Antibody status to poliomyelitis, measles, rubella, diphtheria and tetanus, Ontario, 1969-70: deficiencies discovered and remedies required

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Summary: A serologic survey was made in 15 health unit areas, testing some 5000 individuals in the age groups 4 to 6, 11 to 13, 15 to 17 and 23 to 45 years. Two types of serious deficiency were found.

Only 65% of children 4 to 6 years old had antibodies to all three types of poliovirus, the antibodies being due almost entirely to immunization with Salk vaccine. Even in children who had had six or more doses only 74% had antibodies to the three types. The high percentage of students 11 to 13 and 15 to 17 years old with poliovirus antibodies can be attributed largely to natural infection and to Sabin vaccine in the mass campaign of 1962, as well as to Salk vaccine. In children who had received Sabin vaccine as well as Salk vaccine a very high level of immunity was found. The immunity of the school-age population will decline to an insufficient level unless Sabin vaccine is used after immunization with Salk vaccine.

Of children 4 to 6 years old 18% had no diphtheria antitoxin and 6% had no tetanus antitoxin. Even in those who had had six or more doses of the antigens 5% had no diphtheria antitoxin and 1 to 2% had no tetanus antitoxin. This apparently refractory state is probably due to the use of unadsorbed toxoids, and it is clear that adsorbed toxoids should be used. In the adults, diphtheria antitoxin was found in only 55% and tetanus antitoxin in only 38%.

Résumé: *État des anticorps de poliomyélite, de rougeole, de rubéole, de diphtérie et de tétanos en Ontario en 1969-70: déficiences découvertes et remèdes exigés*

Une enquête sérologique a été faite dans 15 régions sanitaires sur près de 5000 individus dans les groupes d'âge suivants: 4 à 6 ans, 11 à 13 ans, 15 à 17 ans et 23 à 45 ans. Deux types de déficiences graves ont été découverts.

Dans le groupe d'enfants de 4 à 6 ans, seulement 65% avaient des anticorps aux trois types de virus de poliomyélite, ces anticorps étant presqu'entièrement dus à l'immunisation par le vaccin Salk. Même chez les enfants qui avaient eu six doses au moins de vaccin 74% seulement avaient des anticorps aux trois types. Le fort pourcentage d'étudiants âgés de 11 à 13 ans et de 15 à 17 ans qui avaient des anticorps au virus de la polio peut être attribué principalement aux infections naturelles et au vaccin Sabin administré massivement durant la campagne de 1962, ainsi qu'au vaccin Salk. Chez les enfants qui avaient été vaccinés tant par le vaccin Sabin que par le vaccin Salk l'immunité était très élevée. Chez les enfants d'âge scolaire l'immunité déclinera à un niveau insuffisant à moins qu'on ne leur administre le vaccin Sabin après immunisation avec le vaccin Salk.

Parmi les enfants de 4 à 6 ans 18% n'avaient pas d'antitoxine diphtérique et 6%, pas d'antitoxine tétanique. Même chez les enfants qui avaient eu six doses au moins des antigènes 5% n'avaient pas d'antitoxine diphtérique et 1 à 2% n'avaient pas d'antitoxine tétanique. Cet état réfractaire est probablement attribuable à l'emploi de toxoïdes non adsorbés, et il est évident qu'il faut employer des toxoïdes adsorbés. Chez l'adulte on n'a trouvé d'antitoxine diphtérique chez 55% des sujets et d'antitoxine tétanique chez 38%.

To determine the immune status of selected age groups to poliomyelitis, measles, rubella, diphtheria and tetanus, and thereby assess the effectiveness of the immunization programs in Ontario, a serologic survey was made in 15 health unit areas. Eight areas were studied in 1969 and seven in 1970. The survey was designed to examine preschool and school-age children at three stages: shortly before entering school, toward the end of primary school and before leaving secondary school. Because of this plan, and for practical reasons, the groups were selected by grades, or classes, rather than strictly by age. The parents, mostly mothers, of the children about to enter school were also tested. A total of about 5000 individuals were tested.

