ESCMID NEWS

ESCMID

Scientific

New Study Group on Infectious Diseases in Primary Care

Professional

Market Trends in In Vitro Diagnostics

Professional

4th ESCMID School Announcement

Features

Rabies – a Disease with Many Facets

Rabies virus purified from an infected cell culture: negatively stained virions have a characteristic “bullet shape” (see page 16)

ESCMID

Education

Scientific

4 New Study Group on Infectious Diseases in Primary Care

Professional

14 Appeal from the International Red Cross
15 Market Trends in In Vitro Diagnostics

Features

16 Rabies – a Disease with Many Facets

Excerpts

19 News in Brief

Calendar

24 Forthcoming Events

Corrigenda

11 Epidemiology Typing Workshop Report
23 EUCAST Report
Dear Colleagues

The autumn and winter months are those of intense professional activity. The summer is forgotten and the annual round of lecturing, examining, grant applications and congresses is upon us. It is also a time when hospital activity peaks, often as a result of respiratory infections.

Recent epidemics such as SARS and the anticipated future pandemic of H5N1 influenza have kick-started a number of European initiatives. The launching of the European Centre for Disease Prevention and Control on 27 September in Stockholm marked a new era in communicable disease control in Europe. How quickly it is able to bring about closer co-operation between the National Centres and develop a co-ordinated and rapid European response to deal with the next epidemic, will be one of the yardsticks by which it is judged.

Linked to this is the proposed updating of the International Health Regulations, which create a legal framework to prevent the international spread of infectious diseases. International air travel, free movement across national borders and the massive increase in population migration, for whatever reason, have created a truly global village and rendered the old regulations obsolete.

European research funding under the 6th Framework Programme has been substantial and has included identified areas of importance for investigators into infectious diseases. A timetable and topics for the 4th Call of Thematic Priority 1: Life Sciences, Genomics and Biotechnology for Health will be available shortly while the 7th Framework Programme, scheduled for 2006, is under active discussion. The Executive is represented on the Advisory Group and is willing to relay your suggestions and proposals. They will need to be consistent with the published aims and objectives of the overall EU Research Agenda.

The next few months will see major changes in the composition and tasks of the Executive as a result of the recent elections. This will affect many aspects of the Society’s activities such as the organisation of the annual ECCMID, publications and professional affairs. The need to strengthen the operational functions of the Executive Office is also under active discussion. Of one thing I am certain, ESCMID will be strengthened by all these changes and will hopefully continue to enjoy the support of its expanding membership.

Roger Finch
Past President
Chairman, Publications Committee
Message from the President

Marc Struelens

Dear Colleagues

More than ever ESCMID is committed to promote excellence in the art and science of clinical microbiology and infectious diseases. To achieve this goal, we are developing an enlarged repertoire of activities with the enthusiastic involvement of our membership. Key to new ideas and initiatives is the democratic renewal of leadership within the Society. As elections are under way to renew 5 positions in the Executive Committee, we are confident that the high scientific and professional calibre of the candidates and participation of members casting their vote will ensure an excellent representation of Europe's best assets to fulfil our mission.

The preparation of the 15th ECCMID in Copenhagen is progressing well. I invite you to review the preliminary programme on the Society home page. Once again we received a much higher than usual submission of over 2400 abstracts from world wide research in the various fields of microbiology and infection, from bench to the bedside and population level. As in Prague where they proved extremely popular, a series of educational workshops will be organised in Copenhagen by ESCMID Study Groups and partner societies in the afternoon preceding the opening of the Congress. Advance registration is required to participate in this educational programme. Further ahead, the 4th ESCMID School will be held this summer in Szeged, Hungary and will offer an authoritative review of current topics for post-graduate specialty trainees in clinical microbiology or infectious diseases. ESCMID is diligently working together with other European scientific societies to harmonise and improve the efficiency of obtaining European Continuing Medical Education certification through UEMS. Plans are being actively developed with input from the Education Committee to expand our educational programme, which again will be delivered in co-operation with ESCMID Study Groups, learned societies active in related medical fields and other stakeholders in health promotion such as DG SANCO of the European Commission and WHO.

In the scientific arena, the Society provides input to the DG Research consultations regarding priorities of the 7th Framework Programme. ESCMID currently supports 12 Study Groups engaged in promoting co-operative research networks, developing scientific and practice guidelines and organising educational courses and workshops. A new Study Group on the study of infections in primary care is being established and will hold its inaugural assembly of members during 15th ECCMID in Copenhagen (see page 4). In November, a Consensus Conference was organised in Amsterdam by the ARPAC project (Antimicrobial Resistance Prevention and Control). ARPAC is a DG Research supported concerted action conducted by 4 ESCMID Study Groups and coordinated by Dr Ian Gould at the University of Aberdeen. The conference was attended by 150 participants who reviewed and discussed findings from the survey of over 200 hospitals from 32 European countries. Important regional differences were observed with regard to antibiotic consumption and resistance in key pathogens as well as in local antibiotic and infection control policies. Among encouraging observations, was that multidrug-resistant bacterial strain was associated with lower antibiotic use. In addition, infection control policies such as alcohol-based hand hygiene and isolation of patients with MRSA were associated with lower MRSA rates. Recommendations were made based on ARPAC data towards harmonisation and strengthening of local and national antibiotic and infection control policies, as well priorities set for research in control of resistance in the health care setting. The slides from the conference are available at the ARPAC web site accessible through the Society home page, under Science & Education, Study Groups. The recommendations will be published in Clinical Microbiology and Infection. I strongly encourage you to join the study groups active in your main field of interest thereby acquiring more insight into the various approaches taken to manage infectious diseases and contributing to exchange of best practice across Europe.

ESCMID is also active in the field of public health, in conjunction with many partners. EUCAST, now supported by DG SANCO, is progressing steadily in the pan-European harmonisation of breakpoints for antimicrobial agents, and is increasingly involved in scientific discussion with its US counterpart NCCLS. ESCMID is supporting and acts in an advisory capacity to the European surveillance programmes EARSS (European Antimicrobial Resistance Surveillance System) and ESAC (European Surveillance of Antibiotic Consumption) which hold their joint annual meeting recently to review the latest trends in emergence of resistance and antibiotic use. The excellent proficiency in resistance detection of EARSS-participating laboratories as well as the increasingly consistent methods used for drug consumption data collection and analysis by ESAC participating countries is encouraging. Many countries have achieved reduction in annual antibiotic consumption in the outpatient setting, notably those that are developing national campaigns to curb inappropriate use. While some countries experience stabilisation of resistance rates for key pathogens, regional epidemics still do occur with glycopeptide resistant enterococci, ESBL-producing E.coli and MRSA. Again, I encourage you to read the interesting online annual reports of EARSS (www.ears.rivm.nl) and ESAC (www.ua.ac.be/main.asp?c=ESAC). Clearly, a lot more efforts are still needed to improve antibiotic use and control the spread of antibiotic resistance in the community and health care settings.

ESCMID has responded to the public consultation launched by former Commissioner for health David Byrne in his initiative: Enabling Good Health for All. A Reflection Process for a New EU Health Strategy (available at http://europa.eu.int/comm/
ESCMID is pleased to announce the establishment of the ESCMID Study Group on Primary Care Topics (ESPRIT). Infectious diseases are very common in primary care practices and the vast majority of cases is diagnosed and treated in this setting without referral to a hospital. In the past decade research on infectious diseases in primary care has improved considerably, both in quality and quantity. Several university departments of general practice or primary care in Europe have chosen infectious diseases as a major focus for research and have been successful in acquiring funds and publishing papers. This has resulted in a fast growing number of international publications, mainly on respiratory and urinary tract infections, systematic reviews as well as national and international guidelines in this field.

Within primary care meetings and congresses, new insights and controversies on infectious diseases are nowadays frequently discussed and receive adequate attention. However, the dialogue between primary care researchers and microbiologists and infectious disease specialists is still inadequate. Primary care researchers, mainly general practitioners and clinical epidemiologists, only rarely attend international congresses on clinical microbiology and infectious diseases, and presentations by them on these occasions are scarce. More input from primary care specialists in discussions in this field would be very valuable and would enhance both the scope and the scientific relevance of meetings such as ECCMID. In addition, primary care researchers collaborate more and more with infectious disease specialists, microbiologists and immunologists both in research and teaching projects.

Based upon the above, we are very glad that ESCMID has decided to start a study group on infectious diseases in primary care.

Objectives
The objectives will be:
1. to stimulate and coordinate the input of primary care physicians into ESCMID
2. to enhance knowledge on aetiology, diagnosis, prognosis and prevention of infectious diseases in primary care by creating a platform for scientific discussions on these topics within ESCMID
3. to enable, stimulate and improve contacts and cooperation between primary care physicians, infectious diseases specialists, microbiologists, paediatricians and other experts within ESCMID.

Invitation
Our inaugural meeting will take place during the 15th ECCMID in Copenhagen (see next page). The time and place of the meeting will be published in the ECCMID Final Programme and on the ESCMID website under Study Groups. During the meeting an Executive Committee (three members) will be elected and statutes will be established. We will publish the draft statutes and the proposed candidates for the first Executive Committee on the ESCMID website. Plans for future activities and funding of the news study group will also be discussed.

If you are active in clinical work, research or education in the field of infectious diseases in primary care, you are cordially invited to join this new study group and attend the inaugural meeting. For further information please contact the author.

Theo Verheij
T.J.M.Verheij@med.uu.nl
Dear Colleagues and Friends

It is a great pleasure to invite you to participate in the 15th ECCMID in Copenhagen April 2–5, 2005!

