

# Effect of Vaccination of a School-Age Population upon the Course of an A2/Hong Kong Influenza Epidemic \*

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*Children of school age experience the greatest morbidity in influenza outbreaks and are major disseminators of the virus. On this basis, monovalent A2/Aichi/2/68 vaccine was offered to the schoolchildren of Tecumseh, Michigan, to control the anticipated outbreak of Hong Kong influenza. More than 85% of the children were vaccinated. Systemic reactions were rare and 94.5% of those tested exhibited a 4-fold or greater rise in HI titre.*

*The occurrence of respiratory infections in the subsequent outbreak was followed in Tecumseh and the neighbouring unvaccinated community of Adrian, Michigan. Hong Kong influenza virus was isolated during a 10-week period, and, during this time the mean rate of illness in Adrian was 3.0 times higher than in Tecumseh. The protection from illness in Tecumseh was not limited to the vaccinated children; all age-groups experienced lower rates of respiratory infection. Thus vaccination of schoolchildren was shown to produce a marked lowering of illness rates in an entire community.*

Children of school age exhibit the highest attack-rates in influenza outbreaks (Frost, 1920; Parrott & Linder, 1958). They also play a central role in the dissemination of the virus and possibly even in the initiation of the epidemic (Langmuir et al., 1958; Jordan, 1960). Vaccination of schoolchildren should therefore protect the most susceptible segment of the population against the disease and prevent further transmission of the virus to others. Although administration of vaccine to schoolchildren is readily accomplished, this method for community modification of an influenza outbreak has not previously been attempted (Francis, 1967).

The major antigenic shift of influenza virus of 1968 made it likely that an epidemic with a high attack rate would occur. Specific Hong Kong influenza vaccine was available but the supply was so limited that all persons receiving it could easily be identified. These factors contributed to the feasibility of the present study. The vaccine, made available through the National Institutes of Health,

contained 400 CCA units of A2/Aichi/2/68 per 0.5 ml; it had been purified in the zonal ultracentrifuge. Tecumseh, Michigan, was selected for vaccination and Adrian, Michigan, was designated as the comparison community.

## THE COMMUNITIES AND METHODS OF SURVEILLANCE

Tecumseh is a city with a population of 7500, located 28 miles (45 km) south-west of Ann Arbor. Data from the city and the surrounding semi-rural areas have been followed since 1959 as a part of a longitudinal investigation of health and disease in a natural community (Francis, 1961). The study area itself contains a population of approximately 10 000. Since 1965, a surveillance of respiratory infections has been under way in a group of Tecumseh families: 60% of them are recruited randomly and 40% are preselected to contain a person with chronic respiratory disease or a matched control. The families are followed for a period of one year, are questioned weekly on the occurrence of acute disease, and when an illness is reported, specimens for microbial isolation are obtained. At the end of the year of surveillance, the family is replaced by another. During the winter of 1968-69, the number of families being followed at any one time was approximately 360.

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The responsible school officials in Tecumseh were consulted concerning their willingness to permit vaccination in the schools during regular hours and to provide daily absence data.

Adrian, Michigan, the county seat of Lenawee County, is a city of 20 000, just 12 miles (20 km) south of Tecumseh. Adrian was selected as the unvaccinated comparison community for 2 reasons. Both cities share places of employment and other facilities, and therefore population interchange is great. A weekly family surveillance was already in progress in Adrian under the auspices of the Michigan Department of Public Health and the Lenawee County Health Department as part of Project ECHO.

The ECHO programme, an acronym for Evidence for Community Health Organization, is being carried out in 7 localities in Michigan using the same format in each. Families are selected from all households in the community by a system of random sampling for 3 weeks' surveillance. They are visited in the first week and are asked the same questions on respiratory illness as are used in Tecumseh. For the following 2 weeks they are telephoned and the questions on respiratory disease are repeated. Each week new households are visited and started on the 3-week cycle to keep the number of households as constant as possible. In the original ECHO protocol, 36 families were under surveillance in Adrian at any time. In anticipation of the Hong Kong influenza outbreak the number was increased to 150 households. As in Tecumseh, arrangements were made in Adrian for collection of school absence data.

