

World Conference on Dosing of Antiinfectives: 'Dosing the Magic Bullets'

Celebrating the 150th Birthday of Paul Ehrlich, the 'Founder of Chemotherapy',
September 9–11, 2004, Nürnberg, Germany

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It has always been a privilege for this journal to keep the name *Chemotherapy* throughout the years. There are those who still consider 'chemotherapy' as one field and those who speak about 'antiinfectious chemotherapy' and those – due to specialization – who simply speak of 'chemotherapy' when they mean 'antineoplastic chemotherapy'. There is no doubt that the 'founder' or 'father' of chemotherapy and the inventor of this term, Paul Ehrlich, would have loved to have been successful in both areas. However, as we understand today, in his day it was even more difficult to find an antineoplastic chemotherapeutic agent than to find an antiinfective chemotherapeutic agent. Yet 'Ehrlich tumor ascites cells' are a memorable reminder of Ehrlich's successful work in the antineoplastic field. A full book of collected papers is a document of his work in that field [1].

The work of Paul Ehrlich in the infectious diseases field, however, led to the first antibiotic ever developed by systematic research, the antisyphilitic agent called Salvarsan (called '606' in laboratory jargon, since it was found among several hundred compounds; the INN name is arsphenamine). Salvarsan posed great challenges with respect to its appropriate dosing, challenges that Ehrlich met with brilliant published fundamental work that still applies today. Ehrlich used to call his agents 'magic bullets', and his whole life was spent in search of such a

'magic bullet', to which arsphenamine (Salvarsan) came close, at least for him and his times. He also introduced the concept of a 'therapia magna sterilisans' with earlier dyes like methylene blue, trypan red and 'his' Salvarsan (turned out to be yellow, but was not designed as a dye),



Fig. 1. Portrait of Paul Ehrlich (1854–1915). (Reprinted courtesy of the Paul-Ehrlich-Institut, Langen, Germany.)

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where he attempted to eradicate the pathogen with a single dose. This concept was forgotten and long considered obsolete, but has very recently been 'reinvented' [2]. To organize and publish a 'World Conference' is the least that the antiinfective community and this journal can do to honor Paul Ehrlich in the year of his 150th birthday (his birthday is on March 14th; interestingly, Emil von Behring, his friend at times and also an opponent, was born one day later, so it is his 150th birthday too), a man who can truly be called the founder of 'chemotherapy' and probably one of the most ingenious and visionary pharmacologists of the last century. The conference is going to focus on antiinfectives, but the time may be near when chemotherapy specialists in all fields of chemotherapy convene and understand that they are dealing with the same issues when it comes to dosing and that it may be time to learn from each other again.

Chemotherapy and Karger Publishers will be a sponsor of this conference and will in each of the next issues publish papers on areas of modern chemotherapeutic research and also about Ehrlich's role in preparing the ground for modern chemotherapy and also modern pharmacology, when one remembers the fact that Ehrlich and Langley [3], independently of each other, introduced the idea of a receptor that helps explain biological effects of foreign chemicals. Interestingly, Langley's 150th birthday was in 2002.

On behalf of my cochairman George L. Drusano, honorary treasurer Kurt G. Naber and Honorary Secretary Dieter Adam and myself, I invite you to come to Nürnberg to a great scientific conference and a most unusual conference of history and the arts in a pleasant atmosphere. Details available at the time of printing are shown below.

About the Conference

The Conference Logo

The three Ehrlich colors in the conference logo that you may see in color at www.ehrlich2004.org show the three major steps to Ehrlich's magic bullets: methylene blue to fight malaria in the year 1891, trypan red against trypanosomes (1904) and yellow, the color of 'compound 606' (Salvarsan), the first true antibiotic.

The Conference Topic: 'Dosing the Magic Bullets'

There is no doubt that dosing of antiinfectives is still a major issue in the use of these agents. Recently, investigation of the dosing aspect has very much been directed at optimization of antibiotic therapy and resistance issues

by applying the new pharmacokinetics/pharmacodynamics (PK/PD) principles. In previous decades, dosing issues and drug monitoring were more related to predicting adverse events. No conference yet has focused exclusively on dosing by applying the new PK/PD principles that have led to many new insights. This conference gathers the leaders in this field of PK/PD and clinical medicine to exchange views. The PK/PD group will review the concepts and the clinicians will show which principles have been acknowledged and introduced into antimicrobial therapy. Regulatory bodies have also been invited and have agreed to participate. Active participation of the attendees in this conference is assured by using modern technology, each participant having his/her own remote control and being able to express their opinion at their discretion by voting.