ECCMID is the major annual European Congress on Clinical Microbiology and Infectious Diseases in Europe. The yin-yang symbiosis of our two important specialities within modern medicine means that they will always co-operate, although at times compete in the best cultural and scientific traditions, for the benefit of patients the world over.

We are closely interconnected with the environment including animals, birds, fish, and plants and many of the new infectious diseases like SARS originate from animals which have long been domesticated. The programme of the 15th ECCMID will reflect this interconnection between human beings and microbes from the living and innate environment in addition to the major area of recent developments in well-established, emerging and re-emerging infectious diseases. The 15th ECCMID will also focus on the molecular biology revolution. This is causing major changes in our ability to perform rapid diagnostic tests on infectious diseases and in our ability to design exciting new antimicrobials and maybe also to combat the threat of antimicrobial resistance. The 15th ECCMID will be held in Copenhagen Congress Center which housed the EU summit when Denmark chaired the negotiations in December 2002 opening up EU membership in 2004 to many new European countries and thereby a new exciting era also for ECCMID.

On the cultural side Copenhagen is famous for the Tivoli garden, its castles, museums, churches, old city and waterfront. In addition, the impressive new Opera at the waterfront opposite the Royal castle will open in 2005 and welcome the participants of the 15th ECCMID as part of the social programme.

Our opening ceremony of the 15th ECCMID on April 2nd, 2005 takes place on the 200th birthday of Hans Christian Andersen. This is the great author of many world famous fairy tales including “The Little Mermaid” which is the symbol of Copenhagen. We sincerely hope that many of the scientific contributions to the 15th ECCMID will be longstanding evergreens like the fairy tales of Hans Christian Andersen!

Welcome to Copenhagen!

Prof. Niels Hoiby
President 15th ECCMID

www.escmid.org/eccmid2005

Visit the 15th ECCMID website featuring:
• Continuously updated scientific programme
• Online abstract submission (deadline: November 18, 2004)
• Online registration as well as hotel & tours reservation
• Possibility to compose your personal congress programme
• Details regarding the industrial exhibition
• Information on the congress venue and the city of Copenhagen

For further information please contact:

Administrative Secretariat
15th ECCMID 2005
c/o AKM Congress Service
P.O. Box
CH-4005 Basel
Switzerland
Phone +41 61 686 77 11
Fax +41 61 686 77 88
E-mail info@akm.ch
The 14th ECCMID 2004 Prague

The Opinion of the Attendees

The 14th ECCMID 2004 in Prague had the highest attendance ever, with over 5'500 participants. An opinion poll was organised through the internet soon after the meeting: approximately 2500 delegates were asked by email to fill in a short online questionnaire about the Congress. We received 649 replies.

On the positive side, the many compliments on the high scientific level, variety of subjects, interactive sessions, pre-congress workshops, poster walks, perfect organisation and last but not least, European and friendly atmosphere were encouraging.

Among the criticisms and suggestions, people mentioned that some fields such as virology, paediatric infectious diseases or basic sciences were not adequately covered. There was a clear wish for more new research data or for talks on ground-breaking developments in the field of infection.

Some respondents found that the meeting was too dominated by the industry.

The scientific programme succeeded in meeting expectations of getting the latest scientific information / results in the field

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<tr>
<td>Yes</td>
<td>61 %</td>
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<td>No</td>
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<td>Partially</td>
<td>35 %</td>
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Regarding this criticism we would like to emphasise the goal of the Programme Committee to develop a programme as balanced as possible by accommodating the various interests for the benefit of all participants. At any given time the number of industry-sponsored symposia was at most four, parallel with at least 6 other sessions thus allowing ample choice for everyone. But we will also in future keep an eye on the educational character of industry-sponsored symposia.

Despite the generally acknowledged increase in poster quality some respondents still criticised the low grade of too many abstracts and suggested further increasing the rate of rejection. It should be realised that we have to find a compromise between optimal scientific quality and allowing scientists to attend ECCMID and share their data, in line with ESCMID’s educational mission.

Some participants complained about the new category of abstracts accepted for publication only. Among 2644 abstracts received, 1680 were accepted for presentation (oral and poster), an additional 490 for publication in the abstract book only and 474 were rejected. The decision was made for practical reasons as we received too many abstracts to be presented on the available poster premises. In addition, since many of the ‘excess’ abstracts still deserved some attention and most scientists needed some kind of acceptance of their work in order to get funding to attend ECCMID, we introduced this new category, which is common practice at other congresses. People were free to retract their abstract if they wished but very few took advantage of this opportunity.

Whether we will adhere to this policy in future or alternatively raise the rejection rate remains to be decided.

We will do our best to further improve the ECCMIDs taking into consideration your comments and suggestions, and hope very much to see you in Copenhagen at the 15th ECCMID, 1–4 April 2005.

Peter Schoch
ESCMID Managing Director

Patrick Francioli
ECCMID Programme Director

Table 1

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The first Table shows the distribution of the various specialties. As expected, ¾ of the respondents were either Clinical Microbiologists or Infectious Diseases specialists or both. These figures are in agreement with the demographic figures gathered from registration forms at earlier ECCMIDs.

Table 2

Table 2 shows the overall satisfaction rate. Even though almost ¾ of the participants appear to have been fully satisfied in getting the latest scientific information in the field, there is nevertheless room for improvement of the scientific programme, since approximately ⅓ declared that they were only partially satisfied.

According to the figures shown in Table 3, the balance between basic science and practical aspects was thought to be adequate by most respondents.

At the end of the questionnaire, there were open questions for positive or negative comments as well as suggestions for future ECCMIDs. We wish to acknowledge the commitment of the respondents, since a total of 989 remarks was received.

Table 3

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Course Report

Delegates Hail ESCMID / SHEA Meeting Success

This year’s ESCMID/SHEA Training Course in Hospital Epidemiology took place from 17–20 October 2004 at Hotel Schloss Rheinach near the well-known German university town of Freiburg. Possibly motivated by both the beautiful countryside on the foothills of the Black Forest, and, of course, the high reputation of ESCMID/SHEA Training Courses, more than 100 people from over 20 countries worldwide registered for the 4-day event; this was the highest recorded attendance ever.

The Course was chaired by Markus Dettenkofer, Assistant Director of the Institute of Environmental Medicine and Hospital Epidemiology, University Hospital Freiburg, which hosted this year’s meeting. Markus Dettenkofer and Franz Daschner, head of the Institute of Environmental Medicine and Hospital Epidemiology, welcomed all the guests warmly on behalf of ESCMID and SHEA. In numerous lectures, held by leading specialists of international reputation during the following four days, participants were given the opportunity to learn all about the basics, as well as the “secrets”, of hospital epidemiology. To satisfy different requirements, and allow participants to attend a course tailored to their existing knowledge, both basic and advanced modules were again offered, and ESCMID-sponsored scholarships were again awarded to participants with limited resources.

On day one of the basic module, Andreas Voss outlined the history of hospital epidemiology and defined the role of the hospital epidemiologist. On days one and two, Marjolein Kluytmans gave three well-structured lectures on the background of epidemiology. Other highlights of the first day included: a talk by Loreen Herwaldt on the surveillance of nosocomial infections, a presentation on prevention of nosocomial pneumonia by Andreas Voss, the role of molecular typing in infection control by Marc Struelens, control of nosocomial diarrhea by Andreas Widmer and a talk by Petra Gastmeier about the surveillance of nosocomial infections at a national level, which also raised the question as to whether international surveillance is possible.

In summary, this was an excellent course and can be highly recommended for all those who are interested in hospital epidemiology. Next year’s gathering is scheduled to take place in Burgundy, France. The venue will in all probability be the picturesque town of Beaune.

Hotel Schloss Rheinach was an ideal setting for this event and provided a campus-like atmosphere. It offered opportunities to get to know colleagues from all over the world and to discuss infection control issues. The excellent catering also contributed to the well-being of the participants.

On the evening of day three, staff and students met at the Historisches Kaufhaus, the City of Freiburg’s historic Guildhall, for an outstanding buffet dinner. Since ecology is one of the main foci of the hosting Institute for Environmental Medicine and Hospital Epidemiology, Franz Daschner had organised a dinner composed entirely of organic food and wine. After the dinner volunteers from the Netherlands, Norway, Slovenia, Turkey, Poland, Spain and Germany gave presentations on the organisation of infection control in their respective countries. It was interesting to note that while countries in Western Europe predominantly face problems with MRSA and VRE, in Eastern Europe, it is the gram-negatives that often are the most problematic microorganisms.

In summary, this was an excellent course and can be highly recommended for all those who are interested in hospital epidemiology. Next year’s gathering is scheduled to take place in Burgundy, France. The venue will in all probability be the picturesque town of Beaune.

Andreas Dorfmüller, MD
Institute of Environmental Medicine and Hospital Epidemiology, University Hospital Freiburg
The 6th International Meeting on Microbial Epidemiological Markers (IMMEM) was held in Les Diablerets, Switzerland from 27–30 August 2003. This beautiful village in the Swiss Alps welcomed 300 participants from 45 different countries.

The meeting serves as an interactive forum in microbial typing and its various applications in diagnostics, food microbiology, human and veterinary epidemiology, and basic research. It is the only international meeting entirely focused on epidemiological markers and has been regularly organised every 3 to 4 years since 1986.

