Evaluation of the rubella surveillance system in Quebec

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OBJECTIVE: To evaluate the validity of information in the rubella surveillance system in Quebec.

DATA AND METHODS: Cases of rubella in the provincial registry of notifiable diseases, “Maladies à déclaration obligatoire” (MADO), from 1994 to 1996 were matched with laboratory-identified cases and with cases in a reference file created from all case investigation records of regional departments of public health for the same period. Sensitivity and the proportion of cases in agreement were calculated.

RESULTS: Compared with laboratories, the sensitivity of the provincial registry was 56%. Compared with the reference file, global sensitivity (confirmed cases plus clinical cases) was 58% and the positive predictive value was 50%. Of the 356 cases reported to regional public health departments, 65% were classified in the same diagnostic category (confirmed case, clinical case, excluded case) by public health professionals and a group of experts (weighted kappa=0.32). Information on rubella vaccination status was missing in 25% of cases in the MADO file for rubella.

CONCLUSIONS: Notification of positive results for immunoglobulin M antibodies and viral cultures should be required of all laboratories. Uniform procedures should be adopted and applied for the validation of cases that are reported to regional departments of public health. In the context of the rarefaction of rubella, any immunoglobulin M-positive result should be interpreted using all available epidemiological information.

Key Words: Laboratory; Monitoring; Rubella; Validation

Surveillance of rubella is an integral part of efforts to eliminate this contagious, vaccine-preventable disease. In the province of Quebec, rubella cases must be reported to public health authorities by the treating physician (1). Following receipt of a case notification and its validation, professionals of the 18 regional public health departments in...
Quebec enter the case into an electronic provincial registry of notifiable diseases, “Afficher des maladies à déclaration obligatoire” (MADO). Depersonalized data from this file are available for the identification of risk factors, and analysis of geographic and temporal variations.

Objective 14 of the Politique de la Santé et du Bien-être (2) of Quebec targets elimination of rubella by the year 2002. This objective conforms to the Canadian goal of eradicating indigenous rubella infection during pregnancy by the year 2000 as defined during the Rubella and Mumps Consensus Conference (3). Eventual confirmation of elimination or near elimination of this disease requires a monitoring system that is both sensitive and specific. The present study aims to evaluate the validity of information supplied by the Quebec provincial rubella surveillance system and propose measures to improve this system.

### DATA AND METHODS

Depersonalized data were obtained on rubella cases in the MADO file from 1994 to 1996, excluding congenital rubella. These cases were reported as either confirmed or clinical cases. Case definitions used in Quebec (4) during the study period conform to Canadian definitions (5). A confirmed case must fulfill one of the following conditions: in the absence of recent rubella vaccination, it must be confirmed by a laboratory test (either isolation of rubella virus, serological detection of quadrupled titre of anti-rubella virus antibodies or serological detection of rubella immunoglobulin [Ig] M antibodies); in presence of clinical manifestations that meet criteria for a clinical case of rubella, it must have an epidemiological link to a case confirmed by one of the laboratory tests mentioned above. A clinical case must meet four conditions: have clinical manifestations that do not meet the criteria for a case of measles; acute onset of a generalized maculopapular skin eruption; fever; and the presence of one of the following symptoms; joint pain or arthritis, lymphadenopathy or conjunctivitis. For each case, the information recorded was the date of disease onset, sex, birthdate, place of residence, symptoms, vaccination status and serological results.

In the province of Quebec, only four laboratories perform the test for rubella IgM antibodies. Information on positive results from 1994 to 1996 was obtained from these laboratories, but no information was available for tests with a negative result. Variables obtained included the date that the sample was taken; sex, birthdate and place of residence of the patient; serology of measles; and, when available, history of vaccination with the combined mumps-measles-rubella (MMR) vaccine. Cases identified by laboratories were matched to those in the MADO file to assess the sensitivity of the MADO file.

