Evaluation of adverse events after influenza vaccination in hospital personnel

David W. Scheifele, MD; Gordean Bjornson, BSc, MBA; Joyce Johnston, RN, PHN

Reactogenicity of trivalent influenza vaccine prepared for the 1988–89 season was assessed as part of a first-time voluntary influenza prevention program among hospital staff. Of approximately 500 full-time workers in areas with the highest concentrations of patients at high risk for influenza complications offered the vaccine 288 accepted. Of these, 266 (92%) returned a questionnaire regarding any symptoms experienced within 48 hours after vaccination; 238 (90%) of the respondents reported adverse effects. Soreness at the injection site was described by 229 subjects, 58 (25%) of whom had constant aching and 123 (54%) soreness with arm movement. Symptoms resolved in 1 to 2 days, and only 21 (9%) of those who reported symptoms said they took analgesic medication. Systemic adverse effects were described by 130 subjects (49%). Intercurrent illness accounted for some of these complaints, but 65 people (24%) described at least two of the following symptoms: generalized aching, tiredness, nausea, chills or onset of fever within 12 hours after vaccination (a symptom complex previously attributed to influenza vaccine). Systemic symptoms resolved within 0.5 to 2 days. Thirteen subjects (5%) reported missing work because of arm soreness (1 subject) or systemic symptoms (12). Adverse effects were encountered more often than expected, probably because most of the workers were young and lacked immunity to influenza. Acceptability of the program could likely be improved by using a split-virus vaccine.

Le caractère réactogène du vaccin grippal trivalent préparé pour la saison 1988–89 a été évalué dans le cadre d'un programme volontaire de prévention de la grippe entrepris pour la première fois sur du personnel hospitalier. Des quelque 500 personnes travaillant à temps plein dans des secteurs à forte concentration de patients présentant de hauts risques de complications de la grippe 288 ont accepté d'être vaccinées. De ce nombre 266 (92%) ont retourné le questionnaire qui leur avait été remis et qui portait sur les symptômes ressentis dans les 48 heures suivant la vaccination; 238 (90%) des répondants ont fait état de quelques effets secondaires. Une douleur au point d'injection a été rapportée par 229 sujets; pour 58 (25%) d'entre eux la douleur était persistante, et pour 123 autres (54%) la douleur apparaissait dans le bras lors du mouvement. Ces symptômes ont disparu en 1 ou 2 jours, et seulement 21 (9%) de ceux qui s'en sont plaints ont pris des analgésiques. Des réactions systémiques ont été décrivées par 130 sujets (49%). Quelques-uns ont fait état de maladies concomitantes, mais 65 (24%) ont mentionné au moins deux des symptômes suivants: douleur sourde généralisée, fatigue, nausée, frissons ou début de fièvre dans les 12 heures ayant suivi la vaccination (un symptôme complexe antérieurement attribué au vaccin grippal). Ces symptômes systémiques ont disparu dans 0.5 à 2 jours suivants. Treize sujets (5%) ne se sont pas rendus au travail, soit à cause de la douleur localisée dans le bras (1 personne), soit à

From the Vaccine Evaluation Center and the Department of Pediatrics, British Columbia's Children's Hospital, the Employee Health Unit, University Hospital — Shaughnessy site, and the University of British Columbia, Vancouver

Reprint requests to: Dr. David W. Scheifele, Director, Vaccine Evaluation Center, Rm. 303, British Columbia's Children's Hospital Research Center, 950 W 28th Ave., Vancouver, BC V5Z 4H4

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cause de symptômes systémiques (12). Les effets secondaires se sont révélés plus répandus que prévu, probablement parce que la plupart de ces volontaires étaient jeunes et n'avaient pas une bonne immunisation contre la grippe. Ce genre de programme pourrait être mieux accepté si l'on avait recours à un vaccin à virus sous-unitaire.

Vaccination is a useful but underused means of preventing the illness and death associated with influenza. Most likely to benefit from vaccination are people at high risk for complications of influenza because of underlying lung, heart or other chronic disorders. Protection after vaccination is not complete, but it can be supplemented through vaccination of the household members and the health care personnel most likely to interact with those at high risk.

In Canada the National Advisory Committee on Immunization[1] has recommended that hospital personnel and other health care professionals who work with people at high risk for influenza complications be vaccinated annually. This strategy is intended not only to decrease the likelihood of patients being exposed to infected personnel but also to reduce the number of work days lost by personnel as a result of influenza. This is particularly advantageous in critical care areas, where function can be impaired by high rates of absenteeism.[2]

Influenza vaccination programs for hospital workers have not yet become routine in most Canadian hospitals. The plan to introduce such a program is likely to be met by numerous questions from the medically sophisticated target population about adverse reactions to the vaccine. Employers may have concerns about potential vaccination-related work loss. We introduced a program in the fall of 1988 and evaluated adverse reactions to the vaccine.