IMMEM6 was organised by the ESCMID Study Group on Epidemiological Markers (ESGEM) under the auspices of ESCMID, the Federation of the European Microbiology Societies (FEMS), and, for the first time, of the American Society for Microbiology (ASM).

The meeting was opened by a lecture from Prof. Werner Arber, Nobel Prize winner in 1978 for the discovery of restriction enzymes. The sessions were devoted to different subjects, from genomics to the molecular epidemiology of antibiotic-resistant pathogens, including foodborne diseases, zoonoses, nosocomial infections, computerised typing databases, and many others. Active participation from attendees was possible during the workshops on the four most-used typing methods: PFGE, AFLP, PCR-related typing methods, and MLST.

Over 220 original contributions were received, 21 of which were selected for the oral sessions. The others were presented during the poster sessions. The prize for the best abstract, granted by Essex, was awarded to Prof. Jérôme Etienne from Lyon, France, for his work on the intercontinental emergence of community-acquired MRSA carrying the Panton-Valentine leukocidin (PVL) genes. The closing lecture was given by Prof. Sic Andersen on the usefulness of bioinformatics for epidemiological typing. This was the occasion to turn our eyes toward the future.

The magnificent surroundings were very much appreciated by the participants, particularly on the occasion at the Congress dinner which was held on the top of a mountain reached by cable car. The friendly atmosphere allowed for many informal encounters to discuss problems and ideas of mutual interest.

The evaluation of the meeting by the participants revealed that the majority was very satisfied with the meeting. This is a great encouragement for the organisers of IMMEM7, which will be held on 11–14 May 2005 in Victoria, Canada.

For the organising committee
Dominique Blanc and
Patrick Francoli
The 29th ESCMID Postgraduate Education Course, Treatment of ICU Infections, was held on 8–9 October 2004 in Sochi, Russia. For the second time this activity was conducted in Russia within the framework of the Memorandum of Collaboration signed by ESCMID and the Russian Academy of Medical Sciences (RAMS). The course was jointly organised by the ESGARS Study Group and the Interregional Association of Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC) in cooperation with the Institute of Antimicrobial Chemotherapy (IAC) of the Smolensk State Medical Academy.

Overall, 52 participants from various regions of Russia, Latvia, Turkey and the Ukraine, attended the course. Most of them were infectious diseases specialists, clinical microbiologists, ICU specialists, anesthesiologists or clinical pharmacologists.

The course was co-chaired by Prof. Leonid Stratchounski, the President of IACMAC and by Dr. Giuseppe Cornaglia, ESCMID Secretary General who emphasised the importance of collaboration between ESCMID and scientific societies in Eastern Europe.

Lectures were devoted to epidemiology, resistance, diagnosis, proper specimen management of pathogens and antimicrobial treatment of ICU infections. The first day of the course focused on the problems of resistant species: ESBL in Enterobacteriaceae, multiresistant P. aeruginosa and gram-positive bacteria, challenges of immunocompromised hosts in ICU, and several others.

During the second day speakers discussed antibiotic policy in the ICU, choice of antibiotic treatment of sepsis and nosocomial and ventilator-associated pneumonia, de-escalation therapy in peritonitis, and management options for catheter-related infections. Problems in treating invasive fungal infections in the ICU were also covered on this second day. Each lecture was followed by an active discussion.

The lectures were delivered by Giuseppe Cornaglia (Verona, Italy), Andrei Dekhnich (Smolensk, Russia), Mikhail Edelstein (Smolensk, Russia), Nikolay Klimko (Saint Petersburg, Russia), Roman Kozlov (Smolensk, Russia), Philippe Montravers (Bondy, France), Arne Rodloff (Leipzig, Germany), Ethan Rubinstein (Winnipeg, Canada), and Leonid Stratchounski (Smolensk, Russia).

Interesting discussions took place during the case presentation session. Participants and lecturers examined several cases of nosocomial ventilator-associated pneumonia that occurred within a 3-week period in an ICU for trauma patients.

The course was very positively evaluated by all participants and was considered a useful educational opportunity in their professional careers as well as important avenue to expand collaboration between scientists from different parts of Europe.

Dmitry Galkin, MD
General Secretary, IACMAC
Smolensk, Russia
My name is Maksim Mily. I am a clinical pharmacologist at the City Emergency Hospital in Vitebsk, the capital of one of the administrative regions in Belarus. In 2003, the ESCMID Study Group on Antimicrobial Policies (ESGAP) awarded me an International Exchange Grant. I took advantage of this grant during July and August 2004 when I spent six weeks at the Danish National Center for Antimicrobials and Infection Control at the Statens Serum Institut, Copenhagen, Denmark, under the supervision of Dr. Dominique L. Monnet, as well as two weeks of research training for one of my projects at the Department of Medical Microbiology & Infectious Diseases at the Erasmus University Medical Center, Rotterdam, the Netherlands, under the supervision of Dr. Inge C. Gyssens.

A first project Evaluation of trends of antibiotic consumption at Vitebsk City Emergency Hospital provided a quantitative assessment of the utilisation of antimicrobials for systemic use at this typical Belarussian general hospital during the past three years. With 91.2 DDD per 100 bed-days in 2003, Vitebsk City Emergency Hospital can be considered as having a high antibiotic consumption compared with European hospitals that participated in the ARPAC project (preliminary data reported at 14th ECCMID in Prague). The most-used classes were penicillins with extended spectrum (35.2 DDD per 100 bed-days, 39% of total) and aminoglycosides (18.0 DDD per 100 bed-days, 20% of total). Antibiotic consumption was unusually high in surgical departments (general surgery: from 101.1 to 120.2 DDD per 100 bed-days, urology: 170.4 DDD per 100 bed-days), which suggests poor antibiotic prophylaxis practices, most probably unnecessarily prolonged prophylaxis or possibly an excess of infections due to absence of peri-operative prophylaxis. These data will be used to define priorities for future interventions in surgical departments.

The second project Assessment of appropriateness of antibiotic prescribing at Vitebsk City Emergency Hospital was an epidemiological and economic evaluation of antibiotic prescribing for pneumonia. Data indicated that actual practices deviated widely from internationally-accepted clinical guidelines for empiric therapy of community-acquired pneumonia. Inappropriate antimicrobial therapy was quite common. The type of antibiotic prescribed was strongly influenced by patient age, multi-comorbidities and the prescriber, showing a strong need for standardisation of patient care. Antibiotics given orally accounted for only 4.7% of total volume in DDDs. This indicates that large sums of money could be saved by the implementa- tion of a switch-to-oral therapy programme. These results, together with those of a planned microbiological study on antimicrobial resistance in microorganisms responsible for community-acquired pneumonia, will be helpful for the development of local guidelines for empiric therapy of pneumonia. Additionally, I learned about current practices for monitoring antibiotic use and the methodology for auditing antibiotic prescriptions at the Erasmus Medical Center, which will be useful for performing audits and developing an electronic system for monitoring prescriptions at Vitebsk City Emergency Hospital.

Besides these projects, I had the opportunity to upgrade my knowledge in clinical microbiology and to follow everyday routine at the Clinical Microbiology Laboratory at H:S Hvidovre Hospital, Copenhagen, Denmark, thanks to Dr. Henrik Westh. I also learned a lot on practical aspects of the national antibiotic utilisation and resistance surveillance projects in the two visited countries: DANMAP in Denmark and NETHMAP by the Dutch Working Party on Antibiotic Policy (SWAB) in the Netherlands.

This training was very valuable, both for finalising my two research projects and for developing solutions to problems in Belarus where, in the absence of well-structured surveillance-system results, exhaustive and reliable data on antibiotic consumption and on antibiotic resistance among clinically important pathogens are not yet available.

I want to express my deep gratitude to ESGAP for having given me this educational opportunity and thank all persons who helped me during my stay in Denmark and the Netherlands.

Maksim Mily, MD, MPH
Vitebsk, Belarus
ESCMID 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 first combined FEMS/ESCMID fellow is Vladimir Gorbunov from Minsk, Republic of Belarus.

Research Interests

Vladimir Gorbunov’s research interests are antibiotic resistance of bacteria, nosocomial infections and antimicrobial chemotherapy. His current research project focuses on epidemiological monitoring of nosocomial infections examining the properties and circulation of vancomycin intermediate-sensitive *Staphylococcus aureus* (VISA), methicillin-resistant *Staphylococcus aureus* (MRSA), enterobacteria and *Pseudomonas*.

1st Training Course in Multilocus Variable Number Tandem Repeat-Genotyping of *Mycobacterium tuberculosis*

31st ESCMID Postgraduate Education Course
Lille, France, 23 – 28 May 2005

Tuberculosis is the leading cause of death in adults due to a single infectious agent, killing about 3 million people every year. In several regions of the world, there is an alarming rising incidence, linked to the increasing impact of HIV epidemics, deficiencies of current TB control programmes, and emergence of multi-drug resistance. The worldwide development of transport and migration contributes to globalise those threats. In this context powerful approaches in the epidemiological tuberculosis surveillance are needed, which provide quantitative bases to assess or define new control strategies. To achieve this goal, effective methods for accurate identification and monitoring of large numbers of *M. tuberculosis* strains are required. The course will include the theoretical and practical teaching of a novel and highly efficient technology for *M. tuberculosis* multilocus genotyping, analogous to human genotyping techniques, placed into a larger perspective of the use of molecular markers for epidemiological control.

We invite scientists, engineers, technicians, medical doctors, and clinicians who want to expand their knowledge on the state-of-the-art technology and advanced methods of molecular genotyping to participate in this course.