Depersonalized copies of all case investigation records for rubella cases occurring from 1994 to 1996 were obtained from the 18 provincial regional public health departments. Investigation records were unavailable for 25 cases. Using data in these investigation records, one of the researchers (LP) created a reference file by classifying cases into three categories (confirmed case, clinical case, excluded case) using the criteria mentioned above. A positive response to the three questions about skin eruption, fever and the presence of other symptoms was necessary for the case to be classified as a clinical case, even if there was no other information about these symptoms (for example, the maculopapular nature of the eruption). Regarding vaccination status, the person was considered vaccinated if he or she had received a dose of antirubella vaccine with the vaccination date present in the medical file. In the absence of the date of vaccination, the person was considered nonvaccinated. If the person did not know his or her vaccination status, the response was considered unknown. When no response was present, information was considered missing. Cases in the reference file were matched to those in the MADO file to calculate the proportion of cases in agreement.

### RESULTS

For the years of 1994, 1995 and 1996, 63 cases, 48 cases and 56 cases of rubella, respectively, were recorded in the MADO file. This gave a total of 167 cases, 22% confirmed and 78% clinical. Information on vaccination status was missing in 25% of cases in the MADO file, 31% of clinical cases and 8% of confirmed cases. The vaccination status was known for 35 confirmed cases and 90 clinical cases; 47.2% vaccinated, 56% nonvaccinated and 16.8% unknown. The percentage of confirmed patients who were vaccinated was 37.1%.

A total of 38 positive serology tests for rubella IgM antibodies were identified by the laboratories. Only half of these cases (19 of 38) were known to their regional public health departments. Excluding four persons who had received the MMR vaccine in the 56 days (eight weeks) before samples were taken, sensitivity of the MADO file for laboratory-confirmed cases was 56% (19 of 34)

The reference file contained 356 cases, 20 of which were classified as confirmed cases, 103 as clinical cases and 233 cases were excluded (Table 1). Compared with the reference file, overall sensitivity of the MADO file (confirmed cases plus clinical cases) was 58% (71 of 123) and the overall positive predictive value was 50% (71 of 142). Of the 356 cases reported to regional public health departments, 65% were classified in the same diagnostic category (confirmed case, clinical case, excluded case) in public health case investigation records and in the reference file (weighted kappa value=0.32). The main source of disagreement was the records of 11 confirmed and 6 clinical cases in the MADO file for which criteria of the case definition of rubella had not been met.

When the epidemiological indicators calculated from the

### TABLE 1

| MADO file | Confirmed cases | Clinical cases | Excluded cases | Total |
|-----------|----------------|----------------|---------------|-------|
| Confirmed cases | 20 | 1 | 10 | 31 |
| Clinical cases | 0 | 50 | 61 | 111 |
| Excluded cases | 0 | 52 | 162 | 214 |
| Total | 20 | 103 | 233 | 356 |
MADO file were compared with those calculated from the reference file, many differences were observed. Annual average incidences of rubella calculated were 0.8/100,000 versus 0.6/100,000, respectively. The masculine proportion of cases was 51.5% for the MADO file versus 49.2% for the reference file. Distributions of confirmed cases and clinical cases by age groups for the two files are presented in Figures 1 and 2. The MADO file contained a large number of clinical cases in infants younger than one year of age; these cases were not validated by an expert. Thus, there are appreciable differences in specific incidence rates by diagnostic category and age group.

**DISCUSSION**

The present study has shown the lack of validity of the Quebec provincial rubella monitoring system. These conclusions are analogous to results previously reported from other areas (6,7). A study in the state of Vermont, where notification of rubella is the responsibility of physicians, indicates that a maximum of 64% of notifiable diseases were actually reported (6). In Quebec, where notification of cases of rubella identified by laboratories is left to the laboratory’s discretion, sensitivity of the provincial MADO file compared with cases identified by laboratories was 56%. Certain cases were known to Quebec regional public health boards because they had asked for laboratory tests for rubella IgM antibodies. We would expect the proportion of cases diagnosed by laboratories following requests from clinicians and then reported to public health departments to be lower. To increase the sensitivity of the surveillance system, rubella declaration by laboratories should become a legal obligation, adding it to the list of notifiable diseases. Results of the present study illustrate the many problems in obtaining a valid case list for rubella. Differences in disease incidence and age distribution of cases were observed when the same data set was analyzed by health professionals from regional public health departments and experts. The clinical diagnosis of rubella was unreliable, and the notion of clinical case as recommended in the Rubella Consensus Conference (3) should be abandoned. In Finland, in a context of the rarity of measles, rubella and mumps, the positive predictive value of a clinical diagnosis was only 4% (7).

