

The measles epidemic in Calgary 1969-70; the protective effect of vaccination for the individual and the community

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Summary: Twenty per cent of the city's population of 375,000 had had live measles vaccination as pre-school children in the preceding four years. Protection rates for killed-live vaccine schedule (Edmonston) and live vaccine only (Schwarz) were approximately 66%, not diminishing in four years; the rates for killed vaccine only (three doses) were similar for 18 months, diminishing later. As the numbers who have acquired immunity by contracting the disease fall by 10 percentage points, numbers immunized by live vaccines must rise by 15 percentage points to maintain an equivalent balance of immune and susceptible subjects.

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The epidemic of measles in Calgary beginning in December 1969 provided an opportunity to study the epidemiology of this disease in a city of 375,000 where measles immunization has been part of the Health Department's program since February 1966.

Immunization program

The immunization schedule consisted of inactivated measles vaccine (three doses in the earlier phase and one in the later phase of the program) followed by live vaccine (one dose). The minimal interval between doses was four weeks. The first dose of killed vaccine was given at an age not younger than 3 months, the live vaccine not before one year of age. Measles immunization was not given in school, or to school-aged children, but only to infants and preschool children.

From February 1966 to June 30, 1970 (the end of the period covered by this report) 97,784 doses of killed and 26,378 of live vaccine were administered by the Health Department.

Vaccines used

The vaccines used by the Health Department were:

1. Pfizervax Measles K, an alum-precipitated inactivated measles vaccine, produced by Charles Pfizer & Co. Inc.—used from February 1966 to February 1968.
2. Measles vaccine inactivated purified "monovalent" and diphtheria-pertussis-tetanus-polio-measles vaccine purified, "Quint", produced by Connaught Medical Research Laboratories—used from February 1968 to June 1970.
3. Measles virus vaccine, live attenuated (Edmonston B), Lyovac "Rubeovax", produced by Merck Sharpe & Dohme.

During the same period the vaccine most generally used by physicians in their private practices was measles virus vaccine live attenuated (Schwarz) "Lirugen", produced by the Pitman Moore Division of Dow Chemical Company. It was not the practice to give killed vaccine preceding Lirugen. Approximately 1800 doses of Lirugen had been sold in Calgary from its arrival on the market to June 30, 1970.

The epidemic: reporting and diagnosis

After a period of two and a half years during which the incidence of measles was lower than in previous non-epidemic years, there was a substantial increase in the number of case reports received from physicians, parents and public health nurses in December 1969. Diagnoses made by telephone were not accepted as adequate until confirmed at a visit either by an experienced public health nurse or the assistant medical officer of health, or unless the incubation period from contact with a known case was compatible with measles.

Additional evidence that measles was prevalent, (and that other recognizable febrile viral illness of comparable severity was not prevalent) was derived from laboratory reports of hemagglutination inhibition and complement-fixing antibody tests for viral disease on 26 children admitted to hospital because of difficulty in diagnosis or treatment of acute febrile illnesses. Significant increments of measles complement-fixing antibody titres during convalescence were demonstrated in 15 cases; seven had the same titres in both sera, ranging from 256 to 4096, and four showed titres of equal range in single sera. The diagnosis of infectious mononucleosis was subsequently made in one patient; another, whose antibody titre to measles fell from 1 in 1024 to 1 in 128, showed rising antibodies to respiratory syncytial virus. An additional two unhospitalized cases were confirmed by rising levels of complement-fixing antibody.*

Data gathering and definitions

Home visits and telephone calls to homes, clinics and doctors' offices were made to obtain the following information:

A. Pertaining to the case originally reported

1. The complete record of any immunization to measles
2. The severity of the illness with degree and duration of fever, cough and rash
3. Whether this case was the source of infection for other children in the household

B. Pertaining to the household contacts of the originally reported case, children 0 to 11 years

1. The complete record of any immunization to measles
2. Whether any had had the disease previously (such children were not counted in the population at risk in this study)
3. Whether contacts acquired this disease and, if they did, the severity of the illness

For the purpose of this study "population at risk" includes the initial case occurring in the family and any siblings aged 0 to 11 years who had not had the disease previously. "Susceptible contacts" are family contacts under age 12 who have not had the disease. Neither of these terms excludes immunized siblings.