For further information please contact: Marie-José Truong, Phone +33 3 20 43 86 72, Email marie-jose.truong@pasteur-lille.fr or consult the website at www.escmid.org, Courses & Workshops

Corrigenda

Epidemiology Typing Workshop, 25–30 April 2004, Warsaw

In ESCMID News 2-2004 the author of the Report on the Epidemiology Typing Workshop on page 33 was erroneously given as Alex van Belkum. The author of this report was Marek Gniadkowski. As a postscript to this successful course in Warsaw, which may be repeated in the near future, see the corresponding picture with faculty and attendees.
ESCMID Scholarships 2004

The individuals listed below were awarded an ESCMID attendance grant in 2004 for one of the following events:

14th ECCMID 2004 Prague (travel grants and/or free registration)

Andreeva, Irina ................................................. Smolensk, Russia
Araujo, Ricardo ............................................... Porto, Portugal
Awad Al Chikh Hassan, Sawsan Manchester, United Kingdom
Babic, Tatjana ................................. Nis, Serbia and Montenegro
Balda, Joan Miquel ................................................... Boston, USA
Belecheri, Maria .................................................. Athens, Greece
Beren, Ondrej ....................................................... Albany, USA
Bliek, Nicole ............................................................ London, United Kingdom
Blanco, Silvia ......................................................... Badalona, Spain
Brisse, Sylvain ......................................................... Paris, France
Cabrera Ortega, Roberto ........................................... Barcelona, Spain
Camino Ridondo, Nuria .............................................. Madrid, Spain
Cassone, Marco ....................................................... Siena, Italy
Castanheira, Mariana .......................... Bristol, United Kingdom
Cernat, Ramona .................................................. Bucharest, Romania
Corless, Caroline Elizabeth Manchester, United Kingdom
Dobay, Orsolya ......................................................... Edinburgh, United Kingdom
Dominguez, Jose ...................................................... Badalona, Spain
Dragovic, Gordana ................................................. Belgrade, Serbia and Montenegro
Duerink, Daphne Ofira ............................................. Leiden, the Netherlands
Durnová, Eva ......................................................... Ostrava, Czech Republic
Dworniczak, Szymon ............................................. Zabrze, Poland
Ebert, Sandra .................................................. Göttingen, Germany
Edelstein, Inna ....................................................... Smolensk, Russia
Edvinsson, Benjamin ....................................... Stockholm, Sweden
Eisenblätter, Martin ................................................. Berlin, Germany
Ekimov, Alexey ....................................................... Smolensk, Russia
Enne, Verne I. ..................................................... Bristol, United Kingdom
Fitzpatrick, Fidelma .............................................. Dublin, Ireland
Gabunia, Pati ....................................................... Tbilisi, Georgia
Gambotti, Laetitia ................................................. Lyon, France
Garcia Castillo, Maria .............................................. Madrid, Spain
Gattringer, Rainer ................................................. Vienna, Austria
Giske, Christian G. .............................................. Stockholm, Sweden
Gould, Virginia C. .............................................. Bristol, United Kingdom
Grape, Malin .................................................. Stockholm, Sweden
Grygorczuk, Sambor ........................................... Bialystok, Poland
Guinea, Jesús ...................................................... Madrid, Spain
Houhendi, Linda ................................................... Marseille, France
Jover, Francisco .................................................... Alicante, Spain
Jursa, Joanna .................................................. Šczecin, Poland
Kalinina, Olga ....................................................... St. Petersburg, Russia
Kaliiterna, Vanja .................................................. Split, Croatia
Karahan, Ceren ................................................... Ankara, Turkey
Khalaf, Noha ...................................................... Cairo, Egypt
Knobloch, Johannes Karl-Mark .......................... Hamburg, Germany
Kolve, Hedwig .................................................... Münster, Germany
Korona, Izabela ...................................................... Lublin, Poland
Kozh, Iryna ....................................................... Kharkov, Ukraine
Korzh, Oleksiy ....................................................... Kharkov, Ukraine
Kostin, Vladislav A. ............................................. Smolensk, Russia
Kredics, László .................................................... Szeged, Hungary
Krynudshkin, Dmitry ............................................ Moscow, Russia
Lamagni, Theresa ................................................. London, United Kingdom
Libisch, Balázs ....................................................... Budapest, Hungary
Machado, Elisabete .............................................. Porto, Portugal
Markovska, Rumyana ......................................... Sofia, Bulgaria
Marodi, Csaba L. .................................................. Budapest, Hungary
Martella, Vito ..................................................... Bari, Italy
Mediannikov, Oleg .............................................. Moscow, Russian Federation
Meli, Damian N. ..................................................... Bern, Switzerland
Mendes, Rodrigo Elisandro ..................................... Bristol, United Kingdom
Mily, Maksim ....................................................... Umea, Sweden
Mitsura, Viktor ................................................... Gomel, Republic of Belarus
Molvia, Alexandru .............................................. Kishinev, Republic of Moldova
Novais, Carla ...................................................... Porto, Portugal
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Okazaki, Aki ....................................................... Bristol, United Kingdom
Palagin, Ivan ....................................................... Smolensk, Russia
Papp, Tamas ....................................................... Szeged, Hungary
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Terek, Gülfem ....................................................... Izmir, Turkey
Thapar, Mita M. .................................................. Stockholm, Sweden
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Vitorino, Liliana .................................................. Lisboa, Portugal
Voeykova, Anna V. .............................................. St. Petersburg, Russia
Vorobieva, Ekaterina ............................................. St. Petersburg, Russia
Zarnayova-Skopkova, Martina ................................ Bratislava, Slovak Republic
Zinkernagel, Annelies ........................................... Zurich, Switzerland
Postgraduate Education Courses and ESCMID School of Clinical Microbiology & Infectious Diseases and other Conferences co-organised by ESCMID

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Alderson, Shannon ............................................. Albuquerque, USA
Aurbach, Ute ........................................................ Koln, Germany
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Bagrade, Linda ..................................................... Riga, Latvia
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Ni, Oksana ............................................................ Krasnodar, Russia
Nowak, Pawel ..................................................... Krakow, Poland
Olczak, Anna ........................................................ Warsaw, Poland
Palagin, Ivan ........................................................ Smolensk, Russia
Parathon, Harry .................................................... Surabaya, Indonesia
Pawinska, Alicja ................................................... Warsaw, Poland
Petrov, Mihail ........................................................ Sofia, Bulgaria
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Pimkin, Maxim ..................................................... Smolensk, Russia
Prelipecean, Sandra Mihaela ................................ Iassy, Romania
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Rodriguez Villalobos, Hector ................................ Brussels, Belgium
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Sener, Aydogan ..................................................... Izmir, Turkey
Sharma, Rashmi ................................................... Glasgow, United Kingdom
Sibanc, Branko ..................................................... Celje, Slovenia
Sosa, Anibal ........................................................ Boston, USA
Talap, Daniela ....................................................... Bucharest, Romania
Terhes, Gabriella ................................................... Szeged, Hungary
Tomic, Viktorija ..................................................... Gornik, Slovenia
Tormakangas, Liisa ............................................... Oulu, Finland
Virgailis, Marius .................................................... Kaisiadorys, Lithuania
Wiener-Waor, Yonit ............................................... Jerusalem, Israel
Woodford, Eleanor ............................................... Portsmouth, United Kingdom
Zemkova, Marcela ............................................... Hradec Kralove, Czech Republic
Zemlickova, Helena ............................................... Prague, Czech Republic

Clinical Challenges in Diagnosis and Management of Atypical Pneumonia

32nd ESCMID Postgraduate Education Course
Riga, Latvia, 20 – 21 June 2005

The focus of this course is on respiratory tract infections caused by “atypical” bacteria.

For further information please contact:
Dr. Arta Balade, Phone +371 946 08 66,
Email a.balade@stradini.lv or consult the internet at
www.escmid.org, Courses & Workshops.
The International Committee of the Red Cross (ICRC) has a mandate to promote and strengthen international humanitarian law in order to prevent human suffering. In September 2002 it launched a public appeal on Biotechnology, Weapons & Humanity prompted by these concerns. The appeal is intended to promote awareness of the risks, rules and responsibilities associated with the potential for hostile misuse of the life sciences.

Since the launch of the ICRC appeal, the Red Cross and Red Crescent Movement have undertaken work with others in the life sciences to promote the concept of a “web of prevention” against poisoning and deliberate spreading of disease.

The web of prevention entails 3 types of action from individual actors in the life sciences:
1. to acknowledge that minimising the risks from hostile use of advances related to the life sciences is of concern to them and part of their responsibility;
2. to identify and implement the necessary actions within their own sphere of influence that will contribute to risk reduction and that will complement action being taken in other spheres; and
3. to ensure that their actions are well known and will complement the actions of others.

The ICRC has set up a website (www.scienceforhumanity.org) where you can learn more about the aims of the Biotechnology, Weapons & Humanity appeal, and international legal rules on this subject.

The ESCMID Executive supports this appeal and calls on ESCMID members to fulfil their ethical and legal responsibilities by taking measures at the individual and institutional level to prevent the hostile misuse of the life sciences in general and microbiology in particular.

