Prevalence of antibody to current influenza virus strains in a 1992 Canadian serosurvey and crude estimates of 1991-92 season A/Beijing/353/89 infections

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JM WEBER. Prevalence of antibody to current influenza virus strains in a 1992 Canadian serosurvey and crude estimates of 1991-92 season A/Beijing/353/89 infections. Can J Infect Dis 1993:4(5):267-271.

OBJECTIVES: The annual influenza serosurvey was conducted to monitor influenza activity and gauge susceptibility to currently circulating and emerging influenza viruses. **DESIGN:** Six hundred and thirty sera from among specimens received for various tests were selected from all age groups and sent with age and geographic identifiers to the Laboratory Centre for Disease Control. Forty sera per province were selected during a one-week period beginning May 31, 1992 except for the province of Alberta which submitted 80 specimens, and Ontario and Quebec which each submitted 160 sera during a four-week period. Sera were tested for hemagglutination inhibiting (HI) antibodies against the 1992-93 vaccine strains and A/Taiwan/1/86 (H_1N_1). **MAIN RESULTS:** The percentage of sera from all ages having HI antibody to A/Beijing/353/89 (H_3N_2) at a titre of 1:40 or greater more than doubled from 22% in the 1991 sample to 53% in 1992. The percentage of sera in all ages having antibody titre at 1:40 or greater to H_1N_1 strains A/Texas/36/91 and A/Taiwan/1/86 was 55% and 57%, respectively, in 1992, up from 45% with antibody titre 1:40 or greater to A/Taiwan/1/86 in 1991. Twenty-seven per cent of sera had antibody titre 1:40 or greater to B/Panama/45/90 compared with 19% in 1991. **CONCLUSION:** The relative increase in the percentage of sera with antibody with a titre of 1:40 or greater likely reflected vaccination efforts and the relative level of activity of the various influenza types and subtypes during the 1991-92 influenza season. The data also suggested that influenza B had the greatest potential for significant activity during the 1992-93 influenza season. *(Pour résumé, voir page 268)*

Key Words: *A/Beijing/353/89, Immunity, Infection, Influenza, Serosurvey*

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Prévalence de l'anticorps dirigé contre les souches courantes du virus de l'influenza dans une enquête canadienne menée en 1992 et estimations quant aux infections à A/Beijing/353/89 pour la saison 1991-1992

OBJECTIF: Une enquête épidémiologique annuelle sur l'influenza a été menée afin de surveiller l'activité de ce virus et la sensibilité de la population aux virus de l'influenza existants et émergents. **MODÈLE:** Six cent trente spécimens sériques obtenus lors de divers tests ont été sélectionnés parmi tous les groupes d'âge et envoyés au Laboratoire de lutte contre la maladie (LCDC), avec des marqueurs d'âge et des marqueurs géographiques. Quarante spécimens ont été sélectionnés par province durant une période d'une semaine commençant le 31 mai 1992, à l'exception de la province de l'Alberta qui a soumis 80 spécimens et de l'Ontario et du Québec qui ont chacun soumis 160 spécimens durant une période de quatre semaines. Les spécimens ont été analysés à l'égard des anticorps HI contre les souches de vaccin 1992-1993 et A/Taiwan/1/86 (H_1N_1). **PRINCIPAUX RÉSULTATS:** Le pourcentage des spécimens de tous âges porteurs des anticorps HI anti A/Beijing/353/89(H_3N_2) à un titrage de 1:40 et plus ont plus que doublé, passant de 22 % en 1991 à 53 % en 1992. Le pourcentage de spécimens provenant de tous les âges porteurs de titres d'anticorps de 1:40 ou plus et dirigés contre les souches H_1N_1 A/Texas/36/91 et A/Taiwan/1/86 ont été de 55 % et de 57 % respectivement en 1992, comparativement à 45 % avec un titrage d'anticorps de 1:40 ou plus dirigé contre A/Taiwan/1/86 en 1991. Vingt-sept pour cent des spécimens détenaient des titres d'anticorps 1:40 ou plus contre B/Panama/45/90 contre 19 % en 1991. **CONCLUSIONS:** L'augmentation relative du pourcentage de spécimens pourvus d'anticorps avec titrage à 1:40 ou plus a probablement reflété le travail de vaccination et les données relatives à l'activité des divers types d'influenza et de leurs sous-types durant la saison d'influenza 1991-1992. Les résultats ont également suggéré que l'influenza B était doté du potentiel le plus important à l'égard d'une activité importante durant la saison 1992-1993.