Protective effect of live vaccine

Table I shows the number of cases of measles in unimmunized children and in the children vaccinated by the killed-live schedule or by the live only (further attenuated) vaccine. The protective effect of the two live vaccines used as they were in Calgary were approximately equal. Sero-conversion rates for these two vaccines have elsewhere proved to be equal.¹¹ The limited experience in this epidemic with 12 children who had received rubeovax plus gamma globulin, four of whom acquired the disease

suggests that this combination too, gives protection equivalent to the two vaccines of Table I.³

Moderation of severity

When measles occurred in children immunized with live vaccines, it was, on the average, milder than in the unvaccinated cases (Table II).

Cough, fever and rash tended to be less severe in the immunized children (Table III). The grading of severity based on the height of fever was as follows:

- (1) 40°C and over—high
- (2) 34°C to 40°C for two days or more—moderate
- (3) Less than 34°C—mild

If fever was high and cough severe, the illness was classed as severe. If both fever and cough were moderate, or one of the two was moderate and the other severe, the illness was classed as moderate.

Illnesses with combined signs and symptoms of less severity than the above were classed as mild.

The degree of severity of the rash did not enter into the decision about the severity of the illness, although it was observed that the rash was almost always profuse in the severe cases.

Protective effect with killed vaccines

The numbers immunized with killed vaccine only (three doses) were small, but a degree of protection is indicated, and it is greater in those immunized in the years 1969 and 1970 (72%) than in those immunized in 1966, 1967 and 1968 (35%) (Table IV). This diminishing protection from killed vaccine as interval to challenge increases is consistent with the findings of Guinée *et al.*⁹ None of the four children who received four doses of killed vaccine acquired the disease.

Protection of infants

The Connaught Medical Research Laboratories killed measles vaccine was the only active immunizing agent used by the Health Department for children who were under 12 months of age during the epidemic. Table V gives pertinent details for the cases and family contacts who were aged from 6 to 12 months. A smaller proportion (45%) of the immunized (including even those who received only a single dose) than of the unimmunized (73%) acquired the disease. However, it would be unwise to draw any conclusion regarding individual protection from such a small number in view of the various ages and stages of immunization, unknown residual protection from maternal antibody and the difficulty in diagnosis of illnesses and rashes in this age group in the absence of viral tests.

Suppression of infectivity

Contacts were established with 122 families in order to ascertain whether immunized children who developed measles served as the source of infection of other children in their families. In 37 families the other children had already contracted measles; in 13 the index case was the only child. In seven families an immunized child appeared to infect one or more siblings; four of these had received live vaccine and three had received killed vaccine only. The following is a brief account of the four completely immunized cases.

A girl aged 7 years who had received Lirugen in 1967 developed measles on April 20, 1970. The sibling, aged 2 years who had received by injection a total of 3.5 ml. of Connaught measles vaccine in the form of "Quint" in five doses in 1968 and

*The viral serology was performed by the Viral Division of the Provincial Laboratory of Public Health, University of Alberta, Edmonton.

1969, followed in March 1970 by Rubeovax, developed severe measles May 5, 1970.

Measles occurred in an 8-year-old girl on May 7, 1970, despite the administration of three doses of Pfizervax in 1966 and Rubeovax in 1967. The child was moderately ill. Her sister 1 year of age, who had received three injections of killed vaccine ("Quint") and one of Rubeovax, developed moderately severe measles on May 18.

A 7-year-old boy who had received Rubeovax in 1968 following three doses of Pfizervax in 1967, developed moderate measles on May 10, 1970. His sister, aged 11 months, who received three doses of "Quint" in September, October and November 1969, acquired mild measles with scanty atypical rash beginning May 20.

A 7-year-old boy who had received Rubeovax in 1968, following Pfizervax earlier in that year, contracted mild measles on April 4, 1970. His brother, aged 10 years, who had not received measles vaccine, developed severe measles on April 16.