ESCMID Executive Committee

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**4th ESCMID School of Clinical Microbiology and Infectious Diseases**

_Szeged, Hungary, 25 June – 2 July 2005_

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

Organised by the ESCMID Education Committee under the auspices of the University of Szeged
The Place of Microbiological Reagents in the Palette of In Vitro Diagnostics in Europe

In a recent report of the European Diagnostic Manufacturers Association (EDMA) European marketing statistics data were published for 2003. The aim was to better understand the current trends in the in vitro diagnostics (IVD) industry. The figures show that there was an average growth of 5.6% for 2003 (Table 1), which is less than that observed in 2002 (6%). The IVD market increased significantly in most European countries, with the lowest growth rates in Switzerland (1.5%) and Germany (1.7%; Table 1). These two countries are the only ones in Europe to spend more than 10% of their Gross Domestic Product (GDP) on health care. A likely explanation of the low growth rate in these countries is a largely saturated market, a high level of health care services provided and the political efforts to curb health expenditure. In contrast, in the UK, where health care expenditure is low (only 7.6% of the GDP), the growth rate is high: 8.9%. The growth rate is even higher in some central and eastern European countries (Poland >10% and Romania >20%), partly because of inflation and probably also due to the fact that efforts are made to expand health care.

The total IVD market (considering 14 European countries) in 2003 was estimated to be EUR 7633 million (Table 2). The total reagent market for these countries was EUR 6491 million. Of this, only 22% (EUR 1399 million) related to reagents used in microbiology and infectious serology. In most countries, independent of whether they are resource-poor or resource-rich, the reagents used for microbiology (culture) diagnoses account for about 6–7% of all the IVD reagents, and about 15% are spent for the serology of infectious diseases. It is interesting to note that the growth of the infectious serology market (5.3%) is mainly due to the growth of the subcategory of nucleic acid-based reagents (18.9%). The reagents for microbiological cultures increased by a modest 2.1% (Table 2).

It is important to note that IVD expenditure generally represents less than 1% of the total health care expenditure in Europe. Increased laboratory testing in general, and especially in clinical microbiology, does not significantly contribute to increasing health care costs, as the major expenses in health care, also in laboratories, are personnel costs. In vitro diagnosis for infectious and other diseases involves a considerable degree of automation. Valuable data can be obtained at low cost by this means which may help the clinician select appropriate medication, prevent the development of antibiotic resistance, and help avoid the spread of infections in the community and in the hospital.

**Elisabeth Nagy**
ESCMID Professional Affairs Officer,
Clinical Microbiology

Source: European Diagnostic Manufacturers Association, European IVD Market Estimates 2003

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**Table 1**

<table>
<thead>
<tr>
<th></th>
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</tr>
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<tbody>
<tr>
<td>Europe</td>
<td>7366</td>
<td>5.6</td>
</tr>
<tr>
<td>Germany</td>
<td>1755</td>
<td>1.7</td>
</tr>
<tr>
<td>Italy</td>
<td>1366</td>
<td>5.0</td>
</tr>
<tr>
<td>France</td>
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<td>7.5</td>
</tr>
<tr>
<td>Spain</td>
<td>745</td>
<td>7.0</td>
</tr>
<tr>
<td>UK</td>
<td>515</td>
<td>8.9</td>
</tr>
<tr>
<td>Switzerland</td>
<td>228</td>
<td>1.5</td>
</tr>
<tr>
<td>Belgium</td>
<td>243</td>
<td>8.4</td>
</tr>
<tr>
<td>Netherlands</td>
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<tr>
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<td>6.2</td>
</tr>
<tr>
<td>Finland</td>
<td>86</td>
<td>2.9</td>
</tr>
<tr>
<td>Romania</td>
<td>125</td>
<td>24.7</td>
</tr>
</tbody>
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**Table 2**

<table>
<thead>
<tr>
<th>Total IVD Market by Category in 2003</th>
<th>Total</th>
<th>Instruments</th>
<th>Reagents</th>
<th>Reagent Subcategory</th>
<th>Infectious Immunology Subcategory</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mio EUR</td>
<td></td>
<td></td>
<td>Microbiology (culture)</td>
<td>Infectious Immunology</td>
</tr>
<tr>
<td></td>
<td>7366</td>
<td>875</td>
<td>6491</td>
<td>425</td>
<td>974</td>
</tr>
<tr>
<td>Growth in % 2003/2002</td>
<td>5.6</td>
<td>6.0</td>
<td>5.6</td>
<td>2.1</td>
<td>5.3</td>
</tr>
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</table>
The 29-year-old Englishwoman’s neighbours, who lived in the Eppendorf district of Hamburg, did not know which way to turn and notified the on-call physician. Within a few days the much-liked young woman had become depressed, then very aggressive. She was obviously suffering from hallucinations. The on-call physician suspected an acute psychosis and admitted her to the psychiatric ward of the university hospital. Scars on the right arm and buttocks, which looked like healed dog bites, were noticed during the examination. Inquiries showed that the patient had been bitten by a dog three months ago in India. A post-exposure prophylaxis regimen had not been undertaken. This made the psychiatrists suspect rabies. Indeed two weeks after psychological symptoms had begun, rabies virus was isolated from the patient’s saliva.

A 49-year-old Californian went to the city hospital because of increasing pain and paresthesia in his right arm. An atypical nerve inflammation was diagnosed and the patient was dismissed. The next day he noticed that his hand continually cramped up and the right half of his face sweated profusely, while the left side of his body was completely normal. He went back to the emergency room twice, but was sent away each time, because no one could make rhyme or reason of the disease pattern. Only after the patient experienced dysphagia, excessive salivation and became highly agitated, did it dawn on the physicians, that this was possibly a case of rabies. The wife was questioned and reported that a bat had strayed into their house a few months ago. Her husband had caught it in his hands and taken it outside.

The two patients’ fates show how differently rabies first manifests itself and how difficult the clinical diagnosis is. For the patient this has fatal consequences. When the first symptoms of disease are seen (two weeks to twelve months after a bite), any therapy is too late.

A further characteristic of the rabies virus is its unbelievable adaptability. It can proliferate in different animals such as polar foxes, raccoons, cattle and rodents. Indeed there is practically no mammal species from mouse to elephant and from bat to skunk, which cannot contract rabies.

Depending upon geographical region and animal species, the RNA of lyssaviruses differ in certain, well-defined regions. The large number of rabies variants can be interpreted as an evolutionary adaptation of the pathogen to different animal species. After someone has died of rabies, the origin of the pathogen can accordingly be determined by molecular investigations. Hence a previously unknown chain of infection can be explained. In the spring 2003 in Virginia, USA, a young man died of fulminating meningoencephalitis, who had no medical history of contact with a rabid animal. However, isolated and sequenced virus RNA from the patient’s brain showed 100% homology with the virus variant circulating in the local raccoon population.

The underlying principle for the effective spread of the virus is its capacity to adapt. If the infected animal became rabid very quickly and died a few days later, the typically aggressive behaviour of snapping and biting would only be present for a couple of days and the chance of virus transmission to another animal through saliva would decrease. However, if the change of behaviour develops slowly, it is difficult for animals and humans to recognize it and thus increases the chance that the virus is spread by a bite through saliva.

Fig. 1: Rabies virus, purified from an infected cell culture. Negatively stained virions have a characteristic “bullet shape”. Micrograph from F.A. Murphy, School of Veterinary Medicine, University of California, Davis
exposure prophylaxis. Avoided by abatement measures and post-
30,000 to 70,000 cases of rabies worldwide. Annually there are an estimated 10,000 rabies deaths per year from dog bites. India alone reports about 22 persons died from rabies within a few weeks, after having been bitten by vampire bats. Such a cluster of cases of rabies in either Brazil or in another South American country was unprecedented. According to data from the Brazilian Ministry of Health, in the rural communities of Portal Velho and Viseu on the island of Marajó or near the border to the federal state of Maranhão, about one thousand persons were bitten by the flying vampires at night in the preceding 12 months. Only through mass vaccination were further deaths prevented. A similar epidemic was reported from the Baja Baujó district in the Colombian part of the Amazon lowlands and from adjacent areas in Venezuela.

Why the rather timid bats recently started to attack humans at night in places of Pará, 22 persons died from rabies within a few weeks, after having been bitten by vampire bats. Such a cluster of cases of rabies in either Brazil or in another South American country was unprecedented. According to data from the Brazilian Ministry of Health, in the rural communities of Portal Velho and Viseu on the island of Marajó or near the border to the federal state of Maranhão, about one thousand persons were bitten by the flying vampires at night in the preceding 12 months. Only through mass vaccination were further deaths prevented. A similar epidemic was reported from the Baja Baujó district in the Colombian part of the Amazon lowlands and from adjacent areas in Venezuela.

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Meanwhile, Australia, previously considered rabies-free, is no longer a white area but rather a red spot on the rabies map. Some years ago a 39-year-old woman from Queensland, who had cared for several bats unable to fly, died from rabies. And also Great Britain, despite sophisticated veterinary safety precautions at the borders bemoaned the first case of rabies. In 2002 an environmentalist, who had taken care of a sick bat infected with the lyssavirus, died in Lancashire. Another infected animal was caught in September 2004 in the vicinity of Heathrow Airport. In Eastern Europe rabies is also on the advance. The World Health Organization's...
most recent Rabies Bulletin for Europe refers to the alarming increase of rabies cases. Compared to the average for the last 10 years the number of rabid animals in 2003 increased by about: 100% in Romania, 180% in Russia, 310% in Lithuania, 330% in Latvia and as much as 510% in Estonia. These increases were similar for wild and domestic animals. In those five countries a total of 5847 animal rabies cases were reported. The reason for the dramatic rise is unclear.