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Methods

Organization of the survey

The medical officers of health of the 15 areas were requested to participate in the survey and to make the necessary arrangements. The staff of each unit selected the schools and obtained the cooperation of the principals and the consent of the parents. Known likelihood of better or poorer immunization was not a factor in selecting the schools. However, because the subjects were not obtained by random sampling throughout all the schools, the results are not necessarily representative of each health unit area.

Blood samples were collected at the schools on prearranged days by teams from Connaught Laboratories. In each area samples were obtained from about 50 to 100 individuals in each of four groups. For children who were to enter school in September (aged 4 to 6 years) this was done at registration in May and June so that samples would be obtained before the booster dose given after school entry. At the same time samples were obtained from the parents, in most cases the mothers (aged 23 to 45 years), accompanying the children. In three unit areas children previously registered were recalled for blood sample collection. Samples were obtained from students in grades 7 and 8 (aged 11 to 13 years) and 11 and 12 (aged 15 to 17 years) in October and November, except in three unit areas, where samples were collected in May and June.

The immunization history of each school-age child was obtained from health unit records but reliable information could not be obtained on the adults.

The health units that took part in the survey and the municipalities where blood samples were collected are as follows: in 1969, Scarborough (Metro Toronto), Burlington, Ontario County (four centres), Barrie, London, Etobicoke (Metro Toronto), Kitchener and Kingston area (four centres); and in 1970, Cobourg, Stratford, Haldimand-Norfolk County (four centres), Clinton, Perth, Owen Sound and Niagara Falls.

Collecting and testing blood samples

From each subject a blood sample of 0.3 to 0.4 ml was obtained by finger puncture with a disposable lancet and collected in Caraway micro blood-collecting tubes. The sera were tested in cultures of cercopithecus monkey kidney cells for virus-neutralizing antibody to each of the three types of poliovirus by a modification of the method of Sever.[1] Testing for measles antibody in FL cell cultures and for rubella antibody in RK-13 cell cultures was by the micromethods of Moreau and Furesz[2] and Furesz, Moreau and Yarosh,[3] respectively. Tests for diphtheria and tetanus antitoxins were performed in rabbits and mice, respectively, by the methods of Taylor and Moloney;[4] sera were tested for virus-neutralizing antibodies at a dilution of 1/10 and for diphtheria and tetanus antitoxins at a concentration of 0.01 U/ml. Because of the small volume of each blood sample and the variety of tests done these were the lowest test concentrations possible. Also, for the same reasons, measles antibody was sought in sera from males only, and rubella antibody in sera from females only.

Certain individuals with low concentrations of antibody not detected by these tests were undoubtedly immune, though not so designated in this survey. However, there are good grounds for the test concentrations used. Those whose sera were positive could be considered to be immune not only at the time of sampling but also for some period thereafter, the duration depending on the antibody concentration and the type of stimulus, whether infection or inactivated antigen or both. The need to obtain concentrations of antibody higher than the minimal detectable values is recognized in the requirements for vaccine licensing. Thus, to consider a response satisfactory, poliovirus antibodies must be detected at a dilution of 1/16 after administration of oral poliovirus vaccine, and measles antibody at a dilution of 1/8 after administration of live measles vaccine. In any case, the concentrations were those used in most serologic surveys.

Results and discussion

The immune status to poliomyelitis, measles, rubella, diphtheria and tetanus in the four groups is shown in Table I. The results of the survey for 1969 and 1970 were combined because the differences between the findings in the 2 years were small. Results for males and females are not shown separately because the differences in immune status were small and not consistent.

In children aged 11 to 13 and 15 to 17 years the percentages with each antibody were high. In those aged 4 to 6 years the percentage with immunity to the viral infections, particularly rubella, was much less. In contrast, the percentage with immunity to diphtheria and tetanus was relatively low in adults.

Poliomyelitis

We attempted to assess the relative contribution of previous subclinical infections and of immunization to the prevalence of poliovirus antibodies in each age group. The changing incidence of poliovirus infections in recent years is reflected in Table II. Immunization with Salk vaccine was begun in 1955. A mass campaign with Sabin vaccine was conducted in the schools in 1962 but has not beeen repeated.

