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Risk of Acute Respiratory Disease among Pregnant Women During Influenza A Epidemics

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Synopsis....................................

The medical literature contains little information on the occurrence of excess morbidity among pregnant women during recent influenza epidemics.

Rates of medical visits for acute respiratory disease (ARD) among pregnant and nonpregnant members of a large prepaid practice population were examined. Use of medical services for ARD was ascertained for approximately 1,000 pregnant women and 3,000 nonpregnant women during each of four epidemic periods (1975, 1976, 1978, 1979) and a nonepidemic period (1977). Comparing the combined epidemic periods with the nonepidemic period, there were significant excesses of 23.7 (standard error (SE) = 8.1) ARD contacts per 1,000 attributable to epidemic influenza for pregnant women and 10.2 (SE = 3.4) for nonpregnant women. ARD hospitalization rates among pregnant women were low (2 per 1,000), and there were no maternal deaths.

The significant ARD excess among pregnant women was concentrated in the 1978 period with reappearance of the A/Russia H1N1 subtype in the community and was confined to those under age 25 who would not have been previously exposed to this subtype (94.4 (SE = 28.5)). These findings indicate that recent influenza epidemics caused only modest excess ARD morbidity among pregnant women, and significant excess occurred only in association with antigenic shift. These findings support current national policy recommendations with respect to influenza vaccination of pregnant women.

Convincing evidence exists that pregnant women experienced abnormally high mortality during the 1918-19 Spanish influenza pandemic (1-4). Subsequent epidemics have not generally been associated with excess maternal mortality, although several investigators have suggested that significant

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excesses occurred during the 1957 Asian influenza pandemic (5–8). Conflicting opinions regarding influenza-related excess morbidity and mortality among pregnant women have been published (9, 10). In the absence of recent evidence of excess risk among pregnant women, the Public Health Service ceased to recommend routine influenza immunization of pregnant women in the early 1970s. The Immunization Committee of the Infectious Disease Society of America recommends that pregnant women be immunized only when a major antigenic variant is introduced into a susceptible population (11).

In this present study, the impact of recent influenza A epidemics caused by strains of the H3N2 subtype of influenza was examined by comparing rates of medical visits for acute respiratory illness among pregnant and nonpregnant women in a large prepaid group practice program during the influenza seasons between 1975 and 1979. Reappearance of the H1N1 subtype in 1978, after more than 20 years' absence, provided the opportunity to contrast its impact with that of the H3N2 subtype, which had been prevalent for several years prior to the study period.

Materials and Methods

Setting and population. The study population was drawn from Kaiser Permanente (KP) Health Plan, Northwest Region, which enrolls more than 270,000 persons in the Portland, OR, metropolitan area. The health plan population, which is derived primarily through worksite subscription, consists of some 15 to 20 percent of the Portland metropolitan population and is broadly representative of the community in demographic terms (12). Since the membership receives essentially all its medical care within the system (13), the medical records provide a highly reliable accounting of utilization. These data have been previously used to document the impact of epidemic influenza on high-risk and non-high-risk adults and children (14, 15).

This study population was composed of 4,666 women who had pregnancy outcomes during January to September in each of the three years, 1975–77, and from February to September in each of the two years, 1978–79, and were enrolled in the health plan during one or more study periods. Of this total, 2,916 were health plan members during the first quarter of 1975; the number of eligible women increased to 4,475 in 1979.

Study Periods. The study periods include three periods of moderate influenza activity during 1975, 1976, and 1978, a period of low influenza activity during 1979 and a nonepidemic period during 1977. The influenza exposure periods were defined as January 27 to March 10, 1975 (Epi 75), January 25 to March 22, 1976 (Epi 76), December 5, 1977 to March 27, 1978 (Epi 78), and January 1 to February 12, 1979 (Epi 79). The nonepidemic period was defined as January 31 to March 28, 1977 (NonEpi 77).

