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THE EFFICIENCY OF VARIOUS ANTI-TYPHOID VACCINES *

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For over a year the California State Board of Health has been manufacturing at the hygienic laboratory the Gay-Claypole¹ sensitized antityphoid vaccine and distributing it free to physicians. Data cards are sent with the vaccine and physicians are requested to describe reactions and complications and to report any cases of typhoid fever in those who have been vaccinated. When the data cards are not returned, a follow-up postal card is sent. Under this system reports of several cases of typhoid fever in vaccinated persons were received soon after the beginning of the distribution. The investigation here reported was undertaken to determine whether these failures were peculiar to the type of vaccine distributed by the state board of health and also to arrive at a more accurate idea of the value of antityphoid vaccination in the civil population.

The literature on antityphoid vaccination gives little information regarding its value under the conditions of ordinary civil life. For armies there is a rapidly increasing mass of evidence. In five sets of statistics for antityphoid vaccination in the British army, both during the campaigns in South Africa and in selected test-groups of soldiers in India,² there were large numbers of unvaccinated men to serve as controls by indicating the extent of the exposure and the relative protection of the vaccinated men. Among the unvaccinated there were from two to seven times as many cases of typhoid fever as among the vaccinated.

Vincent³ reports more remarkable results for various bodies of troops in the French army. The typhoid morbidity among those vaccinated with a polyvalent vaccine killed with ether varied from nothing to 0.18 per thousand men, while among the unvaccinated it ranged from 2.22 to 225.61 per thousand. In the German army in the Herero campaign in southern

West Africa in 1904 to 1907 there were twice as many cases among the unvaccinated as among the vaccinated.⁴

Brilliant success with typhoid vaccination is shown in the experience of our own army,⁵ the morbidity being reduced to 0.03 per thousand men with no deaths. An almost complete absence of unvaccinated men to serve as controls makes it impossible to state just how far this success is due to improvement in the vaccine and in the method of administration.

There are three important factors which determine how much vaccination will reduce typhoid fever in a community:

1. The efficiency of the vaccination, as shown by the degree of immunity produced in the individual.
2. The proportion of vaccinated individuals in the community.
3. The extent of the exposure to typhoid infection, especially of exposure other than simple contact with individuals within the community.

In analyzing the success of vaccination in our army we cannot give all the credit to the first factor, which depends largely on the kind of vaccine and the method of administration, and also on the power of the individual to respond, because like results are not being obtained by similar methods in the civil population in places where the other factors are unfavorable. In the army the second factor must play a large part, because almost all the men are vaccinated and most of the individuals with whom the soldier comes in daily contact are immune and therefore unlikely to develop typhoid fever and to expose him to contact infection. There is, therefore, little chance for typhoid fever to spread in the army through contact even if it should in rare instances gain entrance to a body of thoroughly vaccinated troops. In the civil population we find that most of our failures are in persons who have lived in the same household with typhoid patients, who have nursed typhoid patients, or who have been exposed to some heavily polluted common food or water supply. The third factor is favorable in the army, especially in time of peace, as heavy and wholesale exposure is being prevented by scientific control of food and water supplies and of the general sanitation of camps and barracks. It is obvious that we cannot expect results similar to those in our army among the civil population where the percentage of the population vaccinated is small, and the exposure to contact infection correspondingly increased, and where there is often serious neglect of the supervision of public water, milk, and food supplies.

* Read before the Section on Pathology and Physiology at the Sixty-Sixth Annual Session of the American Medical Association, San Francisco, June, 1915.

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2. McWeeney, E. J.: Immunity Against Infectious Disease, with Special Reference to Antityphoid Inoculation, *Lancet*, London, Feb. 6, 1915, clxxxviii, 265. Firth, R. H., quoted by Russell, F. F.: Results of Antityphoid Vaccination in the Army in 1911, and Its Suitability for Use in Civil Communities, *THE JOURNAL A. M. A.*, May 4, 1912, p. 1331.

3. Vincent, H.: La vaccination antityphoïdique; résultats donnés par l'emploi du vaccin polyvalent, *Jour. med. franç.*, 1913, vi, 417; Sur la vaccination antityphique, *Jour. State Med.*, 1912, xx, 321.

