without (n=60) HbeAg, HBV DNA was negative at 24 weeks in 75% of patients on the 1mg Entecavir dose. This was significantly more effective than continuation of lamivudine (P<0.001).

Other agents undergoing development include clevudine, an HBV DNA polymerase inhibitor and L-nucleosides, both having shown efficacy against HBV in vitro and in vivo. Viramidine and levovirin are alternatives to ribavirin for the treatment of chronic HCV infection, which seem to be less toxic to red blood cells and thus associated with a reduced incidence of haemolytic anaemia. A different strategy involves attempting to inhibit apoptosis (programmed cell death). IDN-6556 is thus undergoing investigation in both HBV and HCV infection. There is concern, however about the theoretical increased risk of malignancy and further safety data are awaited.


**Antibacterial Agents**

Linezolid was the first member of the novel oxazolidinone class of antibacterials with broad-spectrum Gram-positive activity – including against methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE) –, through inhibition of protein synthesis. Owing to its unique dual mechanism of action resistance problems are rare and there is no cross resistance with other antibacterial agents. Ross et al. recently reported on a longitudinal study in 4 monitored continents. There was sustained, near complete activity against contemporary Gram-positive isolates (7971 strains). Rare linezolid-resistant strains were identified in the United States only (4 strains, 0.05% resistance overall). Linezolid is indicated for treatment of pneumonia and complicated skin and soft tissue infections. Evidence has been accumulating regarding its excellent bioavailability, especially in skin and soft tissue but also in bones, joints, lungs and other tissues. Two recent studies by Weigelt et al. demonstrated that linezolid therapy is well tolerated, equivalent to vancomycin in treating complicated skin and soft tissue infections (CSSTIs), and superior to vancomycin in the treatment of CSSTIs due to MRSA. In the second study, superiority was also demonstrated in surgical site infections. Two further multinational studies concluded that linezolid was associated with better survival and clinical cure rates than vancomycin in nosocomial and ventilator-associated pneumonia (VAP). Recent reports suggest efficacy in orthopaedic infections but further studies are needed before this can be confirmed.


Weigelt J, Itani K, Stevens D et al. Linezolid versus vancomycin in treatment


Levoﬂoxacin is a fluoroquinolone with enhanced Gram-positive activity. The large community outbreak (292 patients) of Legionnaires’ disease in Murcia, Spain (July 2001) afforded an unusual opportunity to compare the clinical response of patients with Legionella pneumonia treated with levofloxacin with that of patients treated with macrolides. Monotherapy with levofloxacin was shown to be a safe and effective treatment for Legionnaires’ disease and appears to be more effective than clarithromycin in those patients with severe disease.


Azithromycin, a long-acting macrolide, was evaluated in a study of children with recurrent respiratory tract infections. Atypical infections (Mycoplasma and Chlamydia spp.) were identified in a surprisingly large number of patients compared to healthy control subjects (190, 54% vs. 83.8%; P < 0.0001). Both short term (1-month) and long term (6-month) clinical success was more frequent among the patients who had received azithromycin together with symptom-specific agents than among those who had received symptom-specific agents alone. This was statistically significant for the subset of patients with atypical bacteria.


New Antibacterial Agents

Over 18 antibacterial agents are currently undergoing clinical trials at or beyond phase 1 development as recently reviewed by Bush et al. The Table below details some of these compounds, the companies responsible and the current development phase.

Carbapenems: Doripenem is a broad-spectrum parenteral carbapenem with better activity against Pseudomonas aeruginosa than imipenem or meropenem. Other carbapenems under development include CS-023.

Cephalosporins: BAL5788 is a novel broad-spectrum cephalosporin, distinguished from current 3rd generation drugs in its enhanced Gram-positive activity, including penicillin-resistant pneumococci (PRSP), MRSA and VRE but not ampicillin-resistant enterococci. It is also effective against extended-spectrum beta-lactamase (ESBL) producing Gram-negative bacteria and was proven effective in skin and soft tissue infections with minimal adverse events. Other cephalosporins under development include RWJ-442831 and TAK-599.

Dihydrofolate reductase (DHFR) inhibitors: Trimethoprim, the established DHFR inhibitor now suffers from widespread resistance. Eclaprime, now under development, has enhanced Gram-positive activity including against MRSA. It has shown efficacy in skin and soft tissue infection and was well tolerated. Furthermore, the potential for development of resistance appears to be rare.