Methods

Trivalent influenza (whole-virion) vaccine prepared for the 1988–89 season was donated by Connaught Laboratories Ltd., Willowdale, Ont., and the Vancouver City Health Department. Vaccine was given at daily clinics held during the first 3 weeks of November in convenient locations within the hospital and at times convenient to workers on all shifts. Promotion consisted of general notices, individual memos and information meetings. For this initial program we invited only full-time employees working in the areas of British Columbia's Children's Hospital that contained the highest concentrations of patients at high risk for influenza complications; these areas included the Special Care Nursery, the Intensive Care Unit, the Oncology Service, the Cardiology Service, the Cystic Fibrosis Clinic, the Allergy Clinic and the Emergency Department. Only personnel in direct contact with patients were invited to take part; these included physicians, nurses, laboratory staff, therapists and radiographers.

The vaccine was injected into the deltoid muscle by nurses of the Employee Health Unit. Pregnancy and allergy to eggs were contraindications to vaccination.

Each subject was asked to complete a questionnaire at home regarding any symptoms of illness experienced during the 48 hours after vaccination and to return it to a special box in the hospital lobby. Reminders were sent to those who failed to reply within 1 week. In prevaccination counselling, volunteers were told that adverse reactions were infrequent: about 30% might have minor local soreness, and fewer than 5% might experience brief systemic symptoms.

Results

Influenza vaccine was administered to 288 of approximately 500 eligible employees. The mean age was 35.5 years. Completed questionnaires were returned by 266, for a response rate of 92%. Most were returned within 1 week; all were returned within 4 weeks. Of the vaccinees 46% were nurses, 10% laboratory staff, 9% physicians and 35% others (e.g., physiotherapists, respiratory therapists, child life specialists and radiologists). The 123 nurses represented 13 hospital areas (an average of 9.5 nurses per area); the largest group comprised 20 nurses from the Special Care Nursery. Only 41 respondents (15%) had previously received influenza vaccine. The vaccine was reported to have been received before or during the work day by 85% of the subjects and at the end of the shift or on days off by 15%.

Adverse effects were reported by 238 (90%) of the respondents (Table 1). Complaints related to the injection site predominated, being present in 232 subjects (87%). Of the 229 subjects who reported soreness at the injection site (Table 2) the maximum pain was described as constant aching by 58 (25%), soreness with arm movement by 123 (54%) and

Table 1: Outcome of voluntary influenza vaccination program among 266 hospital workers

Outcome	No. (and %) of subjects
No adverse effects reported	28 (10)
Injection site morbidity only	108 (41)
Local and systemic adverse effects	124 (47)
Systemic adverse effects only	6 (2)

soreness only to touch by 48 (21%). The pain persisted 1.5 days on average. Of those who reported such symptoms, only 21 (9%) had taken an analgesic. About 20% of those with local soreness also had local redness, swelling or both.

Systemic adverse effects were described by 130 respondents (49%), usually in association with local symptoms (Table 1). Systemic effects were most often multiple (Table 2); the commonest cluster, reported by 65 subjects (24%), consisted of at least two of the following symptoms: generalized aching, tiredness, nausea, chills or onset of fever within 12 hours after vaccination (a symptom complex previously attributed to influenza vaccine). Fever was reported by 35 of those with systemic complaints, but we had not asked subjects to test themselves routinely for fever. Other commonly reported symptoms were headache and dizziness or lightheadedness.

Sixteen subjects reported missing work because of symptoms they attributed to vaccination. In three the symptoms likely resulted from intercurrent infections: bronchitis, beginning 5 days after vaccination; cold, lasting 6 days; and respiratory symptoms, lasting 6 days. Of the other 13 subjects 12 missed work because of systemic adverse effects and 1 because of arm soreness. One person became ill on the day of vaccination, and the others missed work the following day. We believe that each of these subjects missed a single work day following vaccination but lack complete information on this point.