4. Russell, F. F.: Results of Antityphoid Vaccination in the Army in 1911, and Its Suitability for Use in Civil Communities, *THE JOURNAL A. M. A.*, May 4, 1912, p. 1331.

5. Russell, F. F.: Antityphoid Vaccination in the Army During 1913, *THE JOURNAL A. M. A.*, May 2, 1914, p. 1371.

In the civil population, nurses have been more generally immunized than any other class. The exposure of nurses is much greater than that of the general population. Joslin and Overlander⁶ have estimated that a hospital nurse is about eight times as liable to contract typhoid fever as the ordinary citizen. Various reports on the immunization of nurses give morbidities in the vaccinated ranging from nothing to 10.7 per cent. and corresponding morbidities in the unvaccinated varying from 11.4 to 35.8 per cent.^{7, 8}

In epidemics, immunization of the general population has been resorted to frequently. Vincent⁹ reports two epidemics, comprising a total of 712 vaccinated persons with no cases, and 2,793 unvaccinated with a morbidity of 44.4 per thousand. Townsend⁷ reports an epidemic in Torrington, Conn., where there was one case of typhoid among 400 vaccinated persons. In the Sloane Hospital in New York, in a food-borne epidemic⁹ due to a typhoid carrier, there were seven cases (15.9 per cent.) among 44 persons who had been vaccinated with various makes of typhoid vaccine at various lengths of time before exposure. Among 30 unvaccinated persons there were six cases (20 per cent.). Spooner¹⁰ reports a water-borne epidemic in which sixty-five persons were exposed, of whom 29 were vaccinated during the outbreak. Among the vaccinated, one case occurred immediately after the first inoculation (3.4 per cent.). Of the unvaccinated 19 were still well at the time of the vaccinating, and five of these (26.3 per cent.) developed typhoid fever. Wade and McDaniel¹¹ report an epidemic in an institution, one month after the completion of vaccination of the inmates, wherein 1,396 vaccinated persons had 37 cases of typhoid (2.6 per cent.) with 3 deaths, and 304 unvaccinated had 16 cases (5.2 per cent.) with 2 deaths.

There are many reports of vaccination after epidemics, but in a considerable number of them judgment of the efficacy of vaccination is clouded by the fact that while the immunization was being performed other measures were taken to stop the epidemic, for example, the chlorination of a polluted water supply.

Statistics of vaccination among the general public, in the absence of epidemics, are meager. A total record of 26,376 such vaccinations was collected from the literature, with 9 subsequent cases, or 0.34 per 1,000. Most of these were reported in an incidental way that led to the conclusion that no special inquiry had been made to discover cases among the vaccinated.

In a small town in Kentucky¹² there were five cases of typhoid fever in persons who had, within eighteen months, been given vaccines made by at least four different commercial laboratories. About 1,000 persons in the town had been vaccinated. Russell¹³ reports absence of cases in 359 vaccinated children. Among 11,772 vaccinated employees of the Canadian

Pacific Railway on the western lines there were only four cases and one death.¹⁴

In the literature the results of vaccination, varying from apparently complete protection to almost none, bring home the fact that the immunity is relative, and that the severity of the exposure determines to a large degree whether the immunized person will escape. Vaccination seems to be more effective against infection from a slightly polluted water supply or the ordinary contacts of our daily life than against infection from a heavily infected milk or food supply or from continuous close contact with an acute case of typhoid fever.

THE CALIFORNIA STATISTICS

To obtain information regarding the results of antityphoid vaccination in the civil population of California, a questionnaire was sent to 2,400 physicians. Replies were received from 815, and 218 of these had administered antityphoid vaccine to 8,124 patients.

In Table 1 are given the statistics so collected regarding failures to prevent typhoid fever. They are classified according to the type of vaccine and the

