Reinforcing surveillance for vaccine-associated adverse events: The Advisory Committee on Causality Assessment

There is little question that vaccines have had a tremendous impact on the incidence of childhood infectious diseases. However, before 1965, when many vaccines were being introduced, the systematic monitoring for adverse events associated with drug products was not being undertaken. It required an international disaster, the discovery of phocomelia associated with thalidomide use in pregnancy, to stimulate the creation of formal surveillance programs (1).

Today, Canada is a world leader in the postmarketing surveillance of vaccine products. Its Vaccine-Associated Adverse Events (VAAE) program (distinct from the monitoring program for other drug products) is maintained by the Division of Immunization at the federal Laboratory Centre for Disease Control. The division receives case reports of events suspected to be due to the administration of a vaccine that are submitted voluntarily by health care providers through their provincial public health authorities on a specially designed reporting form (2). The program receives about 4000 reports per year, the majority representing minor reactions such as fever or injection site pain and/or swelling (3). Although spontaneous reporting systems are criticized for a number of limitations, including under-reporting, they remain a key first line activity for detecting problems with drugs on the market (4). Time and again, spontaneous monitoring programs have been the first to detect new signals that have later been confirmed.

Continually improving the capacity of spontaneous reporting systems to detect new and rare events is a challenge, especially in a climate of under-reporting. Two activities have more recently been added to supplement the VAAE spontaneous reporting system to address the need for more active surveillance and to evaluate and interpret more fully case reports of new or serious adverse events. The first, started in 1990, is an active, pediatric hospital-based surveillance program known as the Immunization Monitoring Program – Active (IMPACT), which searches admissions for events that may have been due to vaccine administration (5). The second initiative is a multidisciplinary group called the Advisory Committee on Causality Assessment (ACCA), convened to review all case reports meeting criteria for severity or ‘unexpectedness’. This group is composed of specialists in pediatrics, public health, epidemiology, infectious diseases, immunology, neurology and adverse event surveillance. The committee meets for two days, twice a year to review selected cases and discuss vaccine safety issues. Should an emergent concern require more rapid intervention, teleconferences may be arranged. Cases that are reviewed are stripped of all identifiers and distributed to each member in advance. Selection criteria for case review include all cases of meningitis/encephalitis, encephalopathy, afebrile seizures, deaths and other events of a serious nature that have led to hospitalization.

To date, ACCA has met four times and reviewed over 250 cases from the reporting system or submitted directly by provincial public health authorities. Each case is reviewed using a causality assessment rating guide to determine, if given enough information, whether the adverse event was related, possibly related, unlikely to have been related or unrelated to the administration of the vaccine(s) implicated. Cases that are inadequately documented are followed up with the reporter to obtain more information. By using this method, a number of issues have recently been flagged for further detailed research and/or surveillance. If warranted by the results of further work, ACCA can recommend that regulatory action be considered. In addition, ACCA is in a position to recommend increased education in certain areas such as the recognition and diagnosis, management and reporting of cases of anaphylaxis. Summary reports of the case evaluations done by ACCA are made available to the provincial epidemiologists (responsible for immunization programs), to the IMPACT project and for review by the Canadian Paediatric Society Committee on Infectious Diseases and Immunization.

The functioning of ACCA has attracted attention interna-
tionally. A similar expert advisory committee on vaccines is being considered south of the border to explore emergent issues in vaccine safety. A representative from the United States Centers for Disease Control and Prevention attends the ACCA meetings, and a similar exchange is planned when their committee gets underway.

Together with the participation of practitioners who report suspected adverse events, and the IMPACT project that maintains active, hospital-based surveillance, the Advisory Committee on Causality Assessment is a key component in the postmarketing surveillance of vaccine products and in contributing to public and provider confidence in immunization programs.

REFERENCES