Surveillance of the swine influenza vaccination program at the Royal Military College, Kingston

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In a prospective study symptoms appearing in a previously healthy population within 6 weeks after inoculation with monovalent swine influenza vaccine (A/New Jersey/76) were tabulated. Of the 703 persons (ranging in age from 17 to 55 years) participating in the follow-up 54% reported experiencing symptoms, usually within 24 hours of vaccination; the symptoms were usually minor and none of the participants displayed evidence of Guillain–Barré syndrome.

Une étude prospective a permis de relever, au sein d'une population en bonne santé, les symptômes apparus dans les 6 semaines suivant l'inoculation d'un vaccin monovalent contre la grippe porcine (A/New Jersey/76). Des 703 personnes suivis (âgés de 17 à 55 ans) 54% ont ressenti des symptômes, ordinairement dans les 24 heures qui ont suivi la vaccination; la plupart de ces symptômes étaient bénins et aucune personne n'a présenté les symptômes dus au syndrome de Guillain–Barré.

In October 1976 the surgeon general directed the Canadian Forces medical services to vaccinate all members of the Canadian Forces against swine influenza. During the first week of December 1976, 878 doses of monovalent A/New Jersey/76 vaccine (killed) were administered to the students and staff of the Royal Military College (RMC), Canadian Land Forces Command and Staff College and the National Defence College in Kingston, Ont.

There is little information available on the side effects of vaccination in a large group of healthy persons. Because we were responsible for both the primary care and the vaccination of this large, healthy military population, and because at these institutions close medical follow-up is facilitated by a number of geographic, occupational and logistic factors, the setting seemed ideal for a study of the side effects of vaccination. Our findings are presented below.

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Methods

Usual screening procedures were used prior to vaccination, and persons with any contraindication, including a recent upper respiratory tract infection, were not vaccinated at this clinic. No one received the vaccine within 2 weeks of having received any other vaccine. Because the program was compulsory it was not possible to select an unvaccinated control group.

On Dec. 3, 1976, 878 persons were vaccinated with 0.5 mL of monovalent A/New Jersey/76 influenza whole-virus vaccine (Connaught Laboratories, lot 1902-1, expiry date October 1977), which supplied 200 chick-cell agglutinating (CCA) units per dose. The individual syringe and needle method was used with tuberculin syringes and #26 needles. The vaccine was injected into the subcutaneous tissue of the left upper arm above the insertion of the deltoid muscle.

A questionnaire on past medical illnesses and side effects experienced within 24 hours after vaccination, which had been given to each individual on arrival at the clinic, was returned to the outpatient department at RMC 72 to 96 hours after vaccination. The validity and completeness of the answers were assessed from discussion with each individual, and specific complaints were elaborated upon and documented by the senior medical assistant in charge of the outpatient department. This compulsory follow-up was supplemented by a voluntary one; the individuals were instructed to report to the outpatient department at RMC if they experienced any symptoms during the next 6 weeks that required medical attention.

The follow-up data were tabulated according to frequency of the various symptoms and age of the individuals affected.

Results

Of the 878 individuals vaccinated 703 (80%) returned the questionnaire and were available for follow-up.

The 703 ranged in age from 17 to 55 years; most were between 20 and 24 years old (Table I), and the mode of the age distribution was 20 years. Although 170 individuals were less than 20 years old and therefore younger than was recommended for vaccination, we elected to vaccinate them because of their status as military personnel and the possibility that they would be required to provide essential services.

Of the 703 individuals who underwent follow-up 377 (54%) reported apparent side effects of vaccination. The most frequently reported were joint pain and muscle aches, headache, fever and a swollen arm (Table II). Throughout the group joint pain, muscle aches and headache were clinically similar; they usually started approximately 12 hours after

Table I—Age distribution of military populations in Kingston and Trenton, Ont. receiving swine influenza vaccine* and available for follow-up

Age (yr)	No. of persons	
	Kingston	Trenton
15-19	170	1
20-24	340	22
25-29	47	11
30-34	43	10
35-39	43	15
40-49	50	21
50-59	10	1
Total	703	81

*Dose: 0.5 mL of monovalent A/New Jersey/76 influenza whole-virus vaccine supplying 220 chick-cell agglutinating units.

immunization and resolved within 24 to 36 hours.

Of the 590 individuals whose temperatures were recorded within 36 hours of vaccination 128 were then febrile. The temperatures ranged from 37.5 to 39.5°C, and 82 (64%) of the 128 had temperatures between 38.5 and 39.5°C. The fever was transitory, lasting approximately 24 to 36 hours. In 41 patients, those with higher temperatures, the onset of the fever was preceded by chills, typically 6 to 8 hours after immunization.

Few of the patients sought treatment for nausea and vomiting.

The proportion of individuals reporting apparent side effects was greater in the younger age groups; in fact, as Table III shows, the proportion was almost twice as great in the age group 15 to 19 years as in the age group 40 to 49 years.

Of the 878 individuals vaccinated only 50 sought medical attention for symptoms experienced after vaccination. Thirty were assigned light duties, 18 were instructed to rest in bed for 24 hours and 2 (aged 17 and 20 years) were admitted to hospital. All had returned to full duties by 48 hours after vaccination.