Pneumonia

Table VI sets forth data concerning 18 hospitalized cases

of measles complicated by pneumonia, 15 of whom had been vaccinated. Rising measles antibody titres were demonstrated in 10, including seven of the vaccinated cases. All three unimmunized patients had severe cough, while in 10 of those immunized cough was slight or absent. All were aged 3 to 8 years. None were vaccinated later than 1967. Of the 18 cases of pneumonia, 15 had been immunized with Pfizervax, or Pfizervax plus Rubeovax; whereas in the age group 3 to 8, where all these pneumonias occurred, only 102 out of the 886 cases of measles (11%) were vaccinated with Pfizervax and approximately 80% were unvaccinated (Table VII). Thus, 83% of the diagnosed cases of pneumonia occurred in the 11% of the measles cases who had been vaccinated with Pfizervax. No cases of pneumonia or exaggerated local responses^{6, 20} occurred in children vaccinated with Connaught Laboratories killed measles vaccine. The process of manufacture of Pfizervax included adsorption to mineral adjuvant and concentration by alum precipitation, a process that Wil-

Table I
Cases of measles and susceptible family contacts, by immunization status, attack rates and protection rates for those immunized with live vaccines

	No immunization against measles	Completed series of killed measles plus Rubeovax						Lirugen Vaccine only				
		Year of completion						Year of administration				
		1966	1967	1968	1969	1970	Totals	1966	1967	1968	1970	Totals
Cases	1048	2	58	25	13	5	103	7*	6	2	3	18
Non-cases	174	5	132	67	37	9	250	17	18	5	6	46
Population at risk	1222	7	190	92	50	14	353	24*	24	7	9	64
Attack rate %	86	29	30	27	26	36	29	29	25	29	33	28
Protection rate (%)	0	$(\frac{86 - 29}{86} \times 100) = 66^{**}$						$(\frac{86 - 28}{86} \times 100) = 67$				

* One case receiving three doses of killed vaccine followed by Lirugen was included here.

** The degree of protection was equal, approximately 66%, and there was no evidence of diminution of protection with time within these four years.

Table II
Severity of illness of cases of measles in unimmunized children and in those immunized by live vaccines by year of vaccination

	No immunization against measles		Completed series of killed vaccine plus rubeovax							Lirugen vaccine only					
			Year of completion							Year of administration					
			Number	%	1966	1967	1968	1969	1970	Totals	%	1966	1967	1968	1969 & 1970
Severe	276	34	1	12	1	2	0	16	18	0	0	1	1	2	13
Moderate	419	54	1	21	9	3	2	36	40	4	2	1	2	9	60
Mild	102	12	0	19	11	7	1	38	42	2	2	0	0	4	27
Subtotal	797		2	52	21	12	3	90	6	4	2	3	15		
Information on severity not available	251		0	6	4	1	2	13	1*	1	1	0	3		

* This is the case referred to by the asterisk in Table I.

Table III
Cases of measles with three principal signs graded according to severity—by immunization status

	Cough		Fever						Rash			Number for whom information on severity obtained							
	Severe	Moderate	Slight or none		Severe	Moderate	Mild	Severe	Moderate	Slight									
			No.	%							No.		%	No.	%	No.	%	No.	%
No immunization	303	38	308	39	186	23	388	49	280	35	129	16	535	67	189	24	73	9	797
Live vaccine	21	19	18	16	71	65	37	33	34	32	39	35	30	27	18	16	62	56	110

son *et al.*²² have shown to enhance sensitizing activity. The Connaught inactivated measles vaccine was not precipitated on alum.¹⁵ However, in view of unfavourable publicity^{2, 6, 8} surrounding aberrant reactions due to Pfizervax, it was decided to discontinue the use of all killed measles vaccines by the Health Department in June 1970.

In epidemics which occurred elsewhere among unvaccinated subjects, the incidence of pneumonia ranged from 1% in Britain¹⁶ to 36% in Greenland,⁴ and the pneumonia appeared before the initial two days of illness.

Kohn and Koiransky¹² in 1933 reported that in every case of measles, mild or severe, radiology revealed peribronchial infiltration. Partington and Quinton¹⁸ reported in 1958 that in 82 hospitalized measles patients the rash appeared on the eighth to the sixteenth day of the infection, and concluded that both an illness of infection and a long prodromal illness are commoner in measles than usually reported.