Pre-Conference Workshop

The new principles of PK/PD now offer fascinating opportunities to optimize antiinfective therapy. At the conference, participants have two consecutive options to study PK/PD and dosing issues. At the postgraduate workshop from Monday to Thursday, leading experts in PK/PD from the International Society of Antiinfective Pharmacology will lead teaching courses in this field (see program). Everything will be truly 'hands on' – with a computer, the right software and true data sets from the 'real world'. There will also be a bioanalytical component with chromatography, mass spectrometry, microdialysis, protein binding and tissue level determination planned. See how the professionals do this. The whole week can truly be a week of Ehrlich excellence ('Ehrlich' in German also means 'true', 'honest', 'sincere').

Conference Language

English.

Poster Presentations and the 'Magic Bullet Poster Award'

We invite poster submission of new and original data. Interesting case reports and 'opinion' papers that stimulate discussion are also encouraged to be submitted. The conference is the premier place for discussions of your society's or hospital's guidelines. Make yourself heard on a controversial issue where you think science needs a change or new directions. Present a new laboratory method, new calculation methods or simply something you want to have discussed in a nice and stimulating atmosphere.

The best posters will receive the 'Magic Bullet Poster Award'.

Preliminary Program

The Education

September 6–9, 2004:

A 3.5-Day Hands-On Workshop of Bioanalysis and PK/PD of Antiinfectives

Learn from Leading Experts

Laboratory Course

Bioanalysis of antiinfectives in fluids and tissues

Microdialysis, Protein binding

In vitro testing of antiinfectives

Computer Course

PK analysis by different methods and software

Population PK, Monte-Carlo simulation

Discussion

Biostatistics, Bioequivalence statistics

Study design (animal experiments, clinical studies)

FDA, EMEA Guidelines' discussion

The course will also have classes for participants without a strong mathematical background.

The Science

Preliminary Scientific Program

Chemistry and Pharmacology

Chemistry as the basis for pharmacokinetics

Pharmacokinetic basis of individualization of antiinfective therapy

Scientific basis for pharmacodynamics

Drug interactions

Tolerance and its assessment

Microbiology and Its Tools to Determine Doses of Antiinfectives

Clinical Investigations

Dosing rationale for antiinfectives in special populations, gender, weight, age, renal failure, hepatic failure, children, cystic fibrosis, other genetic diseases, sepsis, multiorgan failure, polymorbid; dosing rational in case of no reliable clinical studies

Dosing in RTI, UTI, SST, CNS and intestinal infections

Evidence-based versus individual antiinfective treatment

Clinical studies – present limitations and future trends

Dosing in 'new diseases' where there are no clinical data

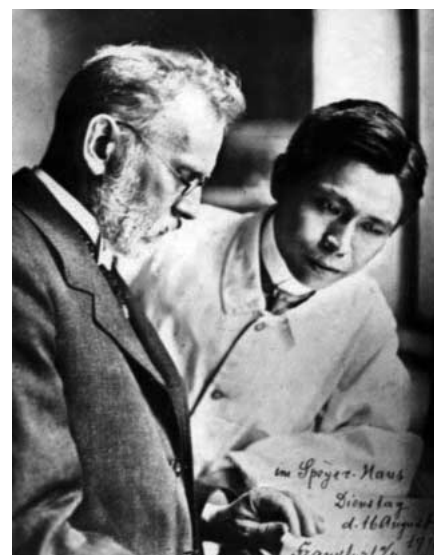


Fig. 2. Paul Ehrlich with Dr. Sahachiro Hata from Japan, who made a great contribution to the development of Salvarsan by testing so carefully and systematically many hundreds of compounds. It is speculated, based on publicly available documents in the Nobel foundation, that, if Ehrlich had not died so early, he and Hata would have received the Nobel Prize for Chemistry. (Photo reprinted courtesy of the Paul-Ehrlich-Institut, Langen, Germany.)



Fig. 3. Typical Paul Ehrlich: studying scientific literature in his office. (Photo reprinted courtesy of Aventis Behring, Germany.)

Communication between Participants

Special areas will be assigned for quiet and pleasant communication between colleagues from around the world. The very special setup of the conference site with small lounge-type areas will create a unique atmosphere. Paul Ehrlich will 'always be around'. The conference site will be decorated to honor Paul Ehrlich's work and achievements. Paul Ehrlich loved colors; as a scientist, he used dyes to fight against infectious agents and as an artist



Fig. 4. Ehrlich in his laboratory testing dye reactions. Ehrlich's laboratory, even for his time, was on a relatively moderate technical level. Many reactions Ehrlich made in reagent vials, but he still made contributions even to discoveries like the structural elucidation of Atoxyl. As a physician (!) he did not avoid hard fights with his chemists, who often gave in and quitted the job when Ehrlich told them what is right and wrong in chemistry. (Photo reprinted courtesy of Histocom, Frankfurt am Main, Germany.)

he liked to play with colors in his laboratory notebooks or sketches, which he prepared whenever he had to explain his ingenious 'colorful' theories. You will have the opportunity to talk directly to the young artists about the ideas they had when preparing their Ehrlich-related artwork. Part of this will be presented in a play during the gala evening.