TABLE 1.—ANTITYPHOID VACCINATION IN CALIFORNIA UP TO APRIL 1, 1915

Manufacturer of Vaccine	Type	Number Vaccinated	Cases among Vaccinated	True Failures	Failures per 1,000 Vaccinations	Deaths, True Failures	Deaths per 1,000 Vaccinations
State Board of Health and University of Calif.	Gay - Claypole, sensitized	4,927	32	21	4.3	2	0.41
B.....	Sensitized...	22	0	0	...	0	
Make not stated....	Sensitized...	18	0	0	...	0	
United States Army	Unsensitized	88	1	1	...	0	
A.....	Unsensitized	2,024	24	15	7.4	2	0.99
B.....	Unsensitized	168	3	3	...	0	
C.....	Unsensitized	188	1	1	...	0	
D.....	Unsensitized	15	0	0	...	0	
E.....	Unsensitized	4	0	0	...	0	
F.....	Unsensitized	55	0	0	...	0	
Four private laboratories	Unsensitized	228	0	0	...	0	
Make not stated....	Unsensitized	136	0	0	...	0	
Make not stated....	Not stated..	251	0	0	...	0	
Total sensitized.....		4,967	32	21	4.3	2	0.41
Total unsensitized.....		2,906	29	20	6.9	2	0.69
Unclassified.....		251	0	0	...	0	
Total.....		8,124	61	41	5.0	4	0.49

manufacturer. All cases reported as typhoid fever and occurring at least thirty days and not more than two and one-half years after the first dose of vaccine are recorded as true failures.

In Table 1 the letters A to E represent well-known commercial biologic laboratories. The letter F represents a municipal laboratory. In the beginning of the table are shown the statistics for the Gay-Claypole vaccine¹ manufactured and distributed at first by the department of pathology of the University of California, but after April 1, 1914, by the hygienic laboratory of the state board of health. The vaccine was made from five virulent strains recently isolated in California, and was sensitized, killed with alcohol, dried, ground, and suspended in weighed amounts in physiologic salt solution. The water-soluble substances were then removed and the sediment was again dried, weighed, and suspended. In the earlier lots of vaccine this last step was not a part of the process of manufacture, and five of the persons who later devel-

6. Joslin, E. P., and Overlander, C. L.: *Separate Nursing and Isolation in Typhoid Fever*, Boston Med. and Surg. Jour., 1907, clviii, 427.

7. Townsend, J. H.: *Antityphoid Vaccination*, Am. Jour. Pub. Health, 1914, iv, 993.

8. Ebersole, R. E.: *The Value of Typhoid Vaccination in Civil Communities*, Med. Rec., New York, 1913, lxxxiv, 894.

9. Ogan, M. L.: *Immunization in a Typhoid Outbreak in the Sloane Hospital for Women*, New York Med. Jour., 1915, ci, 610.

10. Spooner, L. H.: *Antityphoid Inoculation*, THE JOURNAL A. M. A., Oct. 12, 1912, p. 1359.

11. Wade, E. M., and McDaniel, O.: *Observations on the Widal Reaction Following the Administration of Typhoid Vaccine*, Am. Jour. Pub. Health, 1915, v, 136.

12. Gaither, J. G.: *Antityphoid Inoculation*, Correspondence, THE JOURNAL A. M. A., Oct. 10, 1914, p. 1314.

13. Russell, F. F.: *Antityphoid Vaccination in Children*, THE JOURNAL A. M. A., Feb. 1, 1913, p. 344.

14. Medical News, Canada, THE JOURNAL A. M. A., March 27, 1915, p. 1086.

oped typhoid fever received this earlier vaccine. One of these five persons received a vaccine made from a single strain instead of from the five used in the present method.

The firm A which manufactured the greater part of the unsensitized vaccine used in the cases here reported on followed in essentials the United States Army method of manufacture and used the same typhoid culture (Rawlings).

In Table 2 are shown the intervals between the administration of the first dose of vaccine and the onset of typhoid fever in those vaccinated.

In using the table it must be kept in mind that the failures do not in all instances belong to the groups of vaccinations reported. All vaccinations reported, in answers to the questionnaire, as administered up to April 1, 1915, and all failures reported in these answers or afterward by letter up to June 21, 1915, are included in the tables without regard to whether the failures belonged strictly to the particular groups of vaccinations included in the answers to the questionnaire. In some cases the failures were reported by physicians other than those who did the vaccinating, and reports of all the corresponding vaccinations could not be obtained.

In determining whether cases were true failures the interval of time was counted from the date of the first dose of vaccine, because the methods of administration were not alike. The vaccine distributed by the state board of health was given at intervals of two or three days, while most of the other kinds were administered at intervals of ten days.

The basis for determining the diagnosis was in most cases not entirely satisfactory, especially as a positive Widal reaction is not proof of the diagnosis of typhoid fever in a vaccinated person. In all cases the symptoms were regarded by the attending physician as those of typhoid fever. In six of the patients

unvaccinated patients in the same group of cases of typhoid fever.