As the understanding of the epidemiology of rabies in the last decade has expanded, so did knowledge of the illness pathophysiology. It is now clear that the motor end plate is the pathogen’s main entrance into the nervous system. The virus binds to the acetylcholine receptor and is moved retrogradely toward the central nervous system within the microtubules of an axon. This was proven by experiments with colchicine, a substance, which destroys microtubules and is an inhibitor of fast axonal transport. Transportation speed is 50–100mm per day.

Which receptors are responsible for fast retrograde transport within the microtubules has not been resolved. However, the glycoprotein of the pathogen is definitely important for binding to the acetylcholine receptor, transsynaptic propagation, and distribution of the virus along certain neuroanatomical pathways. During retrograde transport the virus is already being replicated.

Once having reached the central nervous system, the virus is disseminated along neural circuits. At the same time transport begins along efferent nerve fibres into the salivary glands. The neurological losses, at the beginning uncharacteristic with a broad range of neuropsychiatric symptoms, are due to neural dysfunction and not due to necrosis or apoptosis of neurons. Experiments by means of subtraction hybridisation show that after infection with rabies virus, 90% of all genes usually active in neurons become down-regulated by at least a factor of 4 while only 1.4% becomes up-regulated.

Two factors determine the incubation period, which is more variable than usual for viral infections. Virus inoculated into muscle remains there for different lengths of time before binding to the motor end plate and beginning fast axonal transport. Once having reached a neuron, transport along the microtubules takes place at a constant speed. Hence it follows that bites near the face and shoulders reach the central nervous system faster than if the virus was inoculated at the end of an extremity.

Since rabies virus is a “master of adaptation”, control measures must be tailored to the respective epidemiological situation in order to achieve success on a long-term basis. For health authorities it is the most difficult in places where stray dogs represent the main reservoir.

Three aspects are of crucial importance: the control measures must be carefully planned and be accepted and actively supported by the population. For example mass killings of feral dogs are completely unacceptable in Buddhist Thailand, in contrast to South America where this is no problem. In order to neutralise the virus, at least 70% of the dog population must be inoculated, no easy task, if dogs do not have owners and wildly roam the streets. And finally each rabies case must be documented and analysed, in order to be able to rapidly recognise the beginning of an epizootic.

With the help of such measures large South American cities have gotten rabies under control. As an example, within five years the number of rabies cases in dogs in São Paulo dropped from 1200 to zero. In Lima the number sank from 1000 and in Buenos Aires even from 5000 to zero.

Hermann Feldmeier

Box 2

**Rabies as a souvenir**

In summer 2004 two French retirees spent a few days in their camper at a campground in southern Morocco. One of the natives offered them a puppy, which they found so cute, that they decided to take it home. Seven weeks after returning from Morocco, the puppy became ill. It had no appetite and began to vomit. A day later the dog became aggressive and began to snap at everything in sight. However it took yet another week before a rabies diagnosis was ascertained.

With the French health authorities alarm bells went off, since it was unclear, with which humans and other animals the puppy had come into contact since crossing the Spanish border. Hundreds of persons along the two Frenchmen’s travel route were visited and numerous domestic animals were preventatively euthanized. The entire district, in which the two dog lovers resided, was placed under quarantine. Additionally they were fined due to illegal import of a health-endangering animal into the European Union and unsatisfactory support of the public authorities.

Box 3

**The twisted path of the rabies virus**

At the beginning of July 2004 four patients at the Baylor University Medical Centre in Houston, Texas developed signs of encephalitis almost simultaneously. They were increasingly confused, had cramps and fell into comas after a few days. Since the preceding liver transplantations were not without complications, the physicians first thought that the neurological symptoms could have something to do with the organ transplants. The situation only became clear after the autopsies. The pathologists discovered typical Negri bodies in brain sections, characteristic of cells infested with rabies virus.

All patients received a donated liver as well as a section of the femoral artery taken from one donor. This artery donor had been bitten in May by a bat, but had died in an accident before rabies broke out. The transplant centre physicians had removed the femoral artery, divided it into several pieces and then used the pieces in different liver transplants. Subsequent investigation of a piece of leftover artery showed the presence of rabies virus in the tissue.

This incident, which received substantial attention in the USA, is remarkable in that it revokes an old dogma. Up until then it was assumed that rabies virus can only reproduce in nerve tissue and is only transmitted through saliva. The observations from Houston show that the pathogen can probably spread through all autonomic nervous system’s efferent fibres into the body’s periphery.
News in Brief

Infectious Diseases and Outbreaks

**C. difficile** outbreak caused by new type of epidemic strain

Increased rates and severity of *C. difficile* disease were observed during the period from 2001 to 2004 in several US hospitals. Also in Canadian hospitals (Quebec) the infection rate increased 5 times in the year 2003 and the number of cases in some hospitals then almost doubled in the year 2004.

A previously uncommon type of *C. difficile* strain was shown to predominate in the geographically dispersed outbreaks in both countries. The new epidemic strain produces an additional toxin and has developed fluoroquinolone resistance, both features previously rare among human *C. difficile* isolates.

Maja Rupnik, ESGCD

**Virulence factor for Group A streptococci discovered**

Group A streptococci (GAS) can cause a rapidly lethal infection, necrotising fasciitis, and are often referred to “flesh eating” bacteria. It is not clear why some strains have this highly virulent potential, but recent work has shed some light on the pathogenic process. Clots are produced by the body as a defence mechanism to the infection and it has been shown that the bacteria can produce streptokinase, which activates plasminogen which destroys the clot. This study showed that mice plasminogen differs from human plasminogen and this imparts a relative resistance to GAS. By using genetically engineered mice with human plasminogen, the group showed that GAS was able to produce the expected systemic infection. These results indicate the possibility of producing inhibitors of streptokinase either as vaccines or as virulence modifying drugs.

Sun et al., Science 2004; 305: 1283

**Outbreak of Yersinia pseudotuberculosis in Finland**

An outbreak of gastroenteritis occurring in Finland was traced to carrots. The outbreak involved 125 people and had two peaks, one in April and a second in July. Investigations into cases in a school traced the source to carrots. A food processing plant and farms in the region were examined. Wild animals are often thought to be a source of the organism and studies are underway to test voles, shrews and mice on the farms.

*Eurosurveillance Weekly* 2004; 8: 41

**Outbreak of Salmonella Newport in the UK**

A marked increase in the number of *Salmonella enterica* serovar Newport has been identified in the UK during late August and September. The outbreak is widespread with cases being reported from Northern Ireland, the Isle of Man and several places in mainland England. A total of 368 infections have been confirmed and molecular typing of 122 of the isolates has shown that 109 are indistinguishable from each other and from 14 isolates from Scotland. Work is underway to find the source. A close association has been found with the consumption of lettuce although its origins are not yet clear.

*Eurosurveillance Weekly* 2004; 8: 41

**Resurgence of syphilis in homosexual men**

Infectious syphilis has been reported from a number of European cities more frequently in recent years in men who have sex with men. Cases have been identified recently in Barcelona (Spain) and in Gloucestershire (UK).

*Eurosurveillance Weekly* 2004; 8: 44.

CDR Weekly 2004; 14: 46

11 November 2004

**Outbreak of Giardiasis in Norway**

*Giardia lambia* has been identified as the cause of an outbreak of gastrointestinal infection in Bergen, Norway. Between September and early November, 365 cases have been identified. The outbreak is associated with the water supply which was found to contain cysts. The source of the contamination of the water treatment plant is under investigation.

*Eurosurveillance Weekly* 2004; 8: 46

**Link between adhesins for Helicobacter pylori and blood groups found**

An understanding of the mechanism of adhesion of *H. pylori* to the gastric mucosa is an essential part of the development of a vaccine to protect from the infection. The group has found that the *H. pylori* strains from Amerindians in that area have lost the ability to adapt and can only bind to blood group O. This has implications in the approach to controlling the adhesion.

Aspholm-Hurtig et al., Science 2004; 305: 519

**Highly virulent community-acquired Staphylococcus aureus strain found in Ireland**

Strains of *S. aureus* carrying the Panton-Valentine leukocidin (PVL) gene are highly virulent and can cause invasive disease, including rapidly progressive soft tissue infections, even in immunocompetent individuals. Three such strains were identified in young men in Galway, Ireland who acquired their infections in the community. The strains were susceptible to methicillin and therapy with flucloxacillin was successful.

*Eurosurveillance Weekly* 2004; 8: 44.

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**EXCERPTS**

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Resistances

Community-associated MRSA strains in neonatal ICU

Methicillin-resistant strains of Staphylococcus aureus (MRSA) are no longer restricted to the hospital environment as a paper published recently from Houston, Texas reveals. A survey of infants in an intensive care unit revealed that 47% of the S. aureus bacteraemic infections were MRSA. Genetic analysis of 6 of the 8 isolates showed that they carried genes characteristic of community-acquired MRSA.

Healy et al., CID 2004; 39: 1460

MRSA spread among college footballers

An outbreak of MRSA infections (cellulitis or skin abscesses) among college footballers in the US was investigated over a period of 2 months. Wound isolates were indistinguishable using PFGE and all carried the same Panton-Valentine leukocidin toxin gene. There was a close association between infection and abrasions from footballing. The proposal is that a green fluorescent dye be inserted into the variola genome in an attempt to speed up and automate drug screening. The proposal will be considered at the World Health Assembly in May 2005.

Wolgate, The Scientist Online update; 11 November 2004

Viral Infections

Haemagglutinin of the 1918 pandemic influenza virus shown to confer virulence

A paper published in Nature shows that the haemagglutinin from the “Spanish flu” pandemic influenza A virus has the ability to confer a marked increase in virulence. Reverse genetics was used to reconstruct the genes of the original viral strain to produce the two virulence factors of influenza, haemagglutinin and neuraminidase. These genes were inserted into a modern influenza virus and mice were infected with the resultant strains. The neuraminidase had little effect on virulence but the haemagglutinin did, producing severe haemorrhaging in the lungs of infected mice.

