

SCRIBE

THE INTERNATIONAL SOCIETY FOR PHARMACOEPIDEMOLOGY

President's Message

By Hubert G.M. Leufkens

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Prescribers have many choices in the drug-treatment of most diseases. Grouping drugs serves to facilitate prescribing. Drug 'classes' are defined on the assumption that we are able to judge whether drugs are closely related, by chemical structure, pharmacology, or actions. Physicians may choose from many β -lactam antibiotics, ACE-inhibitors, statins, NSAIDs, or CCBs. Although individual members of a 'class' share main features, they may have clinically important differences. Herein lies both the benefits and the problems of the concept of drug 'classes'. While the advantages of using a class rubric are evident, it has an unfortunate tendency to hypnotize clinicians and researchers into overlooking aspects of individual drug actions that transcend the characteristics expected of drugs in the 'class'.

Classifying drugs is not an issue limited to indexing medical or pharmacological textbooks. Drug 'classes' are important vehicles for communication about drug effects, labeling, marketing, logistics, and reimbursement. Most pharmacotherapeutic groups contain more than one compound and therefore constitute a 'class'. In drug development, drug 'class' can be an important point of reference. Pharmaceutical innovation is sometimes targeted to bring a new drug to the market with at least the same risk-benefit ratio as other 'class' members. More often, new drugs are designed to show superiority over



existing compounds that populate the 'class', in which case inclusion of the new agent in the same class with the 'old stuff' is not a premium option.

Industry attempts to show evidence for the uniqueness of their newborn, and often considers drug 'class' as an unwanted straitjacket. Bureaucrats usually like drug 'classes'. They provide stability and a frame for regulation, reimbursement or legal action.

Numerous important cases in our field (e.g. NSAIDs and GI risk, safety of inhalational beta-2 agonists, CCBs and coronary risk, psychotropics and car accidents) highlight both the positive and negative aspects of 'class'. Individual differences in drug effects are not easy to interpret. Selective prescribing of certain drugs, drug channelling, and variability of duration of use are factors influencing outcomes of therapy. An interesting study on the issue of a 'class' effect in the context of variable duration of use was the paper of Martinez in the Lancet early this year on lipodystrophy and protease inhibitors¹. They found independent risks of lipodystrophy related to the exposure of protease inhibitors in general, but not with specific antiretroviral drugs. The paper shows clearly that interchangeability is not only a question of

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Demonstration Project in India: Teaching Principles of Epidemiology to Health Professionals in the Developing World.

By Stanley A. Edlavitch and Frank May

In planning sessions at the 15th ICPE and the 16th ICPE, the ISPE Ad Hoc Committee on Global Capacity selected as its first priority the formation of an educational project tailored to the needs of colleagues in developing countries. The committee has met in person and by e-mail several times since its inception in 1998, and recently adopted a program proposed by Professor **Frank May** (University of South Australia). This demonstration project will establish pharmacoepidemiology teaching programmes for pharmacists-in-training in southern India. The program is intended as a model for

similar projects for other health professionals in the developing world. The ISPE Board of Directors has endorsed the proposed program.

Recognizing that unintentional morbidity is a too-frequent feature of use of allopathic medicines in the developing world, this initiative will produce a paper-based, drug-safety-oriented undergraduate curriculum for pharmacists which reflects local clinical circumstances, in this case those pertaining in India. It was decided to develop paper-based educational materials because relatively few Indian pharmacy students have ready access to electronic information resources.

The proposed two-year program will have three salient features:

1. A train-the-trainer module to insure that a core of soundly trained Indian pharmacy academic teachers will be available in the future.
2. A web-based support service for Indian pharmacy academics teaching the programme will be established and maintained as a long-term resource.
3. A network of expert educators in pharmacoepidemiology in the developed world will be matched as ongoing resources for core of nationally respected private Indian providers of education in pharmacy.

The proposal includes detailed performance indicators and milestones for the project. The committee believes that an achievable target has been set to have curricular, learning and

examination materials adopted in Tamil Nadu and Karnataka States as mandatory for students graduating from both the 2-year pharmacy diploma and also the 4-year pharmacy degree courses.

Frank May, who has a successful track-record for educational work with pharmacists in South India, will be the PI. **Stanley Edlavitch**, who recently joined the investigator team on an NIH funded clinical trial in Southern India, will be the Co-PI. An internationally diverse Advisory Reference Panel of ISPE members with interest and experience in working in the developing world also will guide ongoing progress. The panelists are **Michael Lewis**, **Kassim Alriyamy**, **Saad Shakir**, **Arnold Chan**, **Sten Olsson**, **Jean-Paul Collet**, and **Abraham Hartzema**.