Table 2: Adverse effects reported by 266 recipients of influenza vaccine

Adverse effect	No. (and %) of subjects
Injection site	
Any soreness	229 (86)
Soreness to touch*	48 (18)
Soreness with arm movement*	123 (46)
Constant aching*	58 (22)
Redness	42 (16)
Swelling	52 (20)
Systemic effects	
Any	130 (49)
Fever	35 (13)
Chills	16 (6)
Aching or myalgia	39 (15)
Tiredness or weakness	28 (10)
Nausea	28 (10)
Headache	20 (8)
Lightheadedness or dizziness	16 (6)
Sore throat, runny nose or both	10 (4)
Stomach upset or cramps	5 (2)
Vomiting	1 (0.4)
Painful neck glands	2 (0.8)
Insomnia	2 (0.8)
None	28 (10)

*Maximum pain reported.

Discussion

On the basis of information provided in the manufacturer's product monograph, by the National Advisory Committee on Immunization[1] and by the US Public Health Service[3] we expected that soreness at the injection site would occur in fewer than one-third of the vaccinees and that systemic symptoms would occur infrequently, possibly in about 5%.[4,5] We were surprised when nearly 90% of the subjects reported some type of adverse effect, although we asked them to report even minor complaints. Bothersome arm soreness (i.e., constant aching or soreness with movement) was reported by 68% of the respondents. Only 9% of those who reported pain took analgesic medication, and only one subject reported missing work because of arm soreness. Since most of the subjects were injected before or during their work shift they may have been more aware of local soreness, or work-related arm use could have increased its severity. In vaccination studies that included a saline placebo local soreness was reported by 35% to 44% of the placebo recipients.[6,7]

The occurrence of fever, malaise, headache and myalgia beginning 6 to 12 hours after vaccination is well known; the incidence rate is usually reported to be 1% to 7%.[3,5,6] However, two studies have indicated that the age of recipients is important in the development of systemic reactions. Wise and associates[8] reported that the rate was 32% among subjects 18 to 34 years old, as compared with 7% among those more than 35 years old ($p < 0.0005$). Mostow and colleagues[9] reported that 37% of hospital workers under 25 years of age experienced myalgia or malaise, as compared with 21% of those over 40 years ($p < 0.0001$). Older recipients were more likely to have pre-existing antibodies to vaccine components,[8] which may neutralize their reactogenic properties. The relative youth of our subjects and the small number of those who had been previously vaccinated may explain the high incidence (24%) of reported myalgia or malaise.

Some of the reported systemic symptoms, such as stomach cramps, sore throat and coryza, were likely coincidental. Without a placebo control group, vaccination cannot accurately be separated from intercurrent illness as the cause of the excess morbidity. Hospital-based preventive programs do not involve placebo control groups, and program acceptability is judged by participants on the basis of what they experience in the days after vaccination, whether fairly attributed to vaccine or not. The conduct of our program in November, when the season for winter colds was under way, may explain why nearly 5% of the subjects reported the onset of respiratory symptoms within 48 hours after vaccination. Since

influenza vaccine is inactivated it could not have been responsible for such illnesses; however, such misperceptions can tarnish the reputation of the vaccine.

Sixteen subjects (6%) reported missing work because of symptoms they attributed to vaccination, but in three the symptoms clearly indicated intercurrent respiratory tract infection. Mostow and colleagues[9] noted an absenteeism rate of 8.9% among 1565 hospital workers given whole-virus vaccine. The baseline absenteeism rate was not established in either study.

We have no reason to believe that our experience with an influenza prevention program was atypical, apart from being offered for the first time. Participation was voluntary and evenly distributed over a month-long series of clinics. Subjects worked in 15 or more areas of the hospital; thus, the exchange of information would have been limited. There was no apparent hysteria about vaccine-associated adverse reactions in any area group. The type of vaccine in our study was extensively used elsewhere in Canada, and our stock was properly stored. Injections were given by experienced nurses. Prevaccination counselling about adverse reactions was provided in a low-key manner, intended to be reassuring.

To place the experience in perspective we asked the subjects if they would accept influenza vaccine again next year: 91% said "Yes". Further, 92% said they would encourage their colleagues to receive it. We believe the following measures might reduce the incidence of adverse reactions.

- The use of a split-virus vaccine may be advantageous for a new program because of the vaccine's reduced reactogenicity.[1,9] In studies involving young adults this strategy has resulted in reaction rates comparable to those reported by placebo recipients.[8,10]
- Employees should be encouraged to receive the vaccine near the end of their regular work shifts or just before scheduled days off; this would enable those experiencing adverse effects to rest and recover at home.
- The program should be held early in the fall to minimize coincidental association with respiratory tract infections.

Compared with illness associated with influenza the adverse effects in our study were relatively minor and short-lived. We have no hesitation in continuing to support influenza prevention programs for hospital workers, but we plan to take steps to improve the acceptability of our program.

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