Of the children aged 4 to 6 years 65% had antibodies to all three types of poliovirus, probably almost entirely because of immunization with Salk vaccine. Only 52 of 1119 children in this age group had received Sabin

Table I—Antibody status of subjects in 15 Ontario health units, 1969-70

Group (age [yr])	% of subjects immune*				
	With virus-neutralizing antibody (titre, ≥ 1/10)			With antitoxin (≥ 0.01 U/ml)	
	Poliovirus (3 types)	Measles (males)	Rubella (females)	Diphtheria	Tetanus
Entering school (4 - 6)	65 (1119)	65 (553)	20 (558)	82 (1095)	94 (1096)
Grades 7 and 8 (11 - 13)	93 (1290)	97 (612)	72 (673)	94 (1262)	99 (1259)
Grades 11 and 12 (15 - 17)	97 (1349)	99 (668)	79 (680)	94 (1311)	98 (1314)
Adults† (23 - 45)	86 (1239)	100 (52)	80 (1182)	55 (1229)	38 (1225)

*Number tested in parentheses.
†Chiefly mothers of children about to enter school.

Table II—Paralytic poliomyelitis in Ontario, 1949-72

Year	No. of cases	Year	No. of cases	Year	No. of cases	Year	No. of cases
1949	406	1955	75	1961	23	1967	—
1950	113	1956	127	1962	20	1968	—
1951	619	1957	54	1963	—	1969	2
1952	269	1958	20	1964	2	1970	—
1953	985	1959	200	1965	—	1971	1
1954	94	1960	39	1966	—	1972	1

Population: 1949, 4.5 million; 1972, 7.8 million.

vaccine, most of these being in one health unit area. The low incidence of paralytic poliomyelitis after 1962 suggests that children born later had little exposure to poliovirus infection. This is confirmed by the observation that of the 19 children in this age group who had not been immunized only 1 had antibodies to all three types of poliovirus.

The presence of antibodies to all three types of poliovirus in 93% of children aged 11 to 13 years and in 97% of those aged 15 to 17 years can be attributed to immunization with Salk vaccine, to previous subclinical infection, and to administration of one or two doses of Sabin vaccine in the mass campaign in 1962. The incidence of paralytic poliomyelitis up to 1962 indicates the probability of subclinical infections in these two groups of children, who were born in 1956-59 and 1952-55, respectively. Also, it was found that of those who had not been immunized three out of six aged 11 to 13 years and five out of seven aged 15 to 17 years had antibodies to all three types of poliovirus. Some 33% of children aged 11 to 13 years and about 40% of those aged 15 to 17 years had a record of receiving the oral vaccine in 1962. The effect of one or two doses of Sabin vaccine in addition to Salk vaccine is shown in Table III. In each age group the difference in the percentage with antibodies between those who had received Salk vaccine only and those who had also received Sabin vaccine was highly significant ($P < 0.005$; chi-square test).

Though not shown in the tables the adults' antibody status was not related to age and must be attributed largely to previous subclinical infections. Many of those less than 30 years old probably had received Salk vaccine before leaving school but records of immunization could not be obtained.

The percentages of children 4 to 6 years old with antibodies to poliomyelitis varied between the health unit areas, from 71 to 97% for type 1, 77 to 97% for type 2, 58 to 92% for type 3, 55 to 92% for types 1 and 3 combined, and 51 to 92% for all three types. For reasons previously stated the groups tested cannot be considered representative of the health unit areas. Though the importance of the differences between areas is uncertain, in one health unit the percentages with antibody to each type were notably higher than in other areas. In this unit (London) Sabin vaccine was administered in addition to Salk vaccine to 62% of the children.

Of all children 4 to 6 years old in all health unit areas 80, 86 and 74% had antibody to types 1, 2 and 3, respectively. The type 1 component constituted one half of the total poliovirus antigen content of the trivalent vaccine in the period 1958-65 and has constituted two thirds since 1965, the remaining portion being divided between types 2 and 3. Because the immune response to type 3 was lowest and that to type 2 highest the amount of type 3 antigen in Salk vaccine was increased and the amount of type 2 antigen was decreased early in 1974.