THE CANADIAN INFLUENZA SEROSURVEY WAS BEGUN IN 1976. It is one of the surveillance systems used to monitor influenza activity and gauge susceptibility to currently circulating and emerging influenza virus strains. Similar serosurveys are conducted in France and Norway as part of their influenza surveillance systems. In Canada, the influenza serosurvey is part of an annual collaborative influenza surveillance program between provincial laboratories and the Laboratory Centre for Disease Control (LCDC).

MATERIALS AND METHODS

The sampling method does not ensure representation of the entire population but incurs relatively little cost, as sera are aliquots of specimens already submitted to the laboratories for routine monitoring of patient health, screening tests or other diagnostic reasons. Six hundred and thirty sera with age and geographic area identifiers were submitted to the Bureau of Microbiology, LCDC by the provincial public health laboratories.

Laboratories selected 10 sera from each of four age groups (0 to 14 years, 15 to 34 years, 35 to 64 years, and 65 years and older) from among specimens received during a one-week sampling period starting May 31, 1992. The provincial laboratories of public health for Northern Alberta and Southern Alberta each submitted 40 sera. For Ontario and Quebec, a four-week collection period was used so that their relatively larger populations would have a correspondingly larger representation in the total data. The sera collection dates were chosen to fall between influenza seasons and to precede the 1992 vaccine release date. These sera were tested for hemagglutination inhibiting (HI) antibodies against the 1992-93 influenza vaccine strains: A/Beijing/353/89 (H_3N_2); A/Texas/36/91 (H_1N_1); B/Panama/45/90; and A/Taiwan/1/86 (H_1N_1). A similar sample of 640 sera had been collected, beginning on June 4, 1991, and similarly tested against 1991-92 vaccine antigens.

For 1991 and 1992 influenza survey sera, the percentage of samples having titres of 1:40 or greater by the HI antibody test were calculated. HI antibody titres of 1:40 or greater following vaccination have been associated with reduced influenza illness and infection and are widely presumed to indicate some degree of protection against similar strains (1).

RESULTS

Influenza (H_3N_2) immunity: From the data in Table 1 and Figure 1A (all regions), it can be seen that for age group 0 to 14 years there was nearly a threefold increase (from 25% in 1991 to 74% in 1992) in the percentage of sera with protective antibody titre of 1:40 or greater to A/Beijing/353/89 (H_3N_2). The two age groups 15 to 34 and 35 to 64 years showed increases in percentages of sera with protective antibody of greater than twofold and just under twofold for the group aged greater than 65 years (Table 1).

The data of Table 2 show the percentage of sera by age group and geographic region having HI antibody to A/Beijing/353/89 (H_3N_2)-like strains. Comparison of the data for 1992 and 1991 (2) is presented in Figure 1. In each region, the most dramatic differences are among those aged 0 to 14 years. However, in every age group, and in every region except for age groups 15 to 34 and 35 to 64 years in the Atlantic region, there were large increases in the percentages of individuals with HI antibody titres of 1:40 or greater to A/Beijing/353/89 (H_3N_2)-like viruses in 1992 (Figure 1B,C,D,E). This

TABLE 1
Percentage of sera by age group and year having hemagglutinating inhibiting antibody to current influenza strains at a titre of 1:40 or greater

Age group (years)	Number of sera tested	Year	Number and percentage (rounded) A/Beijing/353/89 (H_3N_2)	A/Taiwan/1/86 (H_1N_1)	A/Texas/36/91 (H_1N_1)	B/Panama/45/90
0-14	134	1991	33 (25%)	65 (49%)	–	25 (19%)
	138	1992	102 (74%)	78 (57%)	80 (58%)	39 (28%)
15-34	170	1991	28 (16%)	82 (48%)	–	29 (17%)
	170	1992	65 (38%)	93 (55%)	83 (49%)	34 (20%)
35-64	170	1991	25 (15%)	47 (28%)	–	14 (8%)
	161	1992	60 (37%)	78 (48%)	70 (43%)	31 (19%)
65+	166	1991	56 (34%)	91 (55%)	–	55 (33%)
	161	1992	107 (66%)	112 (70%)	112 (70%)	64 (40%)
All ages	640	1991	142 (22%)	285 (45%)	–	123 (19%)
	630	1992	334 (53%)	361 (57%)	345 (55%)	168 (27%)

TABLE 2
Percentage of sera by age group and region having hemagglutination inhibiting antibody to current influenza strains at a titre of 1:40 or greater