These periods were selected on the basis of the following indices of epidemic influenza in the Portland area:

a. Pneumonia and influenza mortality rates for the Portland metropolitan area, estimated by the Centers for Disease Control, showed marked excesses in Epi 75, Epi 76, and Epi 78, a slight excess during Epi 79, and no excess in NonEpi 77 (16).

b. Reported incidence of acute influenza and influenza-like illness in the state of Oregon and incidences of medically attended influenza and influenza-like illness in KP were high in Epi 75, Epi 76, and Epi 78, moderate in Epi 79, and low in NonEpi 77.

The dominant H3N2 strains isolated from specimens submitted to the Oregon State Health Department's virus laboratory during the study periods were Epi 75-A/Port Chalmers, Epi 76-A/Victoria, Epi 78 and Epi 79-A/Texas. A new H1N1 strain, A/Russia, was frequently isolated during February and March of Epi 78; A/Texas continued to be isolated during this period.

An attempt was made to estimate the separate effects of H3N2 and the new H1N1 influenza on pregnant women by defining two epidemic periods during Epi 78. Based on the bimodal character of

the KP surveillance data and the temporal occurrences of viral isolates in the community, an A/Texas (H3N2) period was defined as December 5, 1977, to January 9, 1978 (Epi 78-T), and an A/Russia (H1N1) period as February 6 to March 27, 1978 (Epi 78-R).

Data collected. Selected for chart review were a 100 percent sample of women having ectopic pregnancies, outside deliveries, spontaneous abortions and stillbirths, and a random sample of 50 percent of women delivering liveborn infants in KP medical centers and having no other type of pregnancy outcomes during the study period. We abstracted data for all pregnancies that occurred during the 5-year period of study, 1975–79, including dates of pregnancy terminations and last menstrual periods. We defined the duration of pregnancy as extending from 2 weeks prior to the date of the last menstrual period up to the date of pregnancy termination. Possible exposure to influenza was quantified by calculating the numbers of trimester-weeks of pregnancy that occurred during the epidemic and nonepidemic periods previously defined.

All medical care services for acute respiratory disease (ARD) that occurred during the epidemic and nonepidemic periods, or up to 3 weeks after the end of the periods, were abstracted by experienced technicians. The ICDA codes for the diagnostic categories of ARD included in the study are given in the box. Data were also abstracted for services at which respiratory or general flu symptoms were noted in the medical chart. Whether the recording of ARD diagnoses and symptoms occurred during medical services for obstetrical care or nonobstetrical care was noted. These data were included to control for the possibility of ARD ascertainment bias due to more frequent opportunities for pregnant women to present illness.

Analysis. Excess rates of medical visits for ARD attributable to pregnancy were estimated by comparing pregnant women with nonpregnant women during the epidemic and nonepidemic study periods. The comparison group for a given period consisted of women who were not pregnant during that period but who were pregnant at other times during the 5 years. Rates of ARD per 1,000 women at risk were calculated for each study period. We calculated rates of total ARD and of the subcategories upper respiratory infection (URI), influenza lower respiratory infections-bronchitis, pneumonia, other viral infections, res-

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piratory tract flu symptoms, and general flu symptoms.

Excess ARD rates attributable to epidemic influenza were defined as the differences between the ARD rates during epidemic periods and the rate during the 1977 nonepidemic period. These excess ARD rates were computed separately for pregnant and nonpregnant women for each epidemic period. Excess ARD rates attributable to epidemic influenza were also calculated for the combined EPI periods. Excess ARD rates attributable to epidemic influenza during the EPI 78-T (Texas) and Epi 78-R (Russia) periods were computed separately for women 25 or younger and 26 or older.

The Standard Normal (Z) test (one-sided) was used to determine the statistical significance of differences between rates. We adjusted ARD rates to a base of 60 days when comparing periods of different duration.

Results

The study included 5,518 pregnancies, 1,277 of which occurred during the 1977 nonepidemic study period. Ninety-five percent of the pregnancies resulted in live births. Spontaneous abortions accounted for 2.6 percent, fetal deaths for 1.3 percent, and ectopic pregnancies for 1.4 percent of the pregnancies. The age distribution of women with pregnancy outcomes in KP was constant from 1975 to 1978. The period vaccination rates were less than 1 percent, except for the nonepidemic period when 6 percent of the study population was vaccinated against swine flu.