#### INOCULATION OF VACCINE AND ANTIBODY RESPONSE

The influenza vaccine was administered in the Tecumseh schools during the week beginning 4 November. A dose of 400 CCA units of A2/Aichi/2/68 in 0.5 ml was given subcutaneously. The community had been well prepared, and participation, based on written parental approval, was excellent: in the elementary schools 91.9% of the enrolment was inoculated. The vaccine was administered to 75% of all high-school students. The over-all rate of acceptance was 85.8%. The total number of doses given was 3159. School absenteeism after vaccination was not significantly increased and, from a limited telephone survey on causes of school absenteeism, it would appear that reactions to vaccination, aside from slight tenderness at the injection site, were infrequent.

Blood specimens obtained before and 2 weeks after vaccination were obtained from 5% of those vaccinated. Results of haemagglutination-inhibition (HI) tests against the homologous antigen showed that although most children had no antibody before vaccination, 4-fold rises in titre occurred in 94.5% of the vaccinated children. The geometric mean post-vaccination titre for the entire school age-group was 61, a level considered to be protective (Salk, Menke & Francis, 1945; Bell et al., 1957).

#### THE HONG KONG INFLUENZA OUTBREAK

The first isolation of Hong Kong influenza in Tecumseh was made from a specimen collected on 18 November, or 2 weeks after vaccination began. Subsequently, the virus was repeatedly isolated and rises in antibody titre were observed in both Adrian and Tecumseh until the week beginning 19 January, a 10-week period. Total school absence rates for this general period in Tecumseh and Adrian are shown in Fig. 1. A line has been drawn at the 8% level which had been established in previous studies as an epidemic threshold value. The initial slight peak of 18 November, the date of the first isolation of influenza, was not maintained in either community. Although influenza was definitely present and 1 school in Adrian had high absenteeism, the 2 curves did not deviate until 9 December. By 11 December the Adrian curve had passed the 8% mark, and rates above 14% were observed from 17 December until 20 December. In January, after the Christmas vacation, the absenteeism in Adrian stayed above 8% for another week.

To enlarge the scope of the analysis to include the experience with adults as well as with children, the weekly reports of total respiratory illness from the Tecumseh and Adrian surveillance programmes were examined. Fig. 2 shows these rates calculated as a 3-week moving mean of all respiratory illnesses per 100 persons contacted. The 21 weeks covered, beginning in the first week of September, were divided into an initial 11-week, base-line period, and starting 17 November, into a 10-week influenza period; the limits of the influenza period were defined by the time of isolation of the virus. Throughout the entire 21 weeks, rates in the ECHO surveillance for Adrian were considerably higher than in the Tecumseh surveillance. Although the questions used in the 2 systems of surveillance to determine if a respiratory illness had occurred were the same, the