Glycopeptides: Dalbavancin is a semi-synthetic derivative of a natural glycopeptide with better activity than existing drugs (vancomycin and teicoplanin) against staphylococci including MRSA as well as PRSP. Phase 2 clinical studies have shown dalbavancin to be effective in skin and soft tissue infections as well as catheter-related bloodstream infections caused by Gram-positive organisms. However, as with teicoplanin, VanA (but not VanB) enterococci (VRE) are resistant. The longer half-life (9-12 days) of dalbavancin will permit once weekly dosing, allowing for early hospital discharge and dispenses with the need for long-term venous access with its associated morbidity. Other glycopeptides under development include oritavancin and relavancin.

Glycolipodepsipeptides: Ramoplanin is an antibiotic produced by Actinoplanes spp. Its mechanism of action is controversial but it appears to inhibit bacterial transglycosylases by binding to a moiety of lipid 2. It is rapidly bactericidal against MRSA and VRE irrespective of the resistance phenotype. Ramoplanin cannot
be injected due to haemolysis and infusion reactions as well as being poorly absorbed orally. Thus development is currently focusing on VRE eradication from the gastrointestinal tract as well as treatment of *C. difficile*-associated diarrhoea.

**Oxazolidinones:** Ranbezolid is being developed for the treatment of hospital-acquired infections due to resistant Gram-positive organisms. It appears to have significant safety advantages over the parent compound, linezolid.

**Peptides:** Iseganan is an antimicrobial peptide originally isolated from leucocytes. It is unique in its broad spectrum of activity against Gram-positive and -negative bacteria as well as yeasts and mycelial fungi. It is undergoing trials as an aerosol for the treatment of respiratory tract infections in cystic fibrosis patients and an oral solution for the prevention of ventilator-associated pneumonia in ICU patients. The latter trial has recently been discontinued due to unacceptable mortality compared to the placebo group. Peptide development in general has been traditionally hampered by rapid clearance and unacceptable toxicity. It is, however, too early to draw conclusions about the fate of iseganan. Other peptides under development include P113.

**Peptide deformylase inhibitors:** These drugs are the only entirely novel class of antibacterial agents currently undergoing clinical trials. LB-415 is one member of the group with undisclosed structure, which has *in vitro* activity against Gram-positive organisms, including those resistant to linezolid and quinupristin-dalfopristin. It appears to be well tolerated but there are no reports yet as to clinical efficacy.

**Quinolones:** Garenoxacin is a broad-spectrum quinolone with both oral and injectable formulations. It has been evaluated for treatment of respiratory- and urinary-tract as well as skin and soft tissue infections and was found to be safe and well tolerated. It appears to be associated with less phototoxicity and CNS toxicity than other quinolones including ciprofloxacin and this may help the drug in establishing a niche in the market. Other quinolones under development include sitafloxacin and WCK-771.

**Tetracyclines:** Tigecycline is an eagerly awaited glycycline developed by Wyeth. It circumvents all previously known tetracycline resistance mechanisms. It is unique in its potency against multi-drug resistant Gram-positive (including MRSA, VRE, PRSP) as well as Gram-negative bacteria (including ESBLs, *Acinetobacter* and *Stenotrophomonas* spp.). Thus tigecycline is the most promising agent of any listed above and is set to be a major asset in the fight against nosocomial infection. This is despite regrettable gaps in its spectrum for *Pseudomonas* and *Proteus* spp., which are due to non-specific efflux mechanisms. It has been evaluated for urinary tract, abdominal and skin infections. It is available in parenteral form only, has a long half-life of 36 hours and side effects appear to be minimal.


### Antifungal Agents

**Polyenes:** Conventional amphotericin B (CAB) and the various lipid formulations derived from it have the broadest spectrum amongst antifungal agents, being effective against most yeasts and mycelial fungi. CAB, however, suffers from serious renal and other side effects and has been largely superseded by newer lipid formulations. Until recently, comparative information regarding the efficacy of these different preparations was lacking due to various factors, chief amongst which is the small number of patients, the rarity of invasive fungal infections and the lack of accurate diagnostic criteria. Recent comparative studies have gone some way towards addressing some of these issues. Data were gathered for CAB and the various lipid preparations: amphotericin B lipid complex (ABLC), liposomal amphotericin B (LAB) and amphotericin B cholesteryl sulfate complex (ABCS). The Collaborative Exchange of Antifungal Research (CLEAR) is an industry-supported patient registry developed in the mid-1990s. Comparative data gathered was mainly for CAB and ABLC. In summary, all the lipid preparations are equally efficacious. However, LAB has the best safety profile – including that for renal toxicity – but is the most expensive. ABCS has the most infusion reactions and ABLC occupies an intermediate ground regarding toxicity and price. Interestingly only 3% of patients on ABLC required renal dialysis compared to 30% of those on CAB. ABLC is probably the drug of choice for zygomycosis.