Approximately 30 percent of the study population was in some stage of pregnancy during the study periods (epidemic or nonepidemic periods). Of these, a small number had first trimester exposure only. This was to be expected from the manner by which the study population was selected.

Respiratory Disease Categories of the 7th Revision of the International Classification of Diseases Adapted and Kaiser Permanente Symptom Codes

Acute upper and lower respiratory infections 470–475, 476.0–476.9
    Acute nasopharyngitis (common cold) 470.0, 512.1–512.6
    Sinusitis 470.2–471.8
    Pharyngitis 472.0–472.6
    Tonsillitis 473.0–473.6
    Laryngitis and tracheitis 474.0–474.3
    Upper respiratory infection 475.0
    Upper and lower respiratory infection 476.0–476.3
    Bronchitis 500.0–500.4
    Viral infection 096.9
Influenza 480.0–484.1
Pneumonia 490.0–493.9

Respiratory tract flu symptoms include:		General flu symptoms include:	
Rhinorrhea	T284	Fever	T010
Nasal congestion	T290	Chills	T016
Sore throat	T311	Malaise	T066
Cough	T410	Chilliness	T015
Chest pain	T401	Headache	T151
Dyspnea	T417	Myalgia	T701
Cold	T415	Joint pain	T891
		General pain	T001

There were only 17 ARD hospitalizations during the five study periods between 1975 and 1979. No hospitalizations occurred during the 1978 epidemic period, and 3 to 4 occurred during each of the other periods. The overall ARD hospitalization rate was 8.9 per 10,000 women. The sample size was too small to estimate the impact of influenza on hospitalization of pregnant women. This study, therefore, assessed the impact of influenza epidemics on rates of outpatient medical services for acute respiratory disease. For brevity we refer to rates of medical visits for acute respiratory disease as ARD rates.

Excess attributable to pregnancy. Pregnant women experienced a higher total ARD rate than nonpregnant women during each of the study periods (table 1). Virtually none of the ARD diagnoses and symptoms were recorded during obstetrical visits. Therefore, the excess ARD rates cannot be attributed to more frequent opportunities for reporting illness. The excess ARD rate among pregnant women achieved statistical significance during the 1978 epidemic periods Epi 78-T, Epi 78-R, and the combined Epi 78 period. Pregnant women had 70 to 80 excess medical care contacts for ARD per 1,000 women per 60 days during these epidemic periods. The excess ARD

rate among pregnant women compared with nonpregnant women during the 1977 nonepidemic period was also statistically significant, but it was only a third of the 1978 excesses. A small statistically significant excess occurred during the 1976 epidemic period but not during the 1975 and 1979 epidemic periods.

Pregnant women experienced significant excesses of outpatient medical services for flu, URI, respiratory symptoms, and general flu symptoms during the 1978 epidemic period. URI and respiratory symptoms each accounted for approximately 37 percent of the total ARD excess rate; general flu symptoms, 15 percent; and clinically diagnosed flu, 7 percent.

During the 1977 nonepidemic period, the only category with a significant excess was general flu symptoms.

Excess attributable to influenza. Aggregating the 4 epidemic periods gave significant excesses of 23.7 total ARD contacts per 1,000 for pregnant women and 10.2 for nonpregnant women (table 2). The difference between pregnant and nonpregnant excesses 13.5 (SE = 8.8) was statistically significant at the $P = .063$ level. Excess rates in the flu, pneumonia, URI, and respiratory symptom categories for the combined epidemic periods were

Table 1. Rates and excesses of medical visits for acute respiratory disease attributable to pregnancy

Epidemic period	Not pregnant		Pregnant		Excess[3]	
	Rate[1]	SE[2]	Rate	SE	Rate	SE
Epi 75......................	[2]74.7	8.4	75.5	11.7	0.8	14.4
Epi 76......................	70.1	6.5	92.3	11.0	[4]22.2	12.8
NonEpi 77..................	55.5	5.5	78.9	9.5	[4]23.4	11.0
Epi 78-A/Texas.............	69.3	7.4	149.4	15.6	[4]80.1	17.3
Epi 78-A/Russian...........	60.3	5.7	137.7	15.5	[4]77.4	16.5
Epi 78 Combined...........	62.9	4.7	134.4	10.5	[4]71.5	11.5
Epi 79......................	61.3	5.7	102.9	27.4	41.6	28.0

[1] Rate per 1,000 women per 60 days.
[2] Standard error of rate.