FIG. 1  
TOTAL SCHOOL ABSENTEEISM IN TECUMSEH AND ADRIAN, MICHIGAN

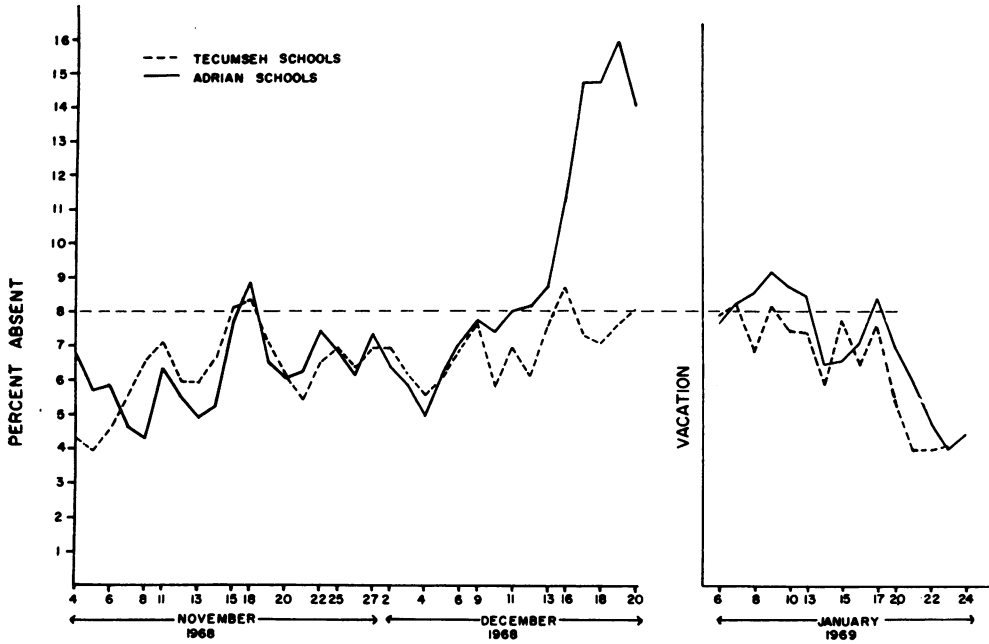


FIG. 2  
INCIDENCE OF RESPIRATORY ILLNESS IN TECUMSEH AND ADRIAN, MICHIGAN: 3-WEEK MOVING MEANS

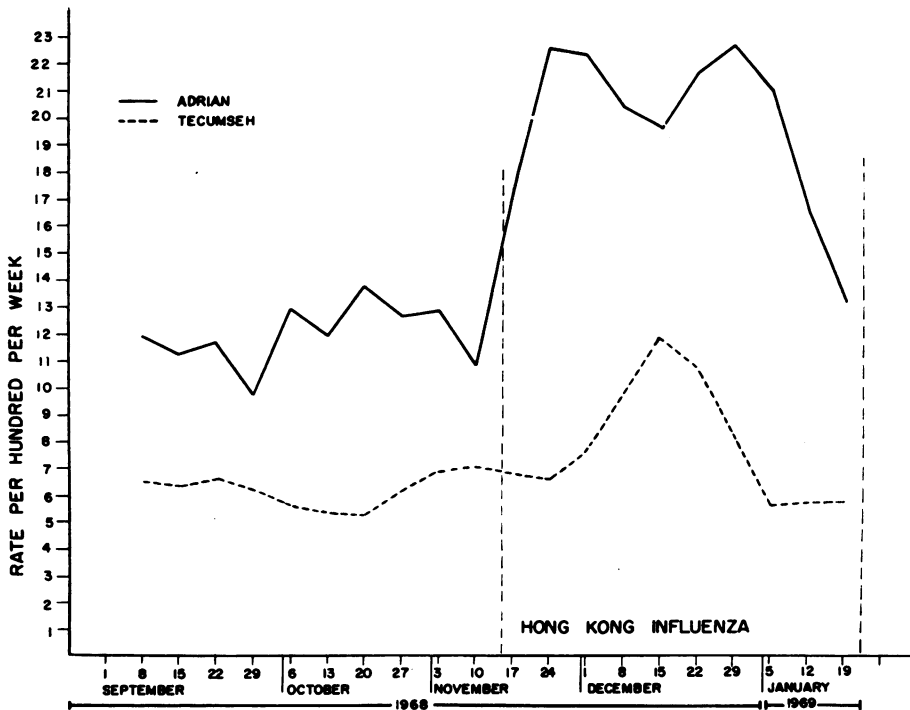


FIG. 3

INCIDENCE OF RESPIRATORY ILLNESS IN TECUMSEH AND ADRIAN, MICHIGAN: ADJUSTED 3-WEEK MOVING MEANS

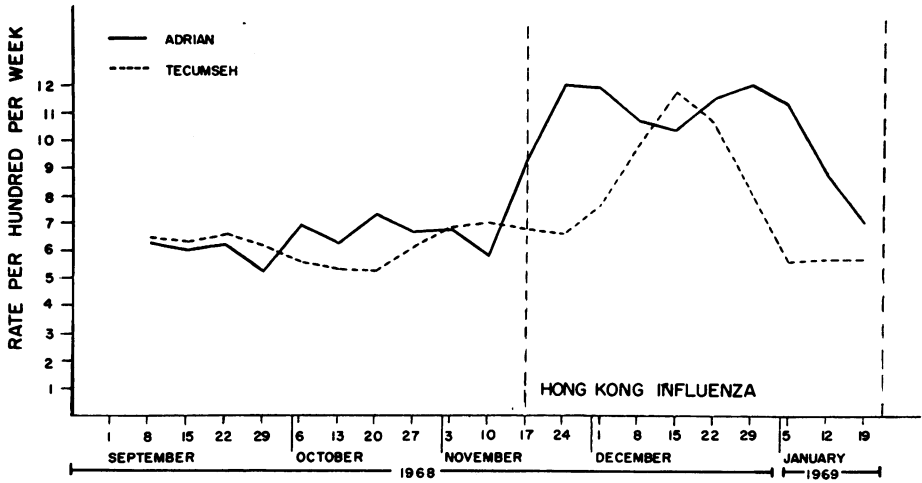
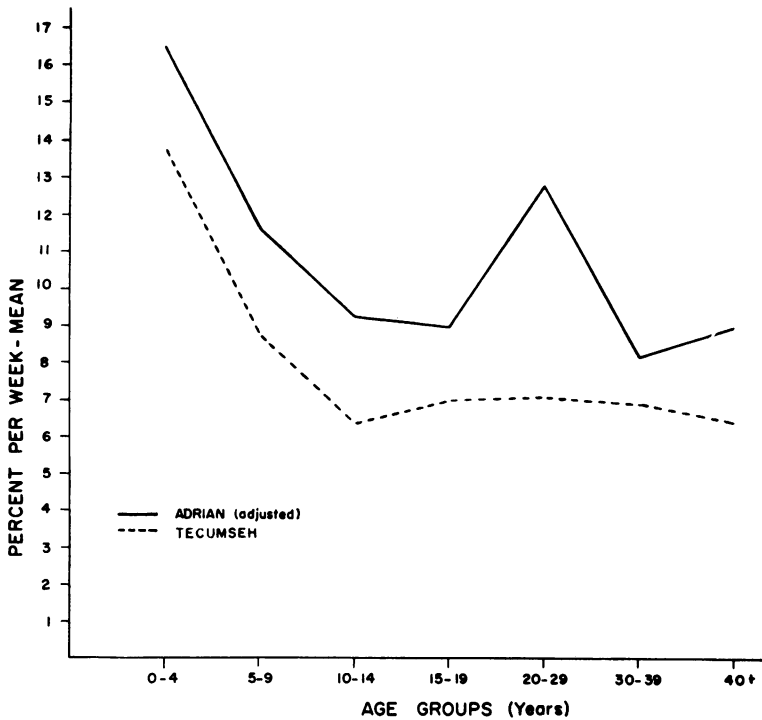


FIG. 4

AGE-SPECIFIC RATES OF RESPIRATORY ILLNESS IN TECUMSEH AND ADRIAN, MICHIGAN, DURING THE INFLUENZA PERIOD



format and follow-up were different. In Tecumseh, a family was followed for a full year, and when an illness was reported in a certain week, a special follow-up series of questions was used in the subsequent week. In Adrian, a family was followed for only 3 weeks, and each week the same questions were used regardless of whether an illness had been previously reported. These differences are believed to have caused over-reporting of illness from Adrian since some of the illnesses may have been counted twice.

During the 11-week base-line period in the early fall, the experience of the 2 communities should have been approximately the same, and the major differences in the reported rates are probably caused solely by differences in the surveillance techniques. This contention is supported by the similarity in the pre-epidemic school-absence data. For the purposes of analysis, it was therefore necessary to bring the rates reported from Adrian to the Tecumseh level. To do so, an adjustment factor was calculated based on the relation of the mean weekly rate for the entire 11-week pre-epidemic period in Adrian to the mean weekly rate for the same base-line period in Tecumseh. Division by this adjustment factor of 1.88 yields a curve for Adrian as seen in Fig. 3. The base-line periods are now similar, but during the influenza period the difference between Adrian and Tecumseh is apparent when the area under the curves is considered.

#### PROTECTIVE EFFECT OF VACCINATION

Clearly, protection by vaccination had been achieved but the crude rates do not identify the benefactors. To determine if protection extended to the adults and pre-school children, age-specific rates were calculated. These rates, shown in Fig. 4, were calculated as a mean of the 10 weekly reports during the influenza period for each age-group in Tecumseh and Adrian. The Adrian rates here are again adjusted by the factor of 1.88. The curve for Tecumseh is consistently lower than the curve for Adrian, emphasizing the difference at all ages. The biggest difference was found in comparisons of persons aged 20-30 years. The young adults in Adrian probably suffered heavily from exposure to their unvaccinated school-age family members.