In Table 3 are shown estimates of the severity of the attacks of typhoid fever in the cases classed as true failures of the vaccination.

EXTENT OF EXPOSURE

The extent of exposure of the vaccinated persons was so very much greater than the average exposure of the citizens of the state, that in spite of the protec-

TABLE 3.—SEVERITY OF TYPHOID FEVER IN FORTY-ONE CASES CLASSED AS TRUE FAILURES

Manufacturer	Mild	Mod- erate	Severe	Hemor- rhage	Perfora- tion of Intestines	Death
State Board of Health and University of Calif.	12	3	6	2	2	2
United States Army	1
A.....	4	4	7	1	0	2
B.....	...	3
C.....	1
Total.....	16	10	15	3	2	4

tion due to the vaccination, the typhoid death rate among vaccinated persons was considerably greater than the typhoid death rate for the state taken as a whole. This is due to the fact that most of the vaccine is sent to the parts of the state having the most typhoid fever and at the seasons of greatest exposure, when the appearance of cases warns the public of the danger of infection. The unusual extent of exposure is indicated by the fact that 824 of the vaccinated persons were nurses, most of them in charge of typhoid cases; 953 were vaccinated in the presence of typhoid fever epidemics; 28 were physicians; 15 were workers in bacteriologic laboratories; and 608 were members of households in which there were acute cases of typhoid fever. Among the 41 true failures, the vaccinated persons were exposed as follows: In 7 cases they received their infection from acute cases of typhoid fever in the same households; in 8 cases they were nurses in charge of cases of typhoid fever; in 2 cases they were bacteriologists working with virulent typhoid cultures; in 6 cases they were exposed to polluted water in water-borne outbreaks; in 5 cases they were exposed in a milk-borne epidemic; one case was that of a physician; and in 12 cases no special history of exposure was obtained. The exposures were similar in the cases of failure after the use of the sensitized and of the unsensitized vaccines. Unfortunately there is no way of estimating with any approach to exactness how many of the vaccinated persons would have developed typhoid fever if not vaccinated.

The extent of the exposure seems to be one of the most important of the factors which determine whether or not a vaccinated person will develop typhoid fever. In a food-borne outbreak like that at the Sloane Hospital in New York⁹ vaccination seems to give inadequate protection, while in the more usual exposures of less severity, we can expect a considerable degree of protection. An instance in which vaccination was apparently of little value is furnished by a recent milk-borne typhoid epidemic in California. On the milk-route under suspicion there were 643 persons, of whom 17 had previously received the anti-typhoid vaccine distributed by the state board of health. There were 23 cases in the outbreak, 5 in

TABLE 2.—INTERVALS BETWEEN THE FIRST DOSE OF VACCINE AND THE ONSET OF TYPHOID FEVER

Manufacturer	Interrupted Vaccinations, Two Doses Only	Early Cases, 1 to 30 Days	True Failures				Totals
			30 to 60 Days	2 to 6 Mos.	6 to 12 Mos.	12 to 30 Mos.	
State Board of Health and University of California	1 (17 mos.)	10	6	4*	4	7	32
United States Army	1	1
A.....	1 (31 days)	8	4	3	5	3†	24
B.....	1	1	1	3
C.....	1	1
Total.....	2	18	10	8	10	13	61

* Includes one case completely vaccinated twice, once fourteen months, and again three months before the onset, and infected in a laboratory.

† One case, a nurse, vaccinated sixteen months before the onset, gave a history of having had typhoid fever twelve years before.

who had received vaccine from the state board of health or the University of California a culture was obtained from the blood or at necropsy and in each case the organism obtained proved to be the typhoid bacillus. Blood cultures demonstrated the presence of the typhoid bacillus in the blood of three of the patients who had received the vaccine of Manufacturer A. In a few cases agglutination tests of the patient's serum were made with paratyphoid A and paratyphoid B bacilli, but with negative results. In a number of cases the diagnosis was strengthened by the fact that there were records of positive Widal reactions in

vaccinated persons (three in one family), and 19 in unvaccinated people. Considering the outbreak by families, we find that there were 76 nonvaccinated families, 17 of which had typhoid fever in at least one person, and 7 vaccinated families, two of which had typhoid fever.