The percentage of subjects in each age group with antibody to each type of poliovirus is given in Table IV. In the school-age groups and adults the percentages with type 1 and with type 3 antibody were equal and only slightly less than the percentage with type 2. Thus, the relation between the three types was different from that in the children about to enter school, indicating a difference in the origin of the antibodies.

The percentage of children 4 to 6 years old with poliovirus antibodies in relation to the number of doses of Salk vaccine, given as DPT (diphtheria–pertussis–tetanus) Polio Vaccine, is shown in Table V. Since 1959 DPT Polio Vaccine has been used for primary courses and booster doses for infants and preschool children. Of children who had received four doses of vaccine 63% had antibodies to all three types of poliovirus, and of those with a record of additional booster doses 75% were triple-positive. But even after six or more doses some 25% did not have satisfactory antibody titres from administration of Salk vaccine. Some 20% of the children about to enter school had not received the basic immunization course of four doses and only 30% had been given more than four doses. The fifth dose, at 3 years of age, was removed from the recommended schedule in 1966.

The results of this survey raise the question whether immunization has been sufficient to ensure a safe level of immunity to poliomyelitis. Only 65% of children 4 to 6 years old had antibodies to all three types of poliovirus; this is not adequate protection. There was evidence that the highly immune status of the children 11 to 13 and 15 to 17 years old was due to previous subclinical infections and to the 1962 Sabin vaccine campaign as well as to immunization with Salk vaccine, whereas the antibodies in the children 4 to 6 years old were the result, almost entirely, of administration of Salk vaccine. One must conclude that, with the current immunization program, the immune status of the school-age population will decline from the high levels in 1969 and 1970. This survey has provided evidence that the administration of Sabin vaccine following primary immunization with Salk vaccine provided a very high level of immunity.

Comparison of the findings of this survey with those of serologic surveys reported from other countries presents

Table III—Effect of giving Sabin vaccine in addition to Salk vaccine

Age group (yr)	% with antibodies (titre, ≥ 1/10) to all 3 types of poliovirus*				
	Salk vaccine only†	Salk vaccine plus Sabin vaccine†			
		1 dose	2 doses	3 doses	1, 2 or 3 doses
4 - 6	65.1 (1013)	94.1 (17)	50.0 (2)	100.0 (28)	95.7 (47)
11 - 13	91.8 (765)	99.6 (249)	100.0 (162)	85.7 (7)	99.5 (413)
15 - 17	95.4 (694)	98.6 (358)	100.0 (160)	100.0 (8)	99.0 (526)

*Number tested in parentheses.
†Differences highly significant ($P < 0.005$; chi-square test) for each age group.

Table IV—Poliovirus antibody status in four age groups

Age group (yr)	No. of subjects tested	% with antibodies to poliovirus (titre, ≥ 1/10)				
		Type 1	Type 2	Type 3	Types 1 & 3	Types 1, 2 & 3
4 - 6	1119	80	86	74	67	65
11 - 13	1290	96	99	96	94	93
15 - 17	1349	98	99	98	97	97
23 - 45	1239	93	97	93	88	86

Table V—Relation of poliovirus antibody status to number of doses of Salk vaccine (DPT Polio Vaccine) in children 4 to 6 years old

Type	% of children with poliovirus antibodies (titre, ≥ 1/10)*						
	0 (1.8)	1 (0.7)	2 (1.1)	3 (16.6)	4 (49.0)	5 (24.9)	≥6 (5.9)
1	11	14	55	76	80	90	84
2	11	43	64	84	87	93	90
3	5	0	82	64	73	81	82
1 & 3	5	0	45	58	66	76	74
1, 2 & 3	5	0	36	57	63	75	74

*Percentage of children with indicated number of doses in parentheses.