Kobasa et al., Nature 2004; 43: 703

WHO asked to approve genetic manipulation of smallpox virus

An Advisory Committee on Variola has recommended to WHO that limited genetic manipulation of variola virus (the causative agent of smallpox) be allowed by two approved laboratories, one in the US (CDC) and the other in Russia (Novosibirsk). The proposal is that a green fluorescent dye be inserted into the variola genome in an attempt to speed up and automate drug screening. The proposal will be considered at the World Health Assembly in May 2005.

Wolgate, The Scientist Online update; 11 November 2004

Rabies imported into Germany

A man who had travelled to India died in Germany in late May of what was subsequently identified as rabies. He had been to India recently and had been in contact with wild dogs but was not aware of ever having been bitten by them. He did report a bite from a monkey on a previous visit (2001). It is known that there can be a very long incubation time for the development of the disease following a monkey bite. This case emphasises the importance of being immunised against rabies when travelling to the Indian subcontinent or other areas with a high incidence of rabies.

Eurosurveillance Weekly 2004; 8: 46

Hepatitis A outbreak in Germany linked to Egyptian hotel

22 cases of hepatitis A in German tourists returning home have been linked to a hotel near the Red Sea in Egypt. The Robert Koch Institute (RKI) issued a European Early Warning on August 24. By August 31 157 cases of hepatitis A had been reported in 39 countries. RKI has requested IgM positive serum samples and/or stool samples from infected people to aid in the detection and sequencing of the virus.

CDR Weekly 14: 36; 3 September 2004

West Nile Virus (WNV)

The numbers of confirmed cases of West Nile fever diseases in the US for 2004 had reached 2282 by early November. There were 77 deaths; 935 cases had classic fever and 809 had neuroinvasive disease. The majority of cases come from the western US with 737 (32%) from California, 381 (17%) from Arizona and 276 (12%) from Colorado. Nearly 7000 dead birds have been found carrying the virus, 5562 of which were corvids. Infected horses have been identified in 46 states and other animals found to be seropositive include dogs, squirrels and one bat. A total of 195 blood donors were found to have potential viraemia, 48 of whom subsequently developed West Nile fever and three neuroinvasive disease.

MMWR 2004; 53: 1050

An outbreak of WNV infections occurred in the Camargue region of southern France during August and September. The total number of suspected cases was 37, with four animals dying or having to be killed. Of the 18 horses tested, the virus was found in 14. This is the same area where an outbreak of WNV occurred previously in 2000. Since that outbreak, surveillance has included the use of sentinel birds and the examination of dead birds. No seroconversions occurred in the sentinel flocks during 2003 but in late July of 2004 the first seroconversion was detected, followed by another in August. By September, over half of the flock was positive for WNV antibodies. Increased surveillance has been instituted and blood donations from those living in or travelling to the region has been restricted.

Eurosurveillance Weekly 2004; 8: 41
Avian influenza

Avian influenza (Influenza A H5N1) has recently been found in various species other than chicken. On 25 August WHO confirmed the presence of the virus in pigs in China. It is not clear how widespread the occurrence of the virus is and WHO has encouraged further studies to assess the role of the pig.

CDR Weekly 14: 36; 3 September 2004

Cats were believed to be resistant to influenza but there were anecdotal reports that domestic cats had contracted avian influenza from eating infected poultry. To investigate the susceptibility of cats to avian flu, workers from Rotterdam infected three cats intratracheally with a human isolate of H5N1. All three animals developed respiratory symptoms and one died. Additional experiments confirmed that cats could contract the disease from eating infected poultry and that it could spread from cat to cat.

Kuiken et al., Science 2004; 306: 241

WHO reports that ducks may play a major role in the transmission of H5N1 to other poultry and to humans. Experiments have shown that the virus replicates in the respiratory and intestinal tracts resulting in shedding of virus. In the majority of infected ducks, no symptoms are evident and there are few deaths although most animals shed sufficient virus to infect chicken. There are indications that the current virus circulating is more stable than earlier versions. WHO has issued public health guidelines for countries affected, drawing attention to the possibility of seemingly healthy ducks being a mode of transmission of the virus.

WHO On line update; 1 November 2004
(www.who.int/csr).

A pair of mountain hawk eagles was imported illegally from Thailand via Vienna to Brussels, where they were noticed by customs officials. The birds were found to be carrying the H5N1 virus and were killed. All other birds in quarantine at the airport, including 200 parrots and 600 other birds that may have come in contact with the eagles were also destroyed. Other birds had already been shipped to Russia and to the Netherlands and attempts are being made to trace them. All contacts with the man transporting the eagles on both flights were traced and advised to get medical advice if they developed any flu-like symptoms. The hawk eagles were ordered by a falconer in Belgium and this raises the possibility that there may be many more birds already in the EU that have been imported illegally and may be carrying the virus.

Eurosurveillance Weekly 2004; 8: 44

On October 25 the Ministry of Public Health in Thailand confirmed that a 14-year-old girl had died of H5N1 influenza. The infection almost certainly was contracted from infected chicken in the household. The total number of confirmed cases in Thailand is 17, 12 of which have been fatal. Three fatal cases of avian influenza were confirmed and reported from Vietnam in August. These deaths follow more outbreaks of avian influenza in poultry, after a quiescent period of some months.

WHO On line update; 25 October 2004
(www.who.int/csr/don/)

Vaccines

Pandemic vaccine for avian influenza

WHO made a prototype seed strain of the virus of H5N1 avian influenza A available for vaccine manufacturers. Only two firms have taken on the work, Aventis Pasteur and Chiron, both funded by the US. WHO reports that small prototype batches of vaccine are available for use in clinical trials, which are not expected to start until the end of 2004. Aventis have been awarded a contract from the US to provide 2 million doses of the vaccine.

WHO On line update; 3 November 2004
(www.who.int/csr/don/)

Work on stable vaccines progresses

The UK company Cambridge Biostability have been awarded £950,000 from the UK government to progress their novel concept of treating the ingredients of a vaccine in a sugary coating to impart stability to extremes of heat. This would be a major asset in many parts of the world where refrigeration and storage of vaccines is a problem. The coating used consists of simple sugars and an amino acid and forms spheres of about 3 microns diameter. These are suspended in an inert anhydrous liquid and when injected the coating dissolves, releasing the active ingredients of the vaccine.

New Scientist on line; 19 October 2004

Compulsory anthrax vaccination for soldiers halted in US

Military personnel in the US sued the Pentagon for enforcing anthrax vaccination for the armed forces claiming that the vaccine should be regarded as an investigational drug, requiring informed consent. This was on the grounds that the approval process for the vaccine was not legal. A US federal judge has agreed with this and has also questioned the efficacy of the vaccine since it has only been shown to be effective against cutaneous anthrax. He has thus ordered the Department of Defense to cease compulsory vaccination.

Dyer, BMJ 2004; 329: 1062

Chiron’s influenza vaccine found to be faulty – US has major shortage of supply

In October the UK regulatory agency suspended the product licence of Chiron’s influenza vaccine, Fluvirin™ at their manufacturing plant in Liverpool because they had identified a risk of contamination to the vaccine. Initially Chiron claimed that the risk was confined to certain batches, but the FDA was not satisfied with this statement. Chiron announced that they are working closely with the UK and American regulatory authorities on a remediation plan for the production of the vaccine. In the meantime, this results in a major shortfall of vaccine supplies for the US since Chiron was expected to supply 48 million doses.

US to purchase extra flu vaccine supplies from Europe

Various states in the US have been negotiating with Aventis in France and GlaxoSmithKline in Germany to purchase extra supplies of flu vaccine to ease the shortage caused by the problems with Chiron. Both of these vaccines are licensed for use in Europe but until recently, not in the US. The Aventis Pasteur vaccine has recently been approved and it will be pro-
duced round the year at the Sanofi-Aventis vaccine unit in France. The agreement includes the stipulation that they will maintain flocks of chicken to produce the eggs continuously.

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**Changes to vaccine development called for**

The consequences of the problems with the Chiron influenza vaccine have been far reaching with suggestions in the US that changes are needed in the government’s approach to vaccine supplies. Vaccines are often unprofitable for drug companies as governments are usually not prepared to pay much for them. The US relies on only two manufacturers for the influenza vaccine, Chiron and Aventis, and the supply is thus highly vulnerable to problems such as the present one. The chair of the US National Vaccine Advisory Committee and the Director of CDC both highlighted the problems and said that long-term plans were needed to improve vaccine development.

*Singer, Nature Medicine 2004; 10: 1148*

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**Prions**

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**Another case of vCJD in France**

The French surveillance system set up to detect vCJD cases has detected a further case, the eighth such case in France since 1996. The patient has donated blood on several occasions over the past few years and the ten people who have received donations from this patient have been contacted.

*Eurosurveillance Weekly 2004; 8: 44*

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**Ireland’s first case of vCJD**

A young male patient in Ireland has been diagnosed with probable vCJD. As the patient has never received a blood transfusion and the case is not related to any operation, it is assumed that this was the first indigenous case in the country. The one previous case was in a patient who had lived in the UK in the 1980s and could therefore have been infected there. Ireland has the second highest rate of BSE in cattle in the world, so it is not surprising that a case has now been detected.