In a recent outbreak due to the drinking of water from a polluted well, out of twelve cases there were two in vaccinated persons. One had received the state board of health vaccine and the other had been given the vaccine of Manufacturer B.

Under the heavy exposure to typhoid fever which occurs in the civil population in various parts of the United States such occurrences as the above will take place from time to time and give rise to a distrust of typhoid vaccination unless more exact information is furnished regarding typhoid immunization in the civil population.

COMPARISON OF THE EFFICIENCY OF THE VARIOUS VACCINES

From the table it would appear that the Gay-Claypole vaccine has greater efficiency, measured by the lower percentage of true failures, than the unsensitized vaccines considered as a group. This is not shown beyond question by the facts at hand because the two sets of figures are not exactly comparable. The methods of distributing the vaccines were different, with the result that more of the Gay-Claypole vaccine than of the unsensitized varieties was used in large groups of people, as in lumber camps and institutions. Another possible source of error is the fact that a large part of the Gay-Claypole vaccine was distributed as late as the summer of 1914 and a certain number of failures are still to be expected in the vaccinated persons reported in the questionnaire. A number of additional failures would also be expected in the persons reported as vaccinated with the other makes. It is, therefore, out of the question to draw any definite conclusions regarding the superiority of one vaccine over another, on the basis of the figures available, but the statistics seem to indicate that there is no great difference between the principal types, and that the reported failures of the vaccine manufactured and distributed by the state board of health were not due to inferiority of the vaccine issued, but rather to limitations common to the several types of vaccine administered to the American public.

REACTIONS AFTER ANTITYPHOID VACCINATION

The severity of the reaction, as valued by the physicians who returned the questionnaire, is shown in Table 4. Observations regarding 2,695 vaccinations of university students and inmates of institutions with the Gay-Claypole vaccine by two physicians were excluded so that the figures might fairly represent a composite of the opinions of a large number of physicians. The fourth column in the table shows how many persons had reactions sufficiently severe, in the opinion of their physicians, to warrant their staying in bed for at least half a day. The classification of reactions as slight, moderate, and severe was intentionally left entirely to the physicians making the reports in order to find out their opinions regarding the amount of annoyance caused by the combined local and general reactions rather than to obtain exact observations on the phenomena. The question of severity of reaction is important when it comes to persuading the public to submit to vaccination in large enough

numbers to make an appreciable reduction in the morbidity from typhoid fever.

It will be seen that the estimates of the severity of the reactions are almost alike for the sensitized and unsensitized vaccines. It was expected that the sensitized vaccines would cause distinctly less discomfort. Similar results have been obtained by E. S. Kilgore, in a series of observations, as yet unpublished and referred to here through his courtesy. Observations were made by Kilgore on the reactions of eighty-five subjects, vaccinated in four nearly equal groups. Two groups received the United States Army vaccine, obtained through the courtesy of Captain Henry J. Nichols, and two groups received the Gay-Claypole vaccine manufactured by the hygienic laboratory of the state board of health.

Of each pair of groups receiving the same kind of vaccine, one received the vaccine at two-day intervals, and the other at ten-day intervals. The reactions were

TABLE 4.—REPORTS OF REACTIONS IN 5,429 VACCINATIONS

Kind of Vaccine	Not Specified	Absent		Slight		Severe		Necessitating Stay in Bed	
		No.	%	No.	%	No.	%	No.	%
Gay-Claypole.....	97	578	28.5	1,159	57.1	294	14.4	49	2.4
A.....	180	591	32.7	979	54.2	235	13.0	92	5.1
B unsensitized.....	0	61	38.1	98	61.3	1	0.6	4	2.5
B sensitized.....	0	16	59.3	11	40.7	0	0	0	0
United States Army.....	1	43	50.0	38	44.2	5	5.8	4	4.7
C.....	0	87	48.1	93	51.3	1	0.6	2	1.1
D.....	0	1	6.7	9	60.0	5	33.3	3	20.0
E.....	0	0	0	3	75.0	1	25.0	1	25.0
F.....	0	23	43.4	27	50.9	3	5.7	3	5.7
Two private laboratories.....	0	122	59.5	82	40.0	1	0.5	1	0.5
Maker not specified.....	190	98	24.9	270	68.5	26	6.6	3	0.7
Total sensitized.....	97	594	28.9	1,170	56.9	294	14.2	49	2.4
Total unsensitized.....	181	928	37.0	1,329	53.0	252	10.0	110	4.4
Total unspecified.....	190	98	24.9	270	68.5	26	6.6	3	0.7
Total.....	468	1,620	32.7	2,769	55.8	572	11.5	162	3.3