certain difficulties, particularly because the age groups tested differ in the various studies. The percentages with type 1 and with type 3 antibody were higher in our children 4 to 6 and 11 to 13 years old than those found by Melnick and colleagues[5] in children 5 to 9 and 10 to 14 years old in a Houston, Texas study in 1968. However, the Houston survey was made in selected low-income groups. The percentage of type 1 susceptibles in our children 11 to 13 years old was less than that found by Galbraith and Fernandes[6] in children mostly 11 to 14 years old in Britain (London area) in 1968. Böttiger, Zetterberg and Salenstedt,[7] from a serologic survey in 1968 in Sweden, where only inactivated vaccine has been used, reported a lower percentage of type 1 susceptibles in children 3 to 8 years old but a higher percentage in children 10 to 14 and 15 to 20 years old (age reported by year of birth only) compared with the groups of approximately similar age in the Ontario survey. In an antibody study of schoolchildren 6 to 9 years old in Ottawa in 1970 Furesz[8] found percentages with each type of antibody that were slightly lower than those found in the children 11 to 13 years old in this survey; thus, our results generally agreed. The results of a study by Wyile, Francis and Devadason[9] in New Brunswick could also be considered similar to those of the Ontario survey. In a recent study in Cleveland, Ohio, Gold and colleagues[10] found that only 43% of children 1 to 4 years old had antibodies to all three types of poliovirus. In all the studies except that in Sweden the authors recommended increased coverage by primary immunization or booster doses.

Measles

The percentage of children about to enter school who had received live measles vaccine and the antibody status of the vaccinated and unvaccinated children are shown in Table VI. Excluded from this table are details of seven children with no immunization records and seven who had received inactivated measles vaccine. Only 43% had been given live measles vaccine; antibody was found in 85% of these children, the percentage being only slightly less in those vaccinated 3 to 5 years before the survey compared with those in whom the interval was less than 3 years. Of the unvaccinated children 51% had antibody, which indicates previous measles infection.

Killed measles vaccine played virtually no part in immunity to measles in this survey, but it has been used in Ontario and Alberta. In Alberta, where Pfizervax had been used in a killed–live (K-L) sequential schedule during 1966 and 1967, Connaught inactivated measles vaccine was used in a similar schedule from January 1968 to May 1970. O'Neil[11] reported the experience with measles vaccine in Calgary. Connaught vaccine was used in a K-L program in Ontario from September 1967 to June 1970. Altogether in the two provinces about 50 000 infants were given Connaught inactivated vaccine; most received live vaccine (Rubeovax or Lirugen) several months later at 1 year of age. Thorough surveillance was maintained in Alberta during and after the period of killed vaccine use. In Ontario surveillance reporting was maintained until about mid-1969. There was virtually no sensitization by the Connaught vaccine. There were only three local reactions and no severe reactions to the subsequent dose of live vaccine such as had been reported with Pfizer vaccine. One possible case of atypical measles pneumonia occurred in Alberta, the causal relation to Connaught vaccine being uncertain. Nevertheless, the use of killed vaccine was discontinued because of the fear of sensitization. However, though the reason was not correct the action was, because of another effect — the rapid decline in antibody titre after administration of live vaccine to children previously given killed vaccine (W.K. Ing, G. Martineau, R.J-P. Belcourt: unpublished data). Observations in Alberta (R.D. Devine: personal communication) indicate that even after a second dose of live vaccine the titre of measles antibody, following an immediate increase, declines rapidly. The reason for this is probably that the small amount of antibody induced by killed vaccine is sufficient to inhibit multiplication of the live vaccine but there is enough antigen mass to act as a booster dose of killed vaccine. Such individuals in all likelihood will eventually lose immunity.

Rubella

The rubella antibody detected in all age groups resulted from previous infection; none of the children in the survey had received rubella vaccine. The immunization program begun in 1970 in Ontario did not at that time include the age groups tested. The results of this survey (Table I) confirm the common observation that rubella infection is largely acquired after a child enters school. In some 20% of adolescents and adults antibody was not detected. Most of these individuals must be regarded as susceptible. Future surveys will show how this pattern changes with the immunization program now in progress.