Table IV

Immunized with inactivated vaccine only: cases of measles and susceptible family contacts, by number of doses and year of administration of last dose

Year of last dose		Number of doses				Totals	Grand total
		1	2	3	4		
1966	Cases	2*	2	10	0	14	
	Non-cases	3	3	8	0	14	
1967	Cases	7**	5	7	0	19	
	Non-cases	2	6	6	3	17	
1968	Cases	7	1	6†	0	14	
	Non-cases	3	1	3	0	7	
Subtotals for 1966, 1967 and 1968							
	Cases	16	8	23	0		
	Non-cases	8	10	17	3		
							Attack rate $\frac{23}{40} = 57\%$
							Protection rate $\frac{86 - 57}{86} \times 100 = 34\%$
1969	Cases	11*	7	4	0	22	
	Non cases	1	1	10	1	12	
1970	Cases	3	1*	0	0	4	
	Non cases	1	5	3	0	9	
Subtotal for 1969 and 1970							
	Cases	14	8	4	0		
	Non cases	2	6	13	1		
							Attack rate $\frac{4}{17} = 24\%$
							Protection rate $\frac{86 - 24}{86} \times 100 = 72\%$
							133

* One severe case in this group

† Two severe cases in this group

** Three severe cases in this group

Table V

Infants aged 6 to 12 months exposed to a case of measles in the family by immunization status (total number 22)

Immunization status	Acquired measles			Did not acquire measles	
	Number	Ages	Severity of illness	Number	Ages
3 doses inactivated plus 1 dose live	0			1	8 months
3 doses inactivated vaccine only	1	11 months	Mild	2	Both 10 months
2 doses inactivated vaccine	2	8 months 6 months	Moderate severe	2	8 months 6 months
1 dose inactivated vaccine	1	7 months	Mild	1	7 months
4 half doses killed vaccine and gamma globulin on exposure	1	11 months	Moderate	0	
Subtotal	5			6	
No measles antigen or antibody*	8	(1) 11 months (6) 10 months (1) 8 months	Moderate 4 moderate* 2 severe Severe	3	(2) 6 months (1) 10 months

* One infant, 10 months of age, who was given Lirugen on the fifth day after onset of illness in sibling was included here.

Because the incidence of pneumonia in this epidemic was so very low, and because it appeared before the diagnosis of measles was made, it is believed that its occurrence was not influenced by prior immunization, but rather that the signs of rash and cough were modified, thus obscuring the diagnosis and leading to admission of the patient to hospital where investigation included a chest x-ray.

Further epidemiological observations and discussion

The vaccination status of the 564 children who did not acquire clinical measles during this epidemic is shown in Table VIII derived from Table VII.

Among children under 6 months of age and in the age group 9 to 11 years, vaccinated subjects outnumbered the unvaccinated. The low attack rate in infants is explained by passively acquired antibody. In the older group this apparent finding may arise from parents' forgetfulness of

previous childhood illnesses. The tendency to forget is mentioned by Hedrick^{10a} in reports of previous studies by Hill and Henderson in London, Ontario, by Chapin in Providence, Rhode Island, and by Krugman *et al.*¹⁸ who

reported a serological survey of 727 presumable susceptible institutionalized children of average age 4 to 9, which revealed immunity in 19%. Another explanation in the older group is a possible cross-immunity from other infections.¹

Table VI
Immunization status related to antibody titres and to cough in 18 cases of measles associated with pneumonia

Previously immunized to measles (total 15)	Killed vaccine only				No measles immunization (total 3)
	1 dose	2 doses	3 doses	Killed plus live (Pfizeravax + Rubeovax)	
Antibody titres					
Rising in 2nd specimen	0	2	2	3	3
Elevated in both specimens	0	0	0	3	0
Only one specimen taken but titre was elevated	0	0	2	2	0
No report available	0	0	0	1	0
Cough moderate to severe	0	1	0	4	3
Cough slight	0	0	1	2	0
No cough	0	1	3	3	0