measured mathematically on the basis of temperatures and measurements of the size of the local reddened area and the slight increase in circumference of the inoculated arm. The vaccines were used in the dosages recommended by their manufacturers and these were not exactly alike. Within the limits of Kilgore's tests and our inquiry no definite diminution of reaction due to sensitization was determined, unless this is indicated by the smaller number of persons (Table 4) who were sick enough to go to bed after receiving the sensitized vaccine.

CONCLUSIONS

1. Antityphoid vaccination is meeting a severe test in the civil population because the vaccine is most used where the exposure is greatest, and because only a small proportion of the people are vaccinated.

2. In California an inquiry has shown that the true failures were 5.0 per thousand vaccinations reported, and the deaths from typhoid fever were 0.49 per thousand. The total number of vaccinations reported was 8,124.

3. The percentage of failures indicated a slight advantage for the Gay-Claypole sensitized vaccine over the unsensitized vaccines, but the superiority was not conclusively demonstrated as the different sets of statistics were not exactly comparable.

4. There is little difference between the vaccines, sensitized and unsensitized, in common use in California with regard to the severity of reactions after inoculation.

5. If widespread and severe exposures are prevented by better supervision over public water, milk, and food supplies, vaccination can be depended on to diminish greatly the residual typhoid fever, especially if a large enough proportion of the people are vaccinated to reduce contact infection to a minimum.

ABSTRACT OF DISCUSSION

DR. GEORGE E. EBRIGHT, San Francisco: The interesting part of Dr. Sawyer's paper consists in his comparison between the use of vaccine in the army and in the civil population. There are three things which we, as clinicians, always naturally bear in mind and consider in giving typhoid vaccine to a patient. First, there is the degree of immunity that will be accomplished. As Dr. Sawyer says, we are not able at present to establish a conclusion from that comparison. Second, is the duration of the time required for the patient to receive a complete vaccination. The sensitized serum has the advantage of requiring a shorter period of time for administration. Then there is the matter of suffering and reaction which the patient will have to undergo. There again we are not able to come to a conclusion. But there are a number of things that arise for comparison between the army and the civil population. There are in civil life a number of things that do not obtain in the army. The civil practitioner has to deal not with the healthy soldier, subject to repeated physical examination in addition to the examination which he undergoes before he joins the army, but persons as well who may be suffering from any of the chronic diseases, such as tuberculosis. From my own experience I am very loth to give antityphoid vaccine to a person with the least degree of active tuberculosis. I have seen three cases in which the reaction was unusually severe in comparison with non-tuberculous people. It would be premature, however, to come to a conclusion at the present time regarding the relation of a vaccine reaction against typhoid and tuberculosis, but inasmuch as the question is still undecided, it is the part of wisdom to be conservative. Finally, it is desirable to be mindful in making comparisons between army vaccine and sensitized vaccine of the possibility of army encampments being under better general sanitary conditions and being less subject to the danger of infection than is the case in civil practice.

DR. H. J. NICHOLS, San Francisco: Dr. Sawyer's paper gives just the sort of results that I personally expected to see in the army in the course of a year or so after vaccination was introduced. I hardly expected that our results would be as good as they have been, but they have continued to be remarkable. The most recent statistics are just as good as they have been for the last three or four years. In other words, up to 1910, since 1904, we had been having between 200 and 300 cases of typhoid a year. During the Spanish War our rate was very high, but it dropped to a minimum of the number stated. Then came the results of vaccination. It is often said that sanitation has had a great deal to do with our results. I beg to differ from that opinion. I am somewhat familiar with conditions in the army, and I can say emphatically that sanitation has made no unusual advance since 1910 in the army; there have been no radical changes. Since 1910 and 1911, when vaccination became compulsory, our rates have dropped remarkably. Last year (1914) we had seven cases of typhoid fever. Four of these were in recruits who were taken into the army during the incubation period of typhoid. Three had been vaccinated, one five years before the attack, one had two doses two years previously, and one, three doses two years previously; but the majority of our cases are now in recruits who are taken in during the period of incubation. In a week or two after they enlist some men develop typhoid fever. Sometimes they have had one inoculation.