When the diagnosis of rubella is suspected, laboratory tests should be performed. Viral culture is a specific method, and a significant rise in specific rubella antibodies provides good evidence of infection. The interpretation of a single IgM-positive result is always difficult, and data are not available to provide precise guidelines. In the Canadian situation, the probability of a false positive IgM result is high in the absence of an epidemiological link to another confirmed case. Following vaccination, as in primary infection, the persistence of IgM is variable and may be very long in a few individuals (8). The measure of avidity of antibodies can be a means in distinguishing between old and recent infections, but it is rarely done in practice (9). Cross-reactions can also occur after recent infections with other viruses, such as the Epstein Barr virus and the cytomegalovirus (8).

To assure that the best possible quality (accuracy, completeness and uniformity) of information is recorded in the surveillance system, the use of a standard case investigation questionnaire is recommended. For all confirmed cases of rubella, the following information should be available: date of disease onset; origin (indigenous or imported); age, sex and place of residence; vaccination status (and when applicable, if two doses of vaccine were received); history of travel; contacts with travellers or sick people; and results of laboratory tests. The final decision to register a rubella case requires a sound medical interpretation combining clinical, epidemiological and laboratory information.

Our study has certain limitations, including the fact that important details may have been missed by the researcher during case classification. It is possible that findings (such as the presence of a specific symptom) were not noted by public health professionals in their case investigation records. This limitation implies that the real proportion of cases in agreement may actually be higher than that indicated in this study. Finally, given that no epidemics of rubella occurred in Quebec during the study period, the conclusions of this study do not apply during an epidemic period of rubella.

The question of the validity, and ultimately the utility, of a monitoring system is crucial for the surveillance of all diseases, especially those on the way to elimination such as rubella, measles and mumps. In 1994, Klaucke (10) noted that: “Determining the most efficient approach to monitoring for a given health event is an art. There is room for creativity and the opportunity to combine scientific rigor with practical realities.”
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DIAGNOSIS
The blood culture from the original septic work-up grew a branching, filamentous, Gram-positive rod. Over the following week, the same branching Gram-positive rod was recovered in three of six blood culture bottles (all aerobic). A modified Kinyoun stain was performed, and the organism was determined to be partially acid-fast. The organism was further identified as Nocardia asteroides.

While in hospital, the patient was started on high dose intravenous trimethoprim/sulphamethoxazole, and his condition gradually improved. He was discharged following three weeks of parenteral antimicrobial therapy, and then continued on oral maintenance antibiotics while at home. Despite the regression of the pulmonary nodule and sterilization of his blood, the patient continued to require periodic admissions to the hospital for numerous other complications from his bone marrow transplant.

DISCUSSION
Whenever branching, beaded, filamentous Gram-positive rods are cultured under aerobic conditions, the possibility of infection with Nocardia species should be raised. If the organisms are partially acid-fast, as was determined in this case, a presumptive identification of Nocardia species can be made. Growth can be observed on most simple media for bacteria, fungi and mycobacteria, while added carbon dioxide promotes more rapid growth. Nocardiae require a minimum of 48 to 72 h incubation before colonies become visible on solid media, and therefore culture plates should be incubated for a minimum of two weeks if a nocardial infection is suspected. Colonial morphology is extremely variable; most colonies have an earthy odour. Laboratories at larger institutions and reference laboratories usually identify Nocardia to the species level using conventional biochemical tests. The most common method (Gordon method) involves hydrolysis of casein, tyrosine, xanthine and hypoxanthine. Newer methods for direct identification of Nocardia species include ELISA techniques, recombinant DNA probes, and polymerase chain reaction-restriction fragment length polymorphism analyses. These methods remain investigational, and are not available for routine use.

As with this case, nocardiosis is primarily recognized in the immunocompromised host. With cell-mediated immunity playing a major role in defending the body against nocardial infection, the majority of infections are reported in patients who have received bone marrow or solid organ transplants, in patients with HIV/AIDS, or in patients with hematopoietic malignancies.

Based primarily on clinical experience, sulphonamides have become the mainstay of therapy in treating nocardiosis. The use of sulphonamides, however, is often complicated by adverse reactions, especially in the HIV/AIDS population. Imipenem/cilastatin, amikacin and other agents (based mainly on the results of in vitro susceptibility tests) are now being used more extensively to treat invasive nocardial disease.

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