Diphtheria

Diphtheria antitoxin was present in 82% of the children about to enter school and in 94% of the school-age population (Table I). The percentages of children 4 to 6 years old with diphtheria antitoxin varied between the health unit areas, from 74 to 91%. The differences were not great and, for the reasons stated previously, no conclusions can be drawn regarding their importance.

The percentage of children 4 to 6 years old with antitoxin in relation to the number of doses of toxoid is given in Table VII. Immunity was obtained in 93% with five doses but only 31% of this group of children had received five or more doses. Of those given as many as six to eight doses of DPT Polio Vaccine 5% had concentrations of diphtheria antitoxin less than 0.01 U/ml. It is probable that in these children, because of the use of plain toxoid for primary immunization, antitoxin can never be maintained at a satisfactory concentration by booster doses given according to the regular schedule.

Only 62% of adults 20 to 29 years old had detectable

Table VI—Measles antibody status in relation to immunization with live measles vaccine in children 4 to 6 years old

Vaccination status	No. of children	% of children	% of children with antibody (titre, ≥ 1/10)
Not vaccinated	308	57	51
Vaccinated	231	43	85
<1-2 years*	83	15	88
3-5 years	148	28	84
Total	539	100	66

*After vaccination.

Table VII—Relation of antibody status to number of doses of diphtheria and tetanus toxoids (DPT Polio Vaccine) in children 4 to 6 years old

	% of children with antitoxin (concentration, ≥ 0.01 U/ml)*						
Antitoxin	0 (2)	1 (1)	2 (1)	3 (17)	4 (48)	5 (25)	≥6 (6)
Diphtheria	0	22	46	80	83	93	95
Tetanus	0	50	86	92	96	99	98

*Percentage of children with indicated number of doses in parentheses.

antitoxin, and immunity was progressively less in the two older age groups (Table VIII), though diphtheria toxoid has been in widespread use since about 1930. This indicates that immunity in the adults resulted chiefly from immunization during school years, with relatively little follow-up after that period.

Tetanus

Immunity to tetanus was found in 94% of children about to enter school and in almost all school-age children (Tables I and VII). The percentages of children 4 to 6 years old with tetanus antitoxin varied between the health unit areas, from 84 to 100%. However, antitoxin was detected in only 60% of women 23 to 29 years old and in only 25% of those 30 to 45 (Table VIII). The presence of tetanus antitoxin can be attributed entirely to immunization with tetanus toxoid because tetanus infection does not produce detectable antitoxin, the lethal dose of tetanus toxin being less than the threshold amount required to stimulate antibody response. Examination of the relation of antitoxin to the number of doses of toxoid (Table VIII) in children 4 to 6 years old shows that 96% of those who had received four doses and 99% of those who had received five doses had detectable antitoxin. However, as with diphtheria antitoxin, because of the use of plain toxoid for primary immunization, tetanus antitoxin cannot be maintained at a detectable concentration even with repeated booster doses in a small number of children — 1 to 2% for tetanus antitoxin.

The deficiencies and the remedies

Two types of serious deficiency were discovered in the immune status of children 4 to 6 years old about to enter school and in adults. The remedies prescribed are neither new nor unusual but are, in fact, the methods of immunization used in almost all countries.

The first deficiency was in poliovirus antibodies. Only 65% of children about to enter school had antibodies to all three types of poliovirus, and even in those with five or more doses of Salk vaccine not more than 75% had antibodies to all three types. With almost no exposure to natural infection or immunization with Sabin vaccine the percentage of children with antibodies cannot be expected to increase beyond this level as the children grow older. Thus, without the use of Sabin vaccine the immunity of the school-age population, due in large part to previous natural infection and the Sabin vaccine mass campaign in 1962, will undoubtedly decline from the high level in 1969-70.

It is clear, therefore, that Sabin vaccine should be used following primary immunization with Salk vaccine. This schedule will provide the greatest possible efficacy and safety. It is also evident that the risk of vaccine-associated illness, albeit extremely low, will increase in the future. Therefore, the addition of Sabin vaccine to the immunization schedule should be made as soon as possible. In Canada, only Ontario and Nova Scotia rely on Salk vaccine alone for immunization against poliomyelitis. The only other countries that do so are Sweden and the Netherlands.