**Azoles:** The prevalent azole, fluconazole is not effective against mycelial fungi and now suffers from resistance especially amongst the “non-albicans” *Candida*, hence the need for new effective agents. Voriconazole is a triazole with broad-spectrum activity against yeasts and mycelial fungi (except *Mucor* spp.). There is also some cross-resistance with fluconazole against *C. krusei* and *C. glabrata*. It has a good safety profile but visual hallucinations occur in up to 30% of cases. Voriconazole is available in both oral and intravenous formulations, is approved for use in invasive aspergillosis and may have a role in preventing breakthrough infections in patients with persistent fever and neutropenia. Posaconazole and ravuconazole are newer azoles undergoing clinical trials.

**Echinocandins:** Caspofungin is a member of this novel class of antifungals, with broad-spectrum activity against yeasts and mycelial fungi (except *Mucor* and *Cryptococcus* spp.). It has the best safety profile of all the agents mentioned here and merits consideration as an alternative – or addition – to the liposomal AB preparations. In a comparative study with LAB, Walsh et al. concluded that caspofungin is as effective as and better tolerated than LAB in patients with persistent fever and neutropenia. It was significantly more effective than LAB in those patients with proven baseline fungal infection. Caspofungin and two more recently introduced echinocandins, micafungin and anidulafungin, are available as intravenous preparations only. Furthermore, for established fungal infection with prolonged neutropenia, GIV or disseminated disease, some authorities now recommend combination therapy with two of the following preparations: any lipid amphotericin B preparation, voriconazole and caspofungin. There is concern about theoretical *in vitro* antagonism between the polyenes and the azoles but no such antagonism exists between the polyenes and the echinocandins.

**Echinocandins**


Vaccines and Probiotics

Vaccine against cervical cancer and genital warts

A randomised double-blind placebo-controlled phase II study was done to assess the efficacy of a prophylactic quadrivalent vaccine targeting the human papillomavirus (HPV) types associated with 70% of cervical cancers (types 16 and 18) and with 90% of genital warts (types 6 and 11). 277 young women were randomly assigned to quadrivalent HPV L1 virus-like particle (VLP) vaccine and 275 to one of two placebo preparations at day 1, month 2, and month 6. The primary endpoint at 36 months was the combined incidence of infection with HPV 6, 11, 16, or 18, or cervical or external genital disease (i.e., persistent HPV infection, HPV detection at the last recorded visit, cervical intraepithelial neoplasia, cervical cancer, or external genital lesions caused by the HPV types in the vaccine). The combined incidence of persistent infection or disease with HPV 6, 11, 16, or 18 fell by 90% (95% CI 71–97, p<0.0001) in those assigned vaccine compared with those assigned placebo. The vaccine could thus substantially reduce the acquisition of infection and clinical disease caused by common HPV types.


Vaccine against C. difficile associated diarrhoea (CDAD)

There is a strong association between serum antibody response to C. difficile toxin A and protection against CDAD. Aboudola et al. used a C. difficile toxoid vaccine which induced high levels of anti-toxin A IgG in sera of 30 healthy volunteers. However, it remains to be seen whether the most susceptible – the elderly population – manages to mount a satisfactory immune response.

Aboudola S, Kotloff KL, Kyne L, et al. Clostridium difficile vaccine and serum immunoglobulin G antibody response to toxin A.

Live lactobacilli in restoration of vaginal flora

Ozkinay et al. evaluated the effectiveness of live lactobacilli in combination with low dose oestriol for restoration of the vaginal flora after anti-infective treatment. Women with the complaints of vaginal infections (bacterial vaginosis, candidiasis, trichomoniasis or fluor vaginalis) were randomly assigned two to seven days after the end of the anti-infective therapy, to therapy with live lactobacilli in combination with low dose oestriol (study group, n= 240) or placebo (n= 120). The Normal Flora Index (NFI), which consists of numbers of lactobacilli, pathogenic microorganisms, leucocytes and vaginal pH, was used as the primary outcome of the study. During restoration therapy, the NFI increased significantly more in the study group than in the control group in both first and second control visits (P = 0.002 and P= 0.006, respectively). The degree of purity of the vaginal flora also increased significantly more in the study group compared with the control group (P < 0.0001 and P= 0.001, respectively). The conclusion was that restoration of the vaginal flora can be significantly enhanced by the administration of live lactobacilli in combination with low dose oestriol.