*Eurosurveillance Weekly 2004; 8: 46*

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**Synthetic prion induces encephalopathy in mice**

A group from the University of California has generated prion proteins from bacteria, folded them into amyloid fibrils and injected these into the brains of mice. Within one to two years the mice developed clinical symptoms similar to those seen in BSE-affected cattle. At autopsy their brains were found to have developed a spongiform encephalopathy and rogue prions could be detected. These prions, when transferred to other healthy mice were also able to produce the disease. This is clear evidence that the proteins alone are capable of transmitting the disease.

*Legname et al. Science 2004; 305: 673*

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**Industry and Drugs**

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**Roche gets approval to market Pegasys for Hepatitis C in Europe**

The EMEA has approved the use of pegylated alfa-2a interferon (Pegasys®) for the treatment of hepatitis C in patients with apparently normal liver function. This is a great advantage for Roche as these patients were previously not treated since it was thought that they only had a mild infection and treatment may even be harmful. Liver function is normally assessed by measuring the release of the enzyme alanine amino transferase (ALT) but it has now been shown that in many infected patients with levels of ALT regarded as normal, there was some liver damage.

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**Lilly to sell vancomycin to ViroPharma**

Eli Lilly is selling the rights to Vancomycin™ (vancomycin) in the US to the drug development firm ViroPharma. The patent to vancomycin in the US expired in 1988 but the natural product is so difficult to make that no generic firm has undertaken the task. The capsule form of vancomycin is used for the control of Clostridium difficile infections in hospitalised patients. Lilly will continue to make the product until 2006 when the contract firm will take over. This will be ViroPharma’s only marketed product and the profit is intended to fund their drug development programme.

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**Roche’s anti-influenza drug effective against avian influenza**

Roche’s drug, oseltamivir (Tamiflu®), which is a neuraminidase inhibitor used for the treatment of influenza, has recently been shown to have activity against the avian and human influenza virus, H5N1. The avian strain is the one circulating currently in the far east and although so far few humans have been infected, the fear is that the avian virus could infect animals or humans also carrying human strains, and reassortment could take place producing a highly virulent strain with the ability to pass from human to human. Roche has announced that they are stepping up production of oseltamivir and have had discussions with various governments to discuss their needs for stockpiles of the drug.

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**European Matters**

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**French biotechnology firms urge government to change approach**

The French government is drafting legislation for a major overhaul of the national science strategy. The biotechnology industry and the pharmaceutical industry have formed a group named Les Entreprises du Medicament and they have put forward a number of proposals to the government to consider. A major request is that 60% of the funds of the new National Research Agency should be allocated to life sciences and a second one is that the government should concentrate biotechnology clusters into two or three centres of excellence. In addition they urge the government to set up some large-scale joint French and European life science projects.

*Burgermeister, The Scientist on line; 10 November 2004*
UK to reform drug regulation – reminder to drug companies to publish clinical trials

A new commission to oversee the drug industry is being planned in the UK. The rules will be tightened, especially those regarding the publication of clinical trial results, an area where the industry has been criticised for dragging its heels.

*BBC News online; 10 November 2004*

EU preparations for pandemic flu inadequate

There are fears that if the avian influenza virus H5N1 co-infected animals or humans also carrying the human influenza strains there could be reassortment of genes resulting in a new highly transmissible and virulent influenza virus. Current vaccines would not protect from such a virus, which could cause the next pandemic. Dr Stöhr, the head of WHO’s global influenza programme has commented that he is concerned about the lack of effort within the EU to prepare a vaccine to protect against this eventuality. Although two vaccine manufacturers in Europe are working on an avian flu vaccine, this work is contracted to the US.

*Stafford, The Scientist online; 2 November 2004*

European Centre for Disease Prevention and Control

The new European Centre for Disease Prevention and Control (ECDC) was officially launched at the end of September, 2004 in Stockholm. An editorial from Dr Gourvras of the Public Health Directorate, EC, outlines the background to the stormy birth of this centre. The SARS emergency in 2003 gave much needed impetus to the setting up of the Centre and the author hopes that it will get the support it needs from the surveillance and control groups. The first meeting of the Centre’s management board was held during which Dr. Marc Sprengen, Director-General of the National Institute for Health and Environment (RIVM) in the Netherlands was elected as Chairman. The immediate main task of the Management Board is the nomination of a Director of the ECDC.

*Eurosurveillance Monthly 2004; 9: 10*

Pamela Hunter Medical Writer

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### Corrigenda

**EUCAST Report**

Due to a typesetting error in the EUCAST Report of ESCMID News 2-2004, page 26–27, some of the symbols were wrongly given in Table 1. We are reprinting the Table below with the correct symbols. We regret any inconvenience caused by these inaccuracies.

Table 1: EUCAST definitions of susceptibility categories and breakpoints

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**Clinical susceptibility categories and breakpoints**

- **Clinically susceptible (S)**
  - a micro-organism is defined as susceptible by a level of antimicrobial activity associated with a high likelihood of therapeutic success
  - a micro-organism is categorized as susceptible (S) by applying the appropriate breakpoint in a defined phenotypic test system

- **Clinically intermediate (I)**
  - a micro-organism is defined as intermediate by a level of antimicrobial activity associated with indeterminate therapeutic effect
  - a micro-organism is categorized as intermediate (I) by applying the appropriate breakpoints in a defined phenotypic test system

- **Clinically resistant (R)**
  - a micro-organism is defined as resistant by a level of antimicrobial activity associated with a high likelihood of therapeutic failure.
  - a micro-organism is categorized as resistant (R) by applying the appropriate breakpoint in a defined phenotypic test system

Clinical breakpoints may be altered with legitimate changes in circumstances.

Clinical breakpoints are presented as $S \leq x$ mg/L; $I > x \leq y$ mg/L; $R > y$ mg/L

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**Epidemiological susceptibility categories and cut-off values**

- **Wild type (WT)**
  - a micro-organism is defined as wild type (WT) for a species by the absence of acquired and mutational resistance mechanisms to the drug in question.
  - a micro-organism is categorized as wild type (WT) for a species by applying the appropriate cut-off value in a defined phenotypic test system.
  - wild type micro-organisms may or may not respond clinically to antimicrobial treatment.

- **Microbiological resistance – non-wild type (NWT)**
  - a micro-organism is defined as non-wild type (NWT) for a species by the presence of an acquired or mutational resistance mechanism to the drug in question.
  - a micro-organism is categorized as non-wild type (NWT) for a species by applying the appropriate cut-off value in a defined phenotypic test system.
  - non-wild type micro-organisms may or may not respond clinically to antimicrobial treatment.

Epidemiological cut off values will not be altered by changing circumstances. The wild type is presented as $WT \leq z$ mg/L and non-wild type as $NWT > z$ mg/L.
Forthcoming ESCMID Events

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

ESCMID events

2–5 April 2005
15th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID)
Place: Copenhagen, Denmark
Contact:
AKM Congress Service
Phone: +41 61 686 77 11
Email: info@akm.ch

23–28 May 2005
31st ESCMID Postgraduate Education Course: 1st Training Course in Multilocus Variable Number Tandem Repeat Genotyping of Mycobacterium tuberculosis
Place: Lille, France
Contact:
Institut Pasteur de Lille
Phone: +33 3 20 43 86 72
Email: marie-jose.truong@pasteur-lille.fr

20–21 June 2005
32nd ESCMID Postgraduate Education Course: Clinical Challenges in Diagnosis and Management of Atypical Pneumonia
Place: Riga, Latvia
Contact: Dr. Arta Balode
Phone: +371 946 08 66

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

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

Supported by ESCMID

28–29 January 2005
10th International Symposium on Infections in the Critically Ill Patient
Place: Porto, Portugal
Contact:
McCann Meetings
Phone: +34 93 206 46 46
Email: infections2004@mccann.es
Internet: www.infections-online.com

1–2 March 2005
1st European Consensus Conference on the Treatment of Chronic Hepatitis B and C in HIV Co-infected Patients
Place: Paris, France
Contact:
Wells Healthcare
Phone: +44 1 892 509521
Email: secretariat@coinfectionecc.org

18–21 June 2005
4th International Conference on Rickettsiae and Rickettsial Diseases
Place: Logroño (La Rioja), Spain
Contact:
Congressos e Incentivos Rioja
Phone: +34 941 202664
Email: cr@rickettsia.net
Internet: www.rickettsia.net

Imprint

ESCMID News: Newsletter of the European Society of Clinical Microbiology and Infectious Diseases

Editors and Editorial Office: Peter Schoch, Managing Director; Roger Finch, Chairman Publication Committee; Dianne White, Publication Assistant; Pamela A. Hunter, Medical Writer; Editorial Office: ESCMID Executive Office, PO Box 6, CH-4005 Basel, Switzerland. Email: info@escmid.org

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Number of Issues & Editorial Deadlines: ESCMID News appears three times per year in April, September and December. Manuscripts must arrive at the Editorial Office (preferably by email) by the 15th of the previous month if they are to be considered for publication in the next month's issue.

Distribution and Circulation Number: ESCMID News is personally distributed to all registered ESCMID members and spread at international conferences for promotion of ESCMID.

Change of Address: Notice of change of address should be sent to Ms B. Menzemer, ESCMID Secretariat, PO Box 1131, D-82018 Taufkirchen, Germany. Email: birgit.menzemer@escmid.org

Printed: ESCMID News is produced by Interrepro AG, Pumpwerkstrasse 11, CH-4142 Münchenstein, Switzerland.

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