Table II—Symptoms after vaccination reported by 377 individuals in Kingston and 49 in Trenton, 54% and 60% of the total number vaccinated

Symptoms	No. (and % of all reporting symptoms)	
	Kingston	Trenton
Joint pain and muscle aches	150 (40)	12 (15)
Headache	143 (38)	11 (14)
Fever	128 (34)	31 (38)
Swollen arm	115 (30)	9 (11)
Nausea and vomiting	58 (15)	6 (7)
Chills or malaise	43 (11)	18 (22)

Table III—Age distribution of individuals reporting apparent side effects

Age (yr)	No. (and % of all who underwent follow-up)	
	Kingston	Trenton
15-19	103 (61)	0 (0)
20-24	191 (56)	18 (82)
25-29	20 (43)	7 (64)
30-34	24 (56)	5 (50)
35-39	19 (44)	7 (47)
40-49	16 (32)	10 (48)
50-59	4 (40)	0 (0)
Total	377 (54)	47 (58)

The case of one of the persons admitted to hospital is presented below.

Case report

A 17-year-old man presented to the outpatient department 12 hours after vaccination. Six hours earlier he had awakened with chills followed by profuse sweating and fever. He was unable to return to sleep, became nauseated and vomited twice before being seen.

He looked unwell; his face was flushed and he had photophobia. His oral temperature was 39.5°C, pulse rate 100 beats/min and regular, respiratory rate 20/min and blood pressure 150/85 mm Hg. There was no meningismus and the ears were clear. Throat injection and rhinitis were noted. The chest was clear and his abdomen was soft.

He was admitted to hospital. The leukocyte count was 13.8×10^9/L with 89% polymorphonuclear forms, the chest roentgenogram was normal and urinalysis showed no abnormal sediment. The fever persisted for 24 hours; he slept for a total of approximately 18 hours, after which he was afebrile and much improved. The leukocyte count 24 hours after admission was 5.9×10^9/L with 49% lymphocytes. The erythrocyte sedimentation rate (ESR) was 6 mm/h (Wintrobe). Cultures of throat secretions grew normal flora.

He was discharged to return to duty approximately 48 hours after vaccination.

This patient demonstrated some unusual but significant side effects of swine influenza vaccination. He had been seen the morning prior to vaccination for final assessment of an old knee injury and at this time was well; hence we could only conclude that his short-lived but severe symptoms were side effects of the vaccination.

An interesting observation was the high leukocyte count, with an elevated proportion of polymorphonuclear forms, in a blood sample drawn 6 hours after the onset of symptoms; this was in keeping with an acute bone marrow reaction. A sample collected 36 hours after vaccination showed a low-normal leukocyte count, with an elevated proportion of lymphocytes, and a normal ESR — the classical pattern of a viral illness.

Discussion

The results of this study show that vaccination with monovalent A/New Jersey/76 influenza vaccine is not without side effects: approximately half of the healthy, active and largely male population reported apparent adverse effects of vaccination, usually mild symptoms that were not disabling.

During August and September 1976 trials were conducted at Canadian Forces Base Trenton to evaluate antibody response to bivalent A/Victoria/76 and A/New Jersey/76 influenza virus vaccines and to two strengths of monovalent A/New Jersey/76 vaccine (Dr. Shirley Johnson, Connaught Laboratories, Toronto: personal communication, 1977). These preparations were part of the initial lots produced by Commonwealth Serum Laboratories, Melbourne, Australia, and were tested mainly to determine the appropriate strength of vaccine commensurate with adequate antibody response and to evaluate reactogenicity prior to the issuing of a notice of compliance by the food and drug directorate of Health and Welfare Canada. Those trials and the vaccination program we conducted are not totally comparable. Our program was not planned as a controlled trial; an unvaccinated control group was not studied and blood was not collected for determination of antibody response. The Trenton trial evaluated three products, only one of which we used; hence we can compare our findings only with those for the persons at Trenton receiving the same vaccine in the same strength — monovalent A/New Jersey/76 whole-virus vaccine supplying 200 CCA units per dose.

The reporting of symptoms among the 81 individuals who received the same vaccine in the same strength as our subjects is shown in Table II. Fever, chills and malaise were the most common complaints of the 47 persons in the Trenton group who reported symptoms; all other symptoms were much less frequent than in the Kingston group.

This finding is likely due to the age difference in the two study populations, which is apparent from Table I. Although the Trenton group had a similar age range (18 to 55 years) the proportion aged less than 25 years was much smaller than in our follow-up group (78% v. 73%). This difference is important since it

has been shown that previous exposure to influenza viruses conditions the anamnestic response to active immunization by any type A influenza virus vaccine. An older individual has had more such exposure and therefore will have lesser reactions to new active antigens.[1-3]

Furthermore, persons aged 25 years or more have usually had some exposure to the hemagglutinin antigens H0 and H1. An antigenic relation has been demonstrated between the two human strains carrying these antigens, which appeared in 1931 and 1947 respectively, and the swine/Wisconsin/30 strain; it is believed that the hemagglutinins are related.[4,5] The swine/Wisconsin/30 strain is clearly related to the A/New Jersey/76 or A/swine strain.

The proportion of persons aged 20 to 24 years reporting side effects was higher in the Trenton group than in our group, and the proportion aged 40 to 49 years was much higher in the Trenton group. These differences probably reflect the more assiduous reporting of very mild symptoms by the personnel monitoring the Trenton trial.

The fact that the persons in the Trenton trial received their vaccine with a "jet-injector gun", whereas our patients received a subcutaneous injection with needle and syringe, is a most unlikely explanation for the observed differences in frequency of clinical reactions.

After about 12 weeks of observation no persons in our study had presented with symptoms of Guillain–Barré syndrome.

Hence, as in recent reports,[6,7] our data suggest that there is a low morbidity associated with A/swine influenza virus vaccination.

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BOOKS

This list is an acknowledgement of books received. It does not preclude review at a later date.

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