Research Update • Le point sur la recherche

Fatal reaction: ADRs a leading cause of death

Serious adverse drug reactions (ADRs) are much more common than previously believed, according to a careful meta-analysis by University of Toronto researchers. They estimate that between about 1.7 and 2.7 million serious ADRs occurred in the US in 1994, resulting in from 76 000 to 137 000 deaths (*JAMA* 1998;279[15]:1200-5). Even the lower estimate would makes ADRs the sixth leading cause of death after heart disease, cancer, stroke, lung disease and accidents. The researchers have also collected worldwide data showing that the scale of the problem is similar in other countries, including Canada.

"There was a lot of suspicion that there was a problem, but there were no numbers," explains co-author Dr. Bruce Pomeranz, a neuroscientist with the Departments of Zoology and Physiology at the U of T who has a special interest in pain and its treatment.

He and co-authors Jason Lazarou and Paul Corey tried to avoid overestimating the incidence of ADRs by including only prospective studies done in US hospitals that looked at ADRs that required admission to or occurred in the hospital. In retrospective studies where researchers look at 1000 charts, he said, ADRs may not be marked on the charts because they were undetected or unrecorded. In contrast, with prospective studies "someone is walking around looking for ADRs."

They found 39 such studies spanning the last 32 years and including 63 000 patients — enough to give the meta-analysis impressive statistical power. Surprisingly, they found that the rate of ADRs did not change over the years. They looked at only ADRs occurring when drugs were given at the proper dosages and excluded administration errors, overdoses, drug abuse and noncompliance. "Our approach was very conservative. We were asking how toxic a properly prescribed and administered drug is."

Pomeranz thinks one of the main reasons that the high incidence of ADRs has not come to light before is a lack of data. In addition to the poor reporting of ADRs on hospital charts, "even more egregious is that reporting to the FDA [US Food and Drug Administration] has been incredibly low." For 1994, the FDA recorded 3500 deaths due to ADRs. Death certificates showed only 159 deaths due to drug reactions that year, although Pomeranz says that this is because certificates must show the immediate cause of death — such as gastrointestinal bleeding — rather than precipitating factors, such as an ADR caused by ASA.

Pomeranz believes the solution may lie in better monitoring. In a Salt Lake City hospital the incidence of ADRs has decreased as a result of tracking them on a computer system. "Drugs have enormous benefits but what is needed is the risk–benefit ratio for each drug," Pomeranz concluded. — *C.J. Brown*

In the news . . .

Race and disease

The role of race in disease and death is not easy to ascertain because race is often associated with income and other health risk factors. Results of a longitudinal study of more than 360 000 men in the US, conducted since 1973, now show that there are some race-related differences in risk of death, even after income and other risk factors are taken into account (*Lancet* 1998;351:934-9). The study showed that black men had a greater relative risk of death from all causes than white men, even after income and health factors were considered. After adjustment for income, the black men in the study had a greater risk of death from cancer (especially prostate cancer and myeloma) and hypertensive heart disease than white men. However, white men had a higher rate of death from coronary heart disease, suicide and melanoma.

JC virus the villain?

JC virus has been found in the cerebrospinal fluid (CSF) of patients with progressive multifocal leukoencephalopathy (PML). However, it has not been clear whether the virus is implicated in the disease or is reactivated by inflammation in the brain. Researchers in Sweden have now found JC virus DNA in the CSF of patients with PML, but not in patients with brain inflammation caused by herpes simplex encephalitis, enteroviral meningitis or multiple sclerosis (*J Clin Microbiol* 1998;36[4]:1137-8). This finding provides evidence that JC virus in the CSF is diagnostic for PML.