Age group	Number and percentage (rounded) A/Beijing/353/90 (H_3N_2) Western provinces	Ontario	Quebec	Atlantic provinces	A/Texas/36/91 (H_1N_1) Western provinces	Ontario	Quebec	Atlantic provinces	B/Panama/45/90 Western provinces	Ontario	Quebec	Atlantic provinces
0-14	37/46	27/40	15/21	23/31	34/46	22/40	7/21	17/31	12/46	9/40	8/21	10/31
	80%	68%	71%	74%	74%	55%	33%	55%	26%	23%	38%	32%
15-34	28/50	14/40	13/40	10/40	32/50	16/40	16/40	19/40	10/50	7/40	7/40	10/40
	56%	35%	33%	25%	64%	40%	40%	48%	20%	18%	18%	25%
35-64	20/50	19/40	11/40	10/31	28/50	17/40	14/40	11/31	12/50	11/40	4/40	4/31
	40%	48%	28%	32%	56%	43%	35%	35%	24%	28%	10%	13%
65+	36/49	21/40	24/38	26/34	40/49	23/40	20/38	29/34	31/49	8/40	12/38	17/34
	73%	53%	63%	76%	82%	58%	53%	85%	63%	20%	32%	50%
All ages	121/195	81/160	63/141	69/136	134/195	78/160	57/141	76/136	65/195	35/160	31/141	41/136
	62%	51%	45%	51%	69%	49%	40%	56%	33%	22%	22%	30%

change in immune status since the beginning of the 1991-92 season is consistent with surveillance data (3) indicating that more than 95% of the 1347 cases of laboratory confirmed influenza were influenza A, and virus isolation data (4) indicating that by far the predominant influenza A strain was A/Beijing/353/89 (H_3N_2)-like.

Crude estimates of past season influenza A/Beijing/353/89 (H_3N_2)-like infections in Canada: Crude estimates of the number of influenza A/Beijing/353/89 (H_3N_2)-like infections during the 1991-92 season may be obtained based on the limited data available. The data of Table 1 indicate that there was an additional 49% of the samples of the 1992 sera from the under-15 year age group that had an antibody titre of 1:40 or greater to A/Beijing/353/89 (H_3N_2) compared with the 25% of samples that had this level of antibody in this age group in 1991. If these samples and their results could be assumed to reflect the change in immune status in those under 15 years of age, and it was further assumed that immunization played little role in the change of immune status, the data would then imply that nearly one of every two, or two-thirds of all susceptible individuals, of the 5.5 million in this age group (5) were infected by A/Beijing/353/89 (H_3N_2)-like virus this past season, leaving only 26% without protective antibody.

It is recognized that the sampling protocol does not provide a truly random sample, that there are weighting biases in the sampling and thus considerable uncertainty in extending the sample findings to the population as a whole. Nevertheless, if the estimated population number (5) in each age group of Table 1 is multiplied by the difference in proportion of sample from that age group that has protective antibody in 1992 relative to 1991, the result is an estimate of 9.4 million more people in 1992 having HI antibody titres of 1:40 or greater to A/Beijing/353/89 than in 1991.

One estimate is that 3.6 million doses of influenza vaccine were distributed in Canada in 1991. If one assumes that 20% of people vaccinated were already immune to A/Beijing/353/89 (Table 1) and another 20% of those vaccinated would not have achieved or maintained an HI antibody titre of at least 1:40 to A/Bei-

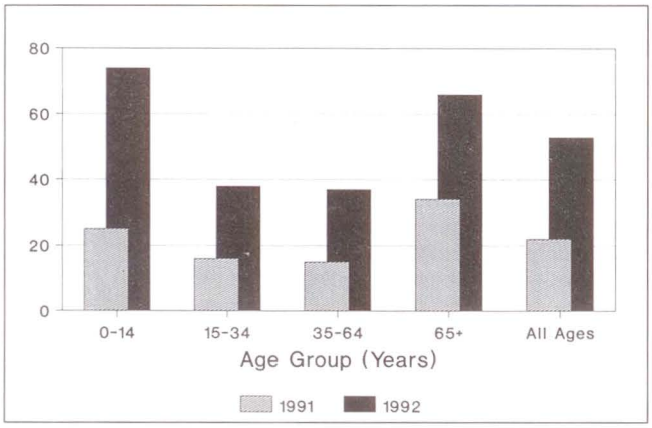

Figure 1A) *Percentage of sera by age group with protective antibody to A/Beijing/353/89 (all regions)*