Any ISPE member with particular interest in the this initiative is invited to contact either Frank May (University of South Australia, Adelaide, Australia 5000, Tel: +61.7.3365.8853, Fax: +61.7.3365.1688, e-mail: frank@pharmacy.uq.edu.au) or Stan Edlavitch (University of Kansas Medical School, 3901 Rainbow Blvd., Kansas City, KS 66160-7313, Tel: +1.913.588.2790, Fax: +1.913.577.2780, e-mail: sedlavit@kumc.edu).

Special Request:

The Committee would appreciate suggestions from any ISPE member about organizations that might be likely funders of this important initiative. Please contact Frank or Stan with your ideas.

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Review of *Monitoring Drug Safety, an Educational CD-ROM*, by J.W. van der Velden, and R.D.T. Farmer.

By Curt Appel and C. Ineke Neutel

Monitoring Drug Safety has been in the works for several years, partly in order to keep up-to-date with various regulatory initiatives in Europe and North America. We hope to give you a flavor of the second edition that is now available.

To start with some negative points, the CD has no formal introduction, and therefore neither objectives nor information about the authors is given. In addition, the opening screen does not adequately guide the user on how to navigate the CD. These are essential elements to any educational CD product.

The approach used in the CD is otherwise user-friendly. The opening screen presents a flow-chart format with “clickable” topic indicators such as passive monitoring (spontaneous reporting & reporting procedures), active monitoring (studies, risk analysis), data sources, web links and presentations (PowerPoint slide shows). When entering the web links area, your Internet browser is automatically opened and shows an array of links to interesting sites. Included are links to pharmaceutical companies, regulatory organizations, journals, and medical search engines. A sampling of the regulatory sites takes you to Food and Drug Administration, USA (FDA), guideline sites (FDA, EMEA, ICH), and rules governing medical products in the European Union (EU). Overall, this is a comprehensive area with valuable links for people working in the area of Pharmacovigilance. One, rather glaring and surprising, omission in the Journals section is that the absence of links to pharmacoepidemiology journals, including Pharmacoepidemiology and Drug Safety.

Working through the flow chart reveals three layers of information. For

example, in the section Passive Monitoring, the second layer “Reporting Procedures”, you find information on Company Safety Units, Expedited Reports, Periodic Reports, Regulations and MedDRA. The last layer provides text material, including terms, definitions with brief explanations. In the sub-section on “What to Report”, there is a statement that is both confusing and partly incorrect. Under expedited reporting is the statement: “All ADRs that are both serious and unexpected are subject to expedited reporting”. Does this apply to all reporting venues? No, and it is incorrect when it comes to reporting in the EU, where Market Authorization Holders are required to report all suspected serious ADRs that occur in any EU country. There are a few other such examples that could lead to confusion by people who are unfamiliar with regulatory

requirements in Pharmacovigilance.

In terms of text material, some sections are more comprehensive than others but in general this is the type of overview of Pharmacovigilance material needed for those working in the field. The above-noted errors need correcting nevertheless. The section on “Studies” is quite good at a basic level. For example, in the description of cohort studies, there is an animation feature that allows a visual representation of such things as, selection of a cohort (exposed/control ratio), and examples of calculation of subject numbers. There is also a good flow-chart of the analysis to obtain an odds ratio.

One difficulty the authors must face in producing such a program is its currency, keeping material up to date.

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ISPE to Award Prize for “Best Paper” Published in *Pharmacoepidemiology and Drug Safety*

Jacques LeLorier and Brian Strom championed the creation of a new Society prize to be awarded annually for the “best” paper published in PDS during the prior calendar year. The ISPE Executive Committee approved the prize at its April 2001 meeting.

Representatives of ISPE, PDS, and John Wiley & Sons are working on the details and exploring funding options. The first PDS prize will be awarded at the 2002 International Conference on Pharmacoepidemiology in Edinburgh, Scotland.

The First Training Course on Pharmacoepidemiology in Russia

By Svetlana Ratchina and Oleg Rozenson

The Interregional Society of Pharmacoepidemiological Researchers (ISPR) and the Russian Society for Pharmaco-economic and Outcomes Research (RSPOR) co-sponsored a training course on pharmacoepidemiology and pharmaco-economics, April 2-4, 2001, in Moscow, Russia. The course was held in conjunction with the Eighth Russian National Congress Human and Medicine.