Ozkinay E, Terek MC, Yaciı M, et al. The effectiveness of live lactobacilli in combination with low dose oestriol (Gynoflor) to restore the vaginal flora after treatment of vaginal infections. BJOG 2005;112(2):234–40

Laboratory Diagnosis

Rapid identification of emerging pathogens, including coronavirus

The emergence of new infectious diseases poses new challenges for laboratory diagnosis. Sampath et al. describe a new approach for infectious disease surveillance that facilitates rapid identification of known and emerging pathogens. The process uses broad-range polymerase chain reaction (PCR) to amplify nucleic acid targets from large groupings of organisms, electrospray ionisation mass spectrometry for accurate mass measurements of PCR products, and base composition signature analysis to identify organisms in a sample. Using 14 isolates of 9 diverse coronavirus spp., including the severe acute respiratory syndrome-associated coronavirus (SARS-CoV), the test could identify and distinguish between SARS and other known CoV, including the human CoV 229E and OC43, individually and in a mixture of all 3 human viruses. The sensitivity of detection, measured by using titered SARS-CoV spiked into human serum, was 1 PFU/mL. The authors concluded that this approach is applicable to the surveillance of bacterial, viral, fungal, or protozoal pathogens and is capable of automated analysis of >900 PCR reactions per day.


Molecular genetic methods for the diagnosis of fastidious microorganisms

PCR may allow quick diagnosis of infections caused by fastidious pathogens for which culture could be extremely difficult. Fenollar and Raoult, however, point to several pitfalls, such as false positives, which underlines the necessity to interpret the results obtained with caution. The recent development of bacterial genome sequencing has provided an important source of potential targets for PCR, allowing rational choice of primers for diagnosis and genotyping. In addition, the development of new techniques such as real-time PCR offers several advantages in comparison to conventional PCR, including speed, simplicity, reproducibility, quantitative capability and low risk of contamination. The article examines the general principles of PCR-based diagnosis and molecular genetic methods for the diagnosis of several hard-to-culture bacteria, such as Rickettsia spp., Ehrlichia spp., Coxiella burnetii, Bartonella spp., Tropheryma whipplei and Yersinia pestis.


The diagnosis of necrotizing fasciitis (NF)

The lack of specific clinical signs of NF leads to a delay in the diagnosis and appropriate treatment with attendant increased morbidity and mortality. Wong and Wang propose a clinical staging to better define the progression of the disease, including hyperacute and sub-acute variants. Imaging techniques, such as magnet-
ic resonance imaging and frozen section biopsies may be of value in the early recognition of NF. However availability and cost limit the routine use of these tests. Recent diagnostic adjuncts include the fasciitis LRINEC (laboratory risk indicator for NF) score and transcutaneous tissue oxygen saturation monitoring. Some may have the potential for widespread application in the assessment of severe soft tissue infections.


Infection Control

Vascular catheter infections
Abundant evidence now exists that there are many interventions that can reduce the risk of vascular catheter infections. In this review, Sherertz examines 22 primary research articles selected from 415 randomised clinical trials and over 2500 others on vascular catheter infections published between January 2002 and March 2004. The recent findings show that: full sterile barriers are not necessary for the insertion of arterial catheters and that subcutaneous tunnels may decrease the risk of femoral catheter infection. The minocycline-rifampin catheter coating still appears to be the most efficacious. Further studies demonstrating that education of MD/RN personnel reduces the risk of catheter infection now exist. A number of studies show that the method of attaching IV tubing to catheters and certain catheter flush solutions can reduce the risk of infection. Differential time to positivity looks increasingly promising as a practical method for diagnosing catheter infection. All catheters suspected of infection do not need to be removed.