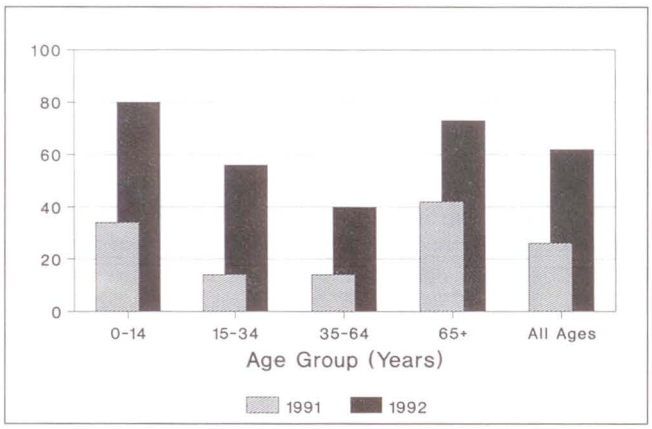

Figure 1B) *Percentage of sera by age group with protective antibody to A/Beijing/353/89 (western provinces)*

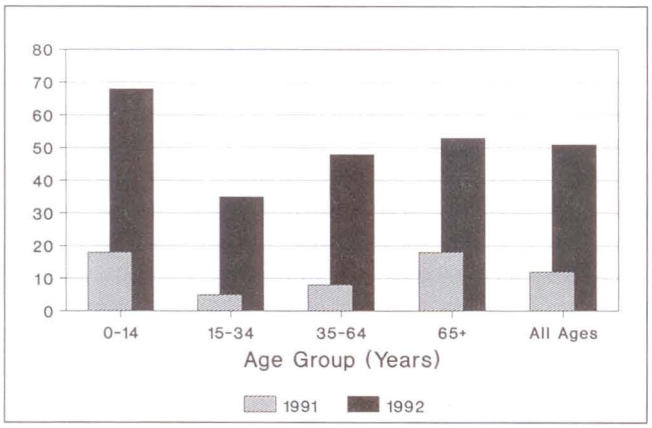

Figure 1C) *Percentage of sera by age group with protective antibody to A/Beijing/353/89 (Ontario)*

jing/353/89 when the serum samples were taken, then the antibody titre of about 60% (2.16 million) of people vaccinated may have risen to at least 1:40 between the 1991 and 1992 sampling times. This figure subtracted from the original estimate of 9.4 million more people having HI antibody titres of 1:40 or greater to A/Beijing/353/89 in 1992 relative to 1991 leaves an estimate of influenza A/Beijing/353/89 infections exceeding 7 million, or about 26% of the Canadian population. An

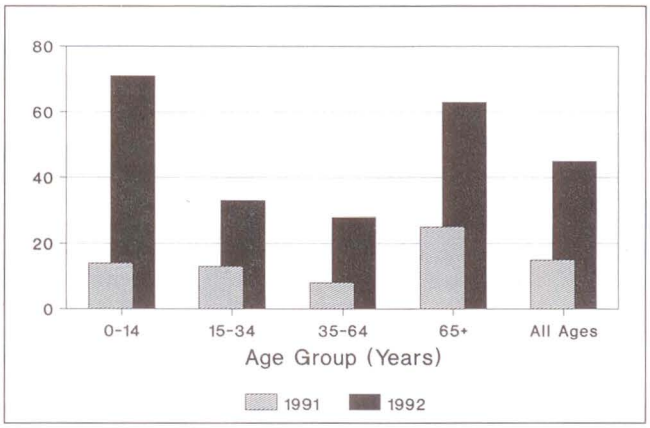

Figure 1D) *Percentage of sera by age group with protective antibody to A/Beijing/353/89 (Quebec)*

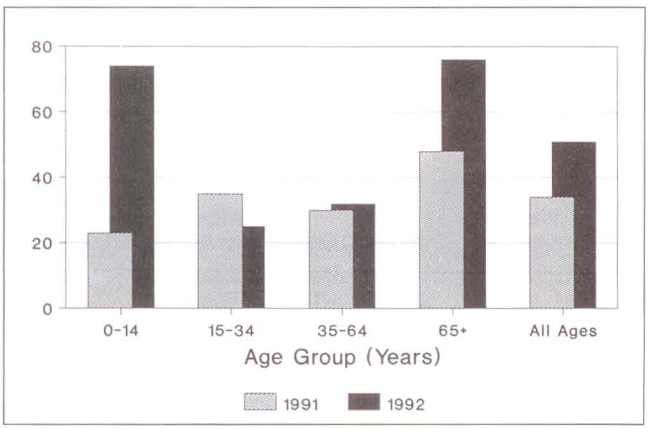

Figure 1E) *Percentage of sera by age group with protective antibody to A/Beijing/353/89 (Atlantic provinces)*

unknown proportion of these infections may have been subclinical. However, 7 million infections have a major effect, without considering the additional impact of influenza A (H_1N_1) or influenza B infections, on lost school and work time, medical and hospitalization costs and influenza-pneumonia related deaths.

