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News roundup

More surveillance of drugs is needed to protect public

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Doctors need to take the risk of psychiatric side effects from prescription drugs far more seriously than they currently do—and to be prepared to listen to patients who report adverse reactions to treatment.

That was the message from a one day conference held in London last week by the charity the Adverse Psychiatric Reactions Information Link (APRIL). The organisation was set up in 1998 by Millie Kieve, whose daughter, Karen, died after falling from a window. Mrs Kieve is convinced that it was her daughter's reactions to various drugs—including sulfasalazine for Crohn's disease and, six years later, co-cyprindiol (Diannette) for hormonal problems—that were to blame for the breakdowns and attacks of psychosis that preceded her death.

Many people in the conference audience had experienced adverse psychiatric reactions themselves or cared for someone who had. They reported negative responses from doctors, who dismissed their concerns as "imagined" and were reluctant to listen to them.

Charles Medawar, coauthor of a controversial study of adverse reactions to antidepressants reported by the BBC's *Panorama* television programme in May 2003, emphasised the importance of surveillance of new drugs after they have been marketed. Currently, he said, the emphasis is on data from clinical trials conducted before drugs are licensed.

"The MHRA [Medicines and Healthcare products Regulatory Agency] spends £9m [$17m; €13m] on postmarketing surveillance," he said. "That is a pretty trivial investment."

By comparison the cost to the NHS of adverse drug reactions leading to hospitalisation was reported to be some £470m a year, he said.

His study, coauthored with Andrew Herxheimer, a clinical pharmacologist and founder of the *Drugs and Therapeutics Bulletin*, showed that reports of suicide linked to the selective serotonin reuptake inhibitor paroxetine (Seroxat) were not being thoroughly investigated by the MHRA. Subsequently the government

announced a review of the yellow card system for reporting adverse drug reactions (*BMJ* 2003;327:308), although plans to allow patients to report directly to the agency rather than through a nurse or doctor are still under trial.

Telling patients the relative risk ratios, the absolute risk, or numbers needed to treat was meaningless, said Dr Herxheimer. "Most people don't understand them —and lots of doctors don't either," he said. Patients needed to be told in language they understood, such as whether they had a 1 in 10 chance of having a problem with a drug, he said. Adverse reactions were often related to dosage, he added, suggesting they may not occur at a lower dose.

Medical students, however, get only limited training in pharmacology, John Halliday, a senior lecturer at Guy's, King's, and St Thomas's School of Medicine, London, told the conference. He argued that more time should be spent on the topic.

"We should encourage students to be sceptical about the benefits of new drugs until we know what their side effects are," he said. But teaching students about every adverse reaction was not straightforward. "It's not very easy to spend a lot of time on a rare drug reaction," he said.

Keith Altman, managing director of Finkelstein and Partners, a US firm of law advisers, believes that drug companies could easily analyse comparative data on adverse reactions, readily available from the US Food and Drug Administration. They would then immediately see a potential problem with a drug, he argued.

"A company has a moral obligation to do something when it sees these signals," he said.

His company has just issued a warning to the FDA about off licence use of gabapentin (Neurontin), an antiepilepsy drug linked to an increase in the risk of suicide. Pfizer, the manufacturer, was recently fined $240m for off-label promotion of the drug (*BMJ* 2004;328:1217).

Data from the FDA show that between 1998 and 2002 eight suicides among people using the drug were reported in the United States, but the number increased markedly in the first six months of last year, when 17 suicides were reported.

After the law firm took out an advertisement in September 2003 on national cable television alerting people to the potential risk from the drug it became aware of even more cases. From September 2003 to August 2004 the firm received reports of 200 suicides among people taking the drug and 2500 attempted

suicides. Despite repeated attempts to alert the FDA to the problem and a request that the information leaflet for patients be altered to reflect this risk the FDA has not changed the leaflet.

Professor Saad Shakin, director of the Drug Safety Research Unit, an independent charity that monitors the safety of new drugs, said that the future lies in drugs designed to meet the different genetic make up of individuals but that this was some way off.

"Some time in the future we are going to have designer drugs, but an enormous amount of work has got to be put in to help us understand what is going on. We need to study the genetics of disease, rather than the pharmacognetics of the drug," he said. "But pharmaceutical companies only fund research for their drugs."

More details of the conference are at www.april.org.uk