Clostridium difficile-associated nosocomial diarrhoea (CDAD)
With the introduction of new antibiotics into clinical practice, confusion has arisen about the risk they pose for CDAD. Strains of C. difficile that fail to produce an active toxin A are an emerging problem and good molecular epidemiology is required to determine whether highly infectious clones exist. Little progress has been made in the treatment of recurrent CDAD but the development of a vaccine is imminent (see below). More effort is being made to rid the hospital environment of C. difficile through infection-control procedures or changes in antibiotic-prescribing policies. Yet even control of the use of third-generation cephalosporins appears to be key. Khan and Cheesbrough looked at the impact of changes in antibiotic policy on CDAD over a five-year period. With the introduction of ceftriaxone for initial treatment of severe sepsis or pneumonia the average number of patients with C. difficile toxin-positive stools per quarter increased from 16 to 39. When levofloxacin was substituted for ceftriaxone, the incidence of CDAD fell progressively to five cases per month by 2000. The observation was also made that a short (typically three dose) course of third-generation cephalosporin poses a similar risk for CDAD as a more prolonged course. A different conclusion was reached by Berild et al. who compared the incidence of CDAD in two university hospitals with the same total antibiotic use. Despite a reduction in the use of broad-spectrum antibiotics in one hospital, the incidence of CDAD increased during 1993–1999. The second hospital had markedly better facilities for infection control (single rooms, WC, hand-basin, etc.). The authors concluded that lack of facilities for infection control and higher bed occupancy could have contributed to the higher incidence of CDAD despite decreased use of broad-spectrum antibiotics and clindamycin. Thus it is probable that there should be a dual pronged focus on both rational antibiotic use and infection control.

Khan R, Cheesbrough J. Impact of changes in antibiotic policy on Clostridium difficile-associated diarrhoea (CDAD) over a five-year period in a district general hospital. J Hosp Infect 2003;54(2):104–8


Extended-spectrum beta-lactamase-producing Klebsiella pneumoniae (ESBLKp)
Lee et al. set out to identify risk factors for the respiratory acquisition of ESBLKp among patients admitted to a neurosurgical intensive care unit (NSICU). Multivariate analysis showed that prior exposure to third generation cephalosporins (TGcs) (OR, 6.0; CI95, 1.9 to 18.6; P = .002) was an independent risk factor of ESBLKp acquisition. TGc use was regulated during the intervention period. The respiratory acquisition of ESBLKp per 1,000 patient-days (13.5 [CI95, 8.9 to 18.1] vs 2.7 [CI95, 0.9 to 4.6]) and the antimicrobial use density of TGcs (38.2 +/- 5.0 vs 17.3 +/- 2.6; P < .001) decreased significantly after the intervention. Thus, prior exposure to TGcs was an independent risk factor for the respiratory acquisition of ESBLKp, and decreased use of TGcs was associated with a decrease in acquisition.


Staphylococcus aureus carriage among participants at the 13th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)
The aim of this study by Nulens et al. was to measure the rate of Staphylococcus aureus nasal colonisation among attendees of the 13th ECCMID, particularly with regard to methicillin-resistant (MRSA) strains. The 31.4% rate of Staphylococcus aureus colonisation detected was as reported previously for healthcare workers. A statistical difference was found between the rates of Staphylococcus aureus carriage in physicians (37.4%) and non-physicians (21.7%) but not between males (35.0%) and females (28.9%). Only one participant was found to carry MRSA. Surprisingly, the rate of methicillin-susceptible Staphylococcus aureus carriage was significantly higher among participants from countries with a low prevalence of MRSA.


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ESCMID events

6–9 November 2005
ESCMID / SHEA Hospital Epidemiology Course 2005
Place: Beaune, France
Contact: Ludwig Serge Aho or Benoist Lejeune
Email: benoist.lejeune@chu-brest.fr
Internet: www.hosp-epi-course.org

1–4 April 2006
16th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)
Place: Nice, France
Contact: AKM Congress Service
Phone: +41 61 686 77 11
Email: info@akm.ch

6–8 September 2006
International Conference on Surgical Infections (ICSI) 2006
Place: Stockholm, Sweden
Contact: Stockholm Convention Bureau (Stocon)
Email: icsi2006@stocon.se
Internet: www.icsi2006.se

31 March – 3 April 2007
17th European Congress of Clinical Microbiology and Infectious Diseases / 25th International Congress of Chemotherapy (ECCMID / ICC)
Place: Munich, Germany
Contact: AKM Congress Service
Phone: +41 61 686 77 11
Email: info@akm.ch

13–14 October 2005
4th European Meeting on Molecular Diagnostics
Place: Scheveningen, the Hague, the Netherlands
Email: molecule@wens.nl
Internet: www.wens.nl/molecule

3–4 February 2006
11th International Symposium on Infections in the Critically Ill Patient
Place: Seville, Spain
Contact: McCann Meetings
Email: info.infections2006@mccann.es
Internet: www.infections-online.com

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