Hedrick, studying the population of Baltimore under 15 years of age, showed a narrow range of fluctuation in the balance of susceptibles and immune subjects. Shortly before major epidemics the proportion of the population under 15 years estimated to be susceptible ranged from 45 to 50%. At the end of epidemics this proportion had fallen only from 30 to 35%. In present Canadian society, with transportation and mobility as they are, there is less likelihood of children remaining in small, remote communities unexposed to measles until 12 or 13 years of age. In a city with a constant age for starting school, a constant rate of migration, and a small but fairly constant proportion attending nursery schools or kindergartens, the data for susceptibility and immunity of children entering first grade would probably have exhibited a similar, even and predictable fluctuation. Such data for Calgary were not collected until 1967, in time to show the effect of measles vaccination. The immunization status of the 9000 students entering school for the first time in September each year from 1967 to 1970 is shown in Table IX.

Almost every child born in Calgary attends the child health centres operated by the Health Department and the immunization offered there is the most widely accepted

Table VII
Age distribution of 1819 of the population at risk, (cases and family contacts classified by antigen or antibody used)

		Under 6 months	6-12 months	1 and 2 years	3-8 years	9-11 years	Totals	Sum of cases plus non-cases
		No antigen or antibody administered	Cases 2 Non-cases 12	7 3	44 7	722 97	265 50	1040 169
Pfizer vaccine alone or followed by Rubeovax	Cases 0 Non-cases 0	0 0	0 2	102 206	4 7	106 215	321	
Connaught measles vaccine alone or followed by Rubeovax	Cases 0 Non-cases 3	6 5	27 33	38 59	0 3	71 103	174	
Lirugen	Cases 0 Non-cases 0	0 1	3 1	13 41	2 3	18 46	64	
Immune serum globulin on exposure	Cases 0 Non-cases 5	0 4	7 5	7 8	2 1	16 23	39	
Rubeovax with gamma globulin	Cases 0 Non-cases 0	0 0	0 0	4 6	0 2	4 8	12	
Totals	Cases 2 Non-cases 20	13 13	81 48	886 417	273 66	1255 564		
Grand totals		22	26	129	1303	339	1819	

Table VIII
Presumed susceptible non-cases in families of cases of measles by age group and vaccination status (total number 564)

Age group	A No antigen	B Gamma globulin on exposure	C Pfizeravax alone or followed by Rubeovax	D Connaught alone or followed by Rubeovax	E Lirugen	F Rubeovax + gamma	Ratio of A to sum of A + C + D + E + F
Under 6 months	12	5	0	3	0	0	12:15
6-12 months	3	4	0	5	1	0	3:9
1 and 2 years	7	5	2	33	1	0	7:43
3-8 years	97	8	206	59	41	6	97:409
9-11 years	50	1	7	3	3	2	50:65
Totals	169	23	215	103	46	8	169:541

service. Each year a number approximating 120% of births in the city are admitted for the first time to the clinic and the average number of subsequent visits per child is five. The fact that such a large number had not had live vaccine in spite of this degree of acceptance of public health services is partly accounted for by mobility—after school opening in September approximately 660 new first-grade students move in and 430 move out of the city before June 30—and partly by the requirement that killed measles vaccine must be given before live vaccine. The achievement of full immunity of a proportion of the population to ensure avoidance of the critical percentage of susceptibles that favours an epidemic requires a progressively higher rate of immunization as the percentage of naturally immune children declines. At the protection rate found in this Calgary study (66%), a rise of 15 percentage points in the number protected by vaccine is required to compensate for a drop of 10 percentage points in the number protected by previous natural infection.

An epidemic began in December 1969, when the ratio of protected to unprotected (D:E in Table IX) among the Grade 1 students was the lowest (52:48) in the four years studied. An epidemic had occurred in late 1966 and early 1967, accounting for the high ratio, 63:37 in September 1967. Although September 1970 was also after an epidemic, the ratio 58:42 was not so high, and a lesser drop will be required for the reaching of the critical pre-epidemic point. This drop can be prevented by extending the immunizing program into schools, kindergartens and nursery schools, rather than depending entirely upon attendance at the Child Health Centres and thereby failing to reach many newcomers to the city.

