Man, Molecules and the Environment – additional information

Adverse "side-effects" of drugs are a constant problem requiring practitioners to make continual risk/benefit analyses when prescribing drugs. Since the MODA course places most emphasis on the mechanisms of actions of drugs, there is little space to cover much on their adverse effects. The MME course therefore seeks to redress this balance by providing an introduction to the variety and nature of such adverse effects. In addition, it will address some of the problems encountered as a result of exposure to potential hazards within our environment, not only the food that we eat but the air that we breathe: these add considerably to the burden placed on the general practitioner.

The course (see outline below) will start by considering general aspects of toxicity (lectures 1 and 2) and then look more specifically at examples of drugs causing particular types of problems (lectures 4 and 5, video and Grace seminar). Lectures 3 and 6 will be concerned with the challenges of developing and testing drugs to avoid such adverse reactions. Lectures 8 -11 (video, Clark seminar and practical) will address the different problems brought about by food and environmental factors.

Lectures:

1a Introduction to course (B Billups)
1b Cellular and molecular basis of toxicity I (M A Barrand)
2 Cellular and molecular basis of toxicity II (M A Barrand)
3 Clinical aspects of drug testing I (C Palmer)
4 Types of adverse drug reactions I (M A Barrand)
5 Types of adverse drug reactions II (M A Barrand)
6 Clinical aspects of drug testing II (C Palmer)
7 Developing safe drugs (A Cahn)
8 Toxicity of insecticides (S B Hladky)
9 Allergy, asthma and the environment (S Nasser)
10 Effects of smoke on the lungs (A Cahn)
11 Environmental assaults on the endocrine system (I Hughes)
12 Resume (M A Barrand, A Cahn, B Billups)

This final lecture/seminar is intended as a session to reflect on the material covered in the course, to allow some discussion, and to provide advice on the types of questioning likely to appear in the examination.

Topics covered in the lectures will be reinforced and extended with material from a practical (this demonstrates the actions of insecticides), a video session concerning thalidomide and two seminars (one entitled: Drugs and sudden cardiac death to be given by Dr A Grace; the other: adverse reactions to foods: the origins, mechanisms and future treatment of food allergy? to be given by Dr A Clark). These seminars are particular useful in providing students with the opportunity to ask questions and discuss issues with the invited speakers.

Background reading (useful also for those providing supervisions)

It is expected that the student will wish to read around the subject ie beyond the information given in the lectures. The following may help with this:

• There are several useful chapters in the latest edition of Rang and Dale (6th edition by Rang, Dale, Ritter and Flower 2007). Chapter 52 covers individual variations based on genetic differences and on other factors and also looks at drug interactions; Chapter 53 discusses the different types of adverse reactions and Chapter 56 dwells on drug discovery and development.

• Introduction to Toxicology by John Timbrell (2002) 3rd edition contains useful background material and has chapters on specific drugs, food and drink, household products, industrial agents, pesticides and other environmental pollutants and toxins of natural origin. This can be viewed in conjunction with Principles of Biochemical Toxicology also by John Timbrell (2002) 3rd edition that emphasizes the biochemical pathways and mechanisms involved in the adverse effects of these agents. A copy of each of these books is kept in the Pharmacology practical classroom and can be consulted there on request to Barney Leake.

• In addition, for the student wishing to explore in more depth on selected topics, a list of suggested review articles is given below. PDF files of these will be posted on the website. These are NOT required reading but should be helpful in providing sources of extra information should the student be interested to know more:

CASIDA JE & QUISTAD GB (1998) Golden age of insecticide research: past, present, or future? Ann Rev Entomol 43, 1-16.

FRANCO R & CIDLOWSKI JA (2009) Review. Apoptosis and glutathione: beyond an oxidant. Cell Death Differentiation 16, 1303-1314.

LIMON-PACHECO J & GONSEBATT ME (2009) Mini review. The role of antioxidants and antioxidant-related enzymes in protective responses to environmentally induced oxidative stress. Mutation Res 674, 137-147.

MEYER UA (2000) Pharmacogenetics and adverse drug reactions. The Lancet 356, 1667-71.

PEREIRA NL & WEINSHILBOUM RM (2009) Cardiovascular pharmacogenomics and individualized drug therapy. Nature Reviews Cardiology 6, 632-638.

STEVENS JL (2006) Future of toxicology – mechanisms of toxicity and drug safety: where do we go from here? Chem Res Toxicol 19, 1393-1401.

RODEN DM & VISWANANATHAN PC (2005) Genetics of acquired long QT syndrome. J Clin Invest 115, 2025-2032.

RODEN DM (2008) Review. Cellular basis of drug-induced torsades de pointes. Br J Pharmacol 154, 1502-1507.

VARGESSON N (2009) Thalidomide-induced limb defects: resolving a 50-year-oldpuzzle. BioEssays 31, 1327-1328.

WILKE RA, LIN DW, RODEN DM, WATKINS PB, FLOCKHART D, ZINEH I, GIACOMINI KM & KRAUSS RM (2007) Identifying genetic risk factors for serious adverse drug reactions: current progress and challenges. Nature Rev/Drug Discov, 6, 904-16.