[3] Excess equals pregnant rate minus nonpregnant rate.
[4] Statistically significant at 5 percent level (one-sided test).

greater for pregnant than nonpregnant women.

Examination of individual years reveals that essentially all of the statistically significant excess attributable to epidemic influenza occurred during the 1978 period (table 2).

A significant excess ARD rate of 55.5 visits per 1,000 occurred among pregnant women during this epidemic period. The excess rate of 7.4 among nonpregnant women was not statistically significant. The difference between the excess for pregnant and nonpregnant women was 48.1 (SE = 15.9), which is statistically significant. Statistically significant excess rates among pregnant women occurred in the categories of flu, pneumonia, URI, and respiratory symptoms during the 1978 epidemic period.

A smaller significant excess (about a quarter of the 1978 excess among pregnant women) occurred among nonpregnant women during the 1976 epidemic period. Pregnant women experienced a similarly small excess during 1976, but it was not statistically significant due to a smaller sample size.

Analysis of the epidemic influenza subperiods in 1978 associated with the A/Texas and A/Russia viruses revealed that the excess flu-attributable illness was largely confined to women under 25 years of age (table 3).

During the 1978 Texas period (Epi 78-T), pregnant women in the two age groups experienced similarly significant excesses of total ARD. URI, respiratory symptoms, and flu contributed significantly to the total excess. Nonpregnant women in the two age groups had similarly insignificant excesses.

The excesses during the Epi 78-R period were 3 to 4 times larger for the 25 and younger women than for the 26 and older. The total ARD excess was significant only for younger pregnant women

[94.4 (SE = 28.5)]; this subgroup experienced statistically significant excess rates of URI, respiratory symptoms, general flu symptoms, and flu.

Discussion

This study, based on more than 5,000 pregnancies exposed to several periods of epidemic influenza in the late 1970s, has shown only a modest and rather selective impact of such epidemics upon the pregnant woman, as compared with her nonpregnant counterparts. Hospitalization occurred at negligible rates, with numbers too small to allow any estimate of possible excess during epidemics. This contrasts strikingly with well-documented rates of excess pneumonia and influenza hospitalization ranging from 3 to 6 per 1,000 among persons of all ages with selected chronic conditions (13), alongside of whom pregnant women were once listed as high priority candidates for influenza vaccine.

The excess ARD rates among pregnant women during influenza epidemics may be partially attributable to a tendency for pregnant women to visit physicians more readily than nonpregnant women when experiencing ARD. However, this is not likely to account for all the observed effect. The differences in excess between pregnant and nonpregnant women were small and not statistically significant during the 1975, 1976, and 1979 epidemics; the difference was significant during the H1N1 portion of the 1978 epidemic (EPI 78-R). Although based on a single nonepidemic year, the excesses are estimated from large stable populations that are representative of the general population.

The apparent lack of excess ARD among pregnant women during the 1975, 1976, and 1979 epidemic periods may be due in part to residual

Table 2. Excess rates of medical visits for acute respiratory disease attributable to epidemic influenza

	Not pregnant		Pregnant	
Epidemic period	Excess[1]	SE[2]	Excess	SE
Epi 75.................................	19.2	10.0	-3.4	15.1
Epi 76.................................	[3]14.6	8.5	13.4	14.5
Epi 78.................................	7.4	7.2	[3]55.5	14.2
Epi 79	5.8	7.9	24.0	29.0
Combined Epi periods	[3]10.2	3.4	[3]23.7	8.1

[1] Excess rate compared with 1977 nonepidemic period; rate per 1,000 women per 60 days.
[2] Standard error of rate.
[3] Statistically significant at 5 percent level (one-sided test).