The duration of individual protection by vaccination will take on importance as these cohorts, the substantial part of whose immunity to measles has been from vaccination, move into adolescence and adulthood. If it is found that vaccine-induced immunity to measles wanes, the susceptibles necessary to the reaching of the critical point may come from older age groups unless reinforcing immunization is accepted.

The difficulty of carrying out adequate immunizing programs in all parts of the world makes unlikely of achievement hopes earlier expressed for the eradication of measles.^{5,7,14,19} Sutherland and Fayers,²¹ analysing data soon to be published,¹⁷ recently reported that vaccination of about 10% of the child population under 15 in Britain deferred an expected epidemic by one year. In Calgary, where approximately 20% of the child population under 15 had been immunized by live measles vaccine (23,000 by the Health Department, 1500 by private physicians), an epidemic, albeit a small one, occurred about 1½ years later than would have been expected before the introduction of measles vaccine.

Conclusions

A protective effect of approximately 66% from immunization with a killed plus live Edmonston strain measles vaccine schedule has been demonstrated in an epidemic of measles in Calgary.

This protective effect did not significantly diminish with increase in interval from vaccination to exposure within the four years of experience.

The findings in the smaller numbers vaccinated by the further attenuated (Schwarz) strain suggest a similar degree and duration of protection.

With killed vaccine the protection was of similar degree but of short duration.

Evidence of individual protection of infants by killed vaccine was only suggestive. The small number of infants intimately exposed to measles and the consequent scarcity of infant cases is an illustration of "herd" protection.

Measles was found to have been transmitted to siblings from cases who had been vaccinated with live vaccine.

Previous measles vaccination tended to modify the severity of fever, cough and rash in cases of the disease.

Although the incidence of diagnosed pneumonia was low in this epidemic and occurred only in the age range 3 to 8 years, in which 72% of the cases of measles occurred, 80% of the cases of pneumonia occurred in the 11% in that age group who had had Pfizervax.

Of the supposedly susceptible children aged 9 to 11 years who did not acquire measles even though intimately exposed 77% had not been immunized, whereas the percentages for children aged 3 to 8 and 1 and 2 are 23% and 16% respectively. Two possible explanations are offered.

High rates of immunization are somewhat diluted by immigration and emigration. The number of naturally immune subjects is diminishing each year.

A relatively high rate of vaccination of preschool children postponed an epidemic by only 1½ years. Still higher rates are necessary to prevent an outbreak. Assiduous programs of vaccination throughout the world would be required to eradicate this disease.

The gathering of data for the study was done as part of their regular work by the public health nurses and their supervisors in the Calgary Health Department. The author is especially grateful to Mrs. Susan McLean and Mrs. Joan Wales for assistance in organizing the data.

Résumé

Etude de l'épidémie de rougeole de Calgary en 1969-70 et remarques sur l'effet protecteur de la vaccination chez l'individu et la collectivité

Sur les 375,000 habitants de Calgary, 20% avaient reçu à l'âge préscolaire un vaccin antirougeoleux (germes vivants atténués) au cours des quatre années précédentes. La protection ainsi assurée, soit par la vaccination à germes tués (Edmonston), soit par celle à germes vivants atténués (Schwarz), s'est élevée à 66% environ et n'a pas diminué durant les quatre années; le taux de protection réalisé par le seul vaccin à germes tués (trois doses) a été semblable pendant 18 mois, mais diminué par la suite. Comme le nombre de sujets ayant acquis l'immunité après avoir

Table IX
Measles immunization status in percentages of children on school entrance in Calgary

Year of birth	1961	1962	1963	1964
Entered school September of year	1967	1968	1969	1970
A. Had live measles vaccine	24	34	46	58
B. Fully protected by vaccine (2/3 of A)	16	22	30	41
C. Had measles	47	35	22	17
D. Estimated fully protected (B + C)	63	57	52	58
E. Estimated unprotected (100 - D)	37	43	48	42

contracté la maladie a diminué de 10%, il s'ensuit que le nombre des sujets immunisés par vaccination doit s'élever de 15% pour maintenir un équilibre correspondant entre les sujets immunisés et les sujets réceptifs.

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Hemoglobin

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The Canadian Medical Association has installed a special night line system in order that our members and divisions may reach the following senior executives after the main switchboard is closed.

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