Table VIII—Diphtheria and tetanus antitoxin status of adults*

Age group (yr)	Diphtheria antitoxin: No. of subjects tested	Diphtheria antitoxin: % with antitoxin (≥ 0.01 U/ml)	Tetanus antitoxin: No. of subjects tested	Tetanus antitoxin: % with antitoxin (≥ 0.01 U/ml)
23 - 29	466	62	468	60
30 - 39	580	54	575	25
40 - 45	183	39	182	25
Total	1229	55	1225	38

*Chiefly women.

The second type of deficiency was in immunity to diphtheria and to tetanus. Of the children 4 to 6 years old 18% had no diphtheria antitoxin and 6% had no tetanus antitoxin. Even after six or more doses of DPT Polio Vaccine, all within about 5 years, 5% had not developed diphtheria antitoxin and 1 to 2% remained without tetanus antitoxin.

These failures can only be explained by the observations of Trinca[12] that, of individuals who had received plain (unadsorbed) tetanus toxoid for primary immunization, some could not subsequently respond properly to booster doses. This may be due to the relatively rapid release of antigen injected in the form of plain toxoid. The slow release of antigen from the adsorbed preparation more closely resembles the release of antigen in natural infection. The remedy for these failures is straightforward — namely, the use of adsorbed toxoids. These have been shown to be more immunogenic than plain toxoids[13] and have been used in most countries for many years. Indeed, Canada is virtually the only country still using unadsorbed toxoids.

Of the adults tested, 45% had no diphtheria antitoxin and 62% lacked immunity to tetanus. Immunization of adults is a difficult problem. However, one measure is to use adsorbed toxoids in schoolchildren to induce higher levels of antitoxins in a larger percentage of individuals and thus provide a longer period of immunity after the individual leaves school.

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References

1. SEVER JL: Application of a microtechnique to viral serological investigations. *J Immunol* 88: 321, 1962

2. MOREAU P, FURESZ J: A rapid micro tissue culture assay in BS-C-1 cells for the titration and neutralization of measles virus. *Can J Microbiol* 13: 313, 1967

3. FURESZ J, MOREAU P, YAROSH W: A micro tissue culture test for the titration and neutralization of rubella virus. *Can J Microbiol* 15: 67, 1969

4. TAYLOR EM, MOLONEY PJ: Assay of diphtheria and tetanus antitoxins in small volumes of blood. *Can J Public Health* 51: 135, 1960

5. MELNICK JL, BURKHARDT M, TABER LH, et al: Developing gap in immunity to poliomyelitis in an urban area. *JAMA* 209: 1181, 1969

6. GALBRAITH NS, FERNANDES R: Polio antibody titres in children aged 7-15 years in London. *Lancet* 2: 792, 1969

7. BÖTTIGER M, ZETTERBERG B, SALENSTEDT C-R: Seroimmunity to poliomyelitis in Sweden after the use of inactivated poliovirus vaccine for 10 years. *Bull WHO* 46: 141, 1972

8. FURESZ J: An antibody survey of children in an Ottawa public school. *Can J Public Health* 64: 398, 1973

9. WYLIE HW, FRANCIS D, DEVADASON C: Immunity study in New Brunswick 1971-72. *Can J Public Health* 65: 124, 1974

10. GOLD E, FEVRIER A, HATCH MH, et al: Immune status of children one to four years of age as determined by history and antibody measurement. *N Engl J Med* 289: 231, 1973

11. O'NEIL AE: The measles epidemic in Calgary 1969-70; the protective effect of vaccination for the individual and the community. *Can Med Assoc J* 105: 819, 1971

12. TRINCA JC: Antibody response to successive booster doses of tetanus toxoid in adults. *Infect Immun* 10: 1, 1974

13. EDSALL G: Bacterial diseases: the problem, and control by vaccine, in *International Conference on the Application of Vaccines Against Viral, Rickettsial, and Bacterial Diseases of Man.* Proceedings. Washington, DC, Dec 14-18, 1970, Pan Am Health Org sci publ no. 226, 1971, pp 319-322