The protective effect of vaccination even on the unvaccinated people in Tecumseh can be demonstrated in yet another way. In the 5-14-year age-groups, 88.1% of the 464 children under surveillance

were vaccinated. There remained 55 children unvaccinated, a number large enough to allow comparisons to be made. The unvaccinated children reported a weekly mean rate of illness in the pre-epidemic period of 6.1%, only slightly lower than the 6.6% mean rate for the vaccinated children. In the epidemic period, the positions were reversed; the vaccinated children had a weekly mean illness rate of 7.2% and the unvaccinated were definitely higher at 9.0%. However, even this figure was lower than the 10.4% adjusted rate for the same age-groups in Adrian. These findings suggest that the high level of vaccine-induced herd immunity may have given some degree of protection to the unvaccinated children as well.

To obtain a summary evaluation of the effect of vaccination in Tecumseh, the following analytical method was adopted: for Tecumseh, the mean weekly illness rate for the total surveillance population in the base-line period was 6.3% per week, and in the 10-week influenza period, 7.7%. The difference in the 2 rates gives the excess morbidity for the epidemic period, 1.4% per week. The excess attack rate of 14.0% is obtained by multiplying this weekly excess morbidity by 10, the number of weeks in the influenza period.

The same procedure was carried out for the Adrian results, with the only variation being the adjustment throughout by the factor of 1.88. The mean weekly rate for the base-line period is, after adjustment, the same as that for Tecumseh at 6.3%. The mean weekly rate in Adrian for the influenza period is 10.5%, which gives an excess morbidity for the influenza period of 4.2% per week. The excess attack rate for the 10-week influenza period is therefore 42.0%. This rate is 3.0 times the 14.0% excess attack rate in Tecumseh. The data may also be looked at in another way; the excess attack rate in Adrian of 42% was 28% higher than the Tecumseh attack rate. Therefore, had the Adrian rate prevailed in Tecumseh, there would have been 2800 more cases of illness in the total area population of 10 000 during the 10-week period.

It is recognized that influenza outbreaks do not occur with uniform severity in different communities. The striking differences between Tecumseh and Adrian would thus gain further significance if it could be shown that in other nearby communities the epidemic behaviour of influenza was more like that found in Adrian than in Tecumseh. The ECHO project also had surveillance programmes in progress in 6 other communities in Michigan. Data were

obtained from 2 of these cities, Lansing and Flint, and were handled in the same manner as those from Adrian. The rates for Lansing were adjusted by 2.0 and for Flint by 2.2, to bring their base-line periods to the Tecumseh levels. The excess attack rate so calculated for Lansing was 36% and for Flint 31%. These rates are 2.2 times higher for Flint, and 2.6 times higher for Lansing than the 14% excess attack rate of Tecumseh.

#### THE TYPE B INFLUENZA OUTBREAK

Weekly rates of illness returned to the usual seasonal level in both communities after the Hong Kong influenza outbreak. However, they did not remain there for more than a few weeks. Type B influenza was isolated from a specimen collected in Tecumseh on 14 February 1969. It was subsequently isolated on repeated occasions in both Tecumseh and Adrian until the week beginning 16 March 1969, a period of 6 weeks. During this 6-week period, the mean weekly rate of illness in Adrian was 14.8%. When adjusted by the same factor of 1.88 used previously, this rate becomes 7.9%. The mean

rate for the same period in Tecumseh was 7.8% per week. The vaccine used in Tecumseh was mono-valent and no effect against type B influenza would be expected. The nearly identical rates of illness in the 2 towns when neither had the advantage of specific vaccine indicate that the adjustment factor properly corrected for artefacts introduced by differences in the surveillance techniques.

#### CONCLUSIONS

Mass vaccination of schoolchildren against influenza has been found to be feasible. Use of influenza virus vaccine in Tecumseh appears to have altered the pattern of Hong Kong influenza in the entire community. The experience of comparison communities confirms this assertion. Had the attack rate in Adrian prevailed among the 10 000 people living in Tecumseh, there would have been 2800 more cases of illness than were actually experienced during the 10-week epidemic period. While vaccination did not prevent the appearance of influenza in Tecumseh, the community benefited markedly by vaccination of schoolchildren.

#### ACKNOWLEDGEMENTS

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