This conference will be held in the city of Dürer, where we will invite young artists to use the Ehrlich colors to decorate and enliven this unique conference.

The Sponsors

Many German and international scientific organizations have accepted the invitation to sponsor this great event. Among these organizations are the International Society of Chemotherapy, International Society of Antiinfective Pharmacology, American Society of Microbiology and Federation of European Societies of Chemotherapy and Infection. Further sponsors are institutions very closely related to Paul Ehrlich: Paul Ehrlich Institute, Langen near Frankfurt am Main, Germany; Robert Koch

Institute, Berlin, Germany, and Georg-Speyer-Haus, Frankfurt am Main, Germany (former institute founded by Paul Ehrlich where he developed Salvarsan). The following German scientific organizations are also sponsors: German Society of Internal Medicine, German Society of Surgery, German Society of Pediatric Infectious Diseases, German Society of Pharmaceutical Sciences, German Society of Chemists, German Society of Hospital Pharmacists and German Society of Tropic Medicine.

We are expecting other organizations to join in the near future and are inviting other organizations from around the world, whether international or national ones, to join this great science conference and celebration of Ehrlich.

Gala Evening to Honor Paul Ehrlich Friday, September 10, 2004

Do not miss this great event to celebrate Paul Ehrlich with many highlights, for example a play on Paul Ehrlich that has been written exclusively for the conference, and hear someone who knew Paul Ehrlich personally speak about him. All this with great-tasting Nürnberg food, wine and beer – a memorable event. As the highlight of the gala evening, receive your 'Magic Gift' for all scientific conference participants that has never been given before.

The History and Celebration

Paul Ehrlich Biography Symposium, Exhibition and Play

Learn more about this great scientist's visionary abilities and lifetime achievements.

Attend the first-ever historians' and chemotherapy researchers' conference on Paul Ehrlich.

View previously unseen exhibits of Paul Ehrlich.

See works from artists using Ehrlich's colors; Ehrlich loved to use and play with colors – in the laboratory and elsewhere.

The Conference Venue

Nürnberg is one of Germany's most enchanting cities. In 1424, Nürnberg was designated as the location for the safekeeping of the imperial jewels and the imperial relics. The Free Imperial City was then at its zenith and was often called the 'Capital of the Middle Ages'. This Euro-

pean metropolis developed into a German center of humanistic sciences, arts and sculpture. Martin Behaim designed the first globe here, and Hans Sachs and the poetry of the Meistersingers reached their peak. Works of art of the highest European level were created by the wood carver Veit Stoss and the sculptor Adam Kraft. Albrecht Dürer, one of the Renaissance's greatest painters, was born in Nürnberg. After a dark episode in the last century, the city rapidly became a modern German city that is particularly focused on human rights, as demonstrated by a prize given each year as well as the 'Strait of Human Rights' in the renowned German National Museum, next to which this conference will be opened. The youth of this now modern German city will welcome scientists and historians from around the world by preparing various events for a most memorable conference.

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Register early to qualify for the following great offers:

Reduced fees of EUR 250 for the conference and EUR 200 (all 3 days) for the pre-conference workshop for early registrants. EUR 400 for the whole week of 'Ehrlich excellence'. See www.ehrlich2004.org for details.

A week of Ehrlich excellence including the complete pre-conference workshop, the conference, the gala eve-

ning and hotel accommodation (three stars) for 6 nights for only EUR 700.

Nürnberg has an international airport with many direct flights from and to major cities in Europe. Flight arrangements from practically all European cities for as little as EUR 20 (!) in some instances, e.g. London, are available through the conference and using Munich International Airport. A bus transfer is planned from Munich airport to Nürnberg (taking approximately 90 min from the airport to the conference hotels or conference site) to allow the use of these special rates. Also, it may be an alternative to fly to other German cities for EUR 30 or 40 and take the train from there to Nürnberg.

Special fees are offered for students, residents and trainee physicians and colleagues from Eastern Europe, as well as for colleagues from the developing world (on request).

These offers are preliminary at the time of editing this editorial. They are not final and binding; for updates, please look at the homepage (www.ehrlich2004.org).

References

- 1 Himmelweit B (ed): The Collected Papers of Paul Ehrlich. Pergamon, London, England, 1956, vol II: Immunology and Cancer Research, pp 148–192.
- 2 Sörgel F: The return of Ehrlich's 'Therapia magna sterilisans' and other Ehrlich concepts? Series of papers honoring Paul Ehrlich on the occasion of his 150th birthday. *Chemotherapy* 2004;50:6–10.
- 3 Maehle AH, Prüll CR, Halliwell RF: The emergence of the drug receptor theory. *Nat Rev Drug Discov* 2002;1:637–641.