Influenza A (H_1N_1) immunity: There were 13 isolations of influenza A (H_1N_1)-like viruses throughout the 1991-92 season, most of these being A/Taiwan/1/86 (H_1N_1) (4). Between the years 1991 and 1992 there was a variable degree of increase in the percentage of samples with protective antibody to A/Taiwan/1/86 in all age groups, and the percentage of individuals in the 1992 sample having immunity to A/Taiwan/1/86 and A/Texas/36/91 was similar (Table 1). In the serosurvey data (not shown) it was noted that individuals who had elevated titres to one of the two H_1N_1 test antigens almost always had a similar titre to the other H_1N_1 antigen. This indicates a great deal of cross-reactivity of human serum antibody with both H_1N_1 antigens used in the survey.

Table 2 indicates that the percentage of sera showing immunity to influenza A (H_1N_1) varied greatly between age groups within and between the various regions of Canada. Most influenza A (H_1N_1) isolates came from

western Canada in the 1991-92 season and the highest percentage of immune individuals (53%) (all ages combined) was seen in western Canada, while the lowest percentage immunity levels (all ages combined) occurred in Quebec and Ontario.

Influenza B immunity: From Table 1, it is seen that there were slightly higher percentages of sera with protective antibody titres to B/Panama/45/90 in 1992 compared with 1991. There was relatively little influenza B activity reported in Canada in the 1991-92 season; however, even when the virus was detected during peak season, it was not successfully cultivated for characterization. Therefore, it is possible that there was limited circulation of influenza B that was not readily detected apart from the reported laboratory diagnoses in Newfoundland, Ontario and Manitoba (3). Alternatively, the 8% increase in 1992 in sera having an antibody titre of at least 1:40 may have resulted partially from vaccination.

DISCUSSION

It is unlikely that A/Beijing/353/89 (H_3N_2) will have the same impact in the 1992-93 season as in the previous season because of the relatively high levels of immunity that presently exist, especially in the youngest age group. More than half of the laboratory confirmed cases of influenza with age of patient given occurred in those under 15 years of age (3). However, tests on serosurvey specimens from the 15 to 34 and 35 to 64 year age groups in various regions of the country indicated that there were also significant numbers of susceptible individuals among those sampled (Table 2, Figure 1).

A/Texas/36/91 (H_1N_1) emerged to cause significant infection along with the closely related A/Taiwan/1/86 in the Atlantic and south Atlantic regions of the United States in the 1991-92 season. We found that there was considerable cross-reactivity in human serum antibodies to both H_1N_1 strains used in the survey, and that a moderately high percentage (49 to 57%) of the two younger age group specimens had antibody to these strains. Therefore, the impact of H_1N_1 strains resembling those in the survey was expected to be light to moderate in the 1992-93 season.

For influenza B, it was seen that considerable potential for activity existed given the relatively low percentage of samples (27% over all ages) that displayed protective antibody.

As of February 5, 1993 laboratory isolation/detection surveillance (Peter Zabchuc, Bureau of Communicable Disease Epidemiology, LCDC) indicated that there were 94 influenza B reports and 14 reports of influenza A indicative of a relatively light influenza activity, but with influenza B predominating. Similarly, the 1991 serosurvey data (2) (Table 1) forewarned of the strong influenza A/Beijing/353/89 (H_3N_2)-like activity seen in the 1991-92 influenza season.

Sample size, selection, origin of specimens within a province and test variation limit the degree to which the percentage immunity figures can be taken to represent the precise level of immunity in any one province and individual age group. However, past experience has shown that the serological data tend to reflect the past year's influenza activity or lack of it for the country as a whole, to contribute to improved prediction of the potential for activity in the coming year, to provide early quantification of the need for vaccination, and to provide specific information for risk communications to the media which helps to control the circulation of false or exaggerated rumours.

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