Table 3. Excess rates of medical visits for acute respiratory disease attributable to A/Texas and A/Russia epidemic periods, 1978: differential effect by age

		Not pregnant				Pregnant			
Epidemic period	Age	Rate[1]	SE[2]	Excess[3]	SE	Rate	SE	Excess	SE
A/Texas .... {	25 or younger	69.8	14.1	14.2	16.6	142.8	21.1	[4]70.1	25.0
	26 or older	69.1	8.4	13.6	11.3	155.8	23.1	[4]71.2	26.7
A/Russia .... {	25 or younger	64.0	9.6	8.4	13.0	167.1	25.1	[4]94.4	28.5
	26 or older	58.4	7.0	2.9	10.3	110.9	18.8	26.3	23.0

[1] Rate per 1,000 women per 60 days.
[2] Standard error.
[3] Excess compared with 1977 NonEpi period.
[4] Statistically significant at 5 percent level (one-sided test).

immunity from prior exposure to variants of the H3N2 influenza virus which may have offset decreased protective factors due to pregnancy. Both H3N2 virus and H1N1 virus co-circulated during the 1978 epidemic period. The ARD excess, however, was concentrated in the period dominated by the latter strain during which it was limited to young pregnant women. This suggests that the effect was due to H1N1 virus to which women 25 or younger would have had no previous exposure. These findings are compatible with the national experience in which the impact of the H1N1 A/Russia strain, which appeared in 1978, was almost entirely confined to persons who were not alive at the time of the last H1N1 epidemic 20 years earlier (17).

In summary, these observations on large numbers of pregnant and nonpregnant women during several influenza epidemics reveal a relatively modest excess of medically attended ARD among the former, almost entirely confined to the appearance of a new viral strain. Some of the apparent excess may simply reflect a lower threshold for seeking medical attention for ARD during influenza epidemics on the part of pregnant women. These findings provide empirical support for the recom-

mendations of the Public Health Service and the Immunization Committee of the Infectious Disease Society of America with respect to influenza vaccination of pregnant women.

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Foodborne Streptococcal Pharyngitis After a Party

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Synopsis......................................

Following a private party in Río Piedras, PR, 23 (56 percent) of those who attended developed an illness characterized by pharyngitis, myalgia, fatigue, headache, and fever. Consumption of carrucho (conch) salad was significantly associated with illness (P = 0.013, Fisher's exact test). Group A beta-hemolytic streptococci (M nontypable T12, serum opacity factor positive) were isolated both from throat cultures in 11 of 47 persons who attended the party and from the implicated food. The original source of contamination of the conch salad was not identified. Because complications may still occur from such infections and only a small percentage of persons with sore throats seek medical attention and ultimately receive treatment for their illnesses, it is important to recognize these outbreaks.

Before the advent of pasteurization of milk and the general availability of adequate refrigeration, foodborne streptococcal outbreaks were common. Outbreaks have been reported that resulted in cases of scarlet fever, rheumatic fever, and suppurative complications (1–3). Since the institution of these sanitary control measures, foodborne streptococcal outbreaks have become relatively uncommon. Recent outbreaks have been reported primarily from institutions or community-associated events (3–6) and have occurred when there has been a breakdown in normal refrigeration practices. Because complications may still occur from such infections and only a small percentage of persons with sore throats seek medical attention and ultimately receive treatment for their illnesses, it is important to recognize these outbreaks. We report an outbreak of streptococcal pharyngitis that occurred after a private party; its source was a marinated conch salad.

The Outbreak

On the evening of Friday, August 3, 1984, 47 persons attended a party in a private home in Río Piedras, PR, to celebrate the birthdays of three persons who worked in a large office. Over the weekend numerous people who had attended the party developed pharyngitis, fever, lymphadenopathy, and myalgia. Because of the large number of persons who became ill, the office director recognized the existence of an outbreak and notified the Division of Epidemiology of the Puerto Rico Department of Health on August 8. It was suspected that a cold marinated "carrucho" (conch) salad was the vehicle of transmission because several persons who were friends of the hosts had not attended the party and did not work at the office but became ill after eating leftover carrucho.