The audience included general practitioners, pharmacists, representatives of public, governmental and non-government organization and pharmaceutical companies. The objectives of the course were to introduce the basic principles of pharmacoepidemiology and pharmaco-economics, and to present the results of local studies as examples of practical application of pharmacoepidemiology and pharmaco-economics.

The first part of the training course was dedicated to the general principles and application of pharmacoepidemiology. Professor **Pavel Vorobjov**, Moscow State Medical Academy and co-chair of the course, welcomed the more than 120 participants and reviewed the course agenda. Professor **Leonid Strachounski**, Smolensk State Medical Academy, gave an overview of main definitions in pharmacoepidemiology, types of research, and some specific approaches to the pharmaco-epidemiological studies in Russia. **Ulf Bergman**, Karolinska Institute, Huddinge University Hospital, Sweden, discussed differences between drug utilization research and pharmacoepidemiology, and the importance of drug utilization studies in the implementation of rational use

of drugs. **Dr Svetlana Ratchina** and **Dr Alexandr Bedenkov** (both from Smolensk State Medical Academy) introduced the ATC/DDD methodology with some examples of its application to drug utilization studies. The first part of the course was concluded by presentation the results of multicentral pharmacoepidemiologic study "Patterns of drug prescribing in outpatient adults with acute exacerbation of chronic bronchitis" by **Dr Sergei Kozlov**, Smolensk State Medical Academy.

Professor **Pavel Vorobjov's** lecture on the "General introduction to pharmaco-economics" began the second day. **Ulf Bergman** then presented "The characteristics of

pharmaceuticals as value components". **Dr Oleg Rozenson** (Smolensk State Medical Academy) and **Dr Maria Avksentyeva** (Moscow State Medical Academy) gave an overview of types of economic analyses (cost-minimization, cost-utility, cost-effectiveness, cost-benefit). And **Dr Oleg Rozenson** concluded the day with a discussion of the application of the cost-effectiveness analysis for the assessment the different approaches to the management of chronic hepatitis B. A lively and interesting discussion followed.

The participants expressed their gratitude to the lecturers and organizers for a well-planned, useful course and expressed their interest in having more meetings.

FUTURE ISPE MEETINGS

2002

- **Mid-Year Symposium: Risk Communication**
April 19, 2001
Hotel Wyndham Montreal
Montreal, Quebec, CANADA
 - **18th International Conference on Pharmacoepidemiology**
August 17-21
Edinburgh Conference Centre
Edinburgh, Scotland, UK
- Abstract Submission Deadline: February 22, 2002*

2003

- **19th International Conference on Pharmacoepidemiology**
August TBA
Wynham Philadelphia at Franklin Plaza
Philadelphia, Pennsylvania, USA

Visit the ISPE website (www.pharmacoepi.org) for information about these meetings and abstract submissions.

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the drug as such, but a function of both the molecule's action and the way it is used.

The question whether drugs within a class are fully interchangeable is dynamic. In the early days of statin treatment for hyperlipidemias, most data showed comparable effects of individual statins. Today we know that statins might have other pharmacological effects as well, which appear to differ from one drug to another. Perceived differences may influence prescribing decisions, making comparisons between patient outcomes of different drugs from one 'class' difficult. Comparisons are the

sinew of research in pharmacoepidemiology, but they depend on comparing like with like. The practice of medicine ought to be based on solid data on 'class' effects, but assessment of individual drug actions should not be fettered by preconceptions based on 'class' effects.

The research agenda of pharmacoepidemiology should address this topic in a more extensive way.

¹ Martinez E. et al. Risk of lipodystrophy in HIV-1 infected patients treated with protease inhibitors: a prospective cohort study. *Lancet* 2001; 357: 592-98.

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In the "Databases and Records" section, the description of the WHO monitoring program is out of date – there are now over 50 countries participating in the WHO program and a new website is available. Perhaps consideration could be given to selling the CD with periodic updates.

The PowerPoint presentations are an intriguing part of this program. They seem to be taken from presentations that the authors have made to various audiences. While the slides are refreshing and original, viewing slide presentations without anyone to answer questions can be unfulfilling. Some technical points: The program

can be run from the CD or installed on your computer. We had difficulty accessing the CD from one of our computers. In several text sections there are areas where text is run off the visible page (overlapping a border), and several sections require proof reading.

In conclusion, with corrections as noted and possibly periodic updating, *Monitoring Drug Safety* can be a good effort at providing a basic introductory teaching guide for those in industry and regulatory agencies who are beginning in the field of Pharmacovigilance, and perhaps to those who need easy to access references.

ELECTION 2001 RESULTS

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Congratulations to the Class of 2004 and to all ISPE members who stood for election.



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