The fact is that our results are just as good today as they were when typhoid vaccination was first impressed on

the public as being of great value. We have had no such bad luck as Dr. Sawyer reports in California. I do not pretend to say what his results are due to, but I do feel like emphasizing the fact that our vaccine is made with great care. It is a very simple matter, but it is made according to definite principles and they are rigidly adhered to. It is not an experiment with us any more. It is too valuable to experiment with, and we do not allow any changes to be made.

Another thing, we do not allow any vaccine to be used after four months. A great many of the commercial houses are allowed by law to put a year's limit on the vaccine. I do not know what effect this may have had in Dr. Sawyer's results. Again some persons receive only one dose or two. Our men take three doses, or they hear from us. All these factors are to be considered. Of course we are all in the same boat and the same principles must hold inside or outside of the service. I do not feel, however, that the explanations which are given for our success, such as lack of exposure, etc., are at all conclusive. Our men certainly are subject to the same infection that anyone is. Our soldiers go down town and go into restaurants, and everywhere they are subject to the same contamination as any other citizen. I cannot help believing myself, personally, that our vaccine is somewhat superior to the vaccines in general use. At any rate, the fact is that we have not had any such setback as is mentioned by Dr. Sawyer.

DR. E. S. KILGORE, San Francisco: It is unfortunate that it was not possible to obtain reliable returns from another 8,000 unvaccinated subjects living in the same communities and under the same conditions as those included in this analysis. They would be the only group with which it would be fair to compare these results, and for reasons given in the paper they would undoubtedly have shown a much greater morbidity than the population at large. As it stands, the sensational fact which will stick in the mind of the ordinary reader is that there is actually more typhoid fever among the civil population who have received antityphoid vaccination than among those who have not. This impression will be false and dangerous unless the reasons for it given in the paper are duly appreciated. A factor not mentioned by Dr. Sawyer which may account for some of the morbidity among vaccinated subjects is the feeling of security which they have and the consequent relaxation of hygienic measures they would otherwise employ. The feeling has been widespread that antityphoid inoculation is a sure preventive, and the individual who considers himself already safe will not take troublesome precautionary measures. Therefore, an important practical lesson to be taken from this paper is that whenever we immunize people against typhoid fever (or any other infection) particular pains should be taken to make them understand that the protection conferred is not absolute and does not remove the necessity for ordinary hygienic precautions. In view of the presumable necessity of vaccinating every two or three years in order to maintain protection against typhoid, the question of relative severity of reactions following subsequent vaccinations has some importance. Some have been restrained from revaccination on account of the prevalent idea that later vaccinations produce greater discomfort than initial ones. Our experience at the University of California Hospital is that this is not true about as often as it is true, and that the average reactions from first and from later inoculations is practically the same.

DR. L. B. WILSON, Rochester, Minn.: At the meeting of the Colorado State Medical Society last September, Jolley reported the results obtained by the use of typhoid vaccine in the National Guard while encamped during a strike in immediate proximity to a village in which a large number of cases of typhoid were occurring among private citizens. I do not remember the exact figures, but my impression is that the results were excellent, though there was abundant opportunity for the vaccinated men to become infected.

DR. W. A. SAWYER, Berkeley, Calif.: I believe with Dr. Nichols that antityphoid vaccination was a very important

factor, perhaps the most important single factor, in the astonishing success in the reduction of typhoid fever in the army. If it is claimed that the vaccine used in the army is superior to the vaccines manufactured by commercial houses which follow in their way the methods of the army laboratories, I wish it could be arranged that a large amount of the army vaccine, say enough for 10,000 people, could be distributed for use in the civil population of California. Then we should soon know whether the vaccine of the army is more efficient than the material now in use. If it is, the fact should be ascertained as soon as possible, so that the public will receive the most efficient antityphoid vaccine which can be manufactured.

THE CHOICE AND TECHNIC OF THE ANESTHETIC

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It is the purpose of this paper to analyze the many existing methods of anesthesia with the object of determining if possible in a judicial way what anesthetics should be selected and what technic should be employed in a general surgical clinic. In making this analysis and in arriving at conclusions, we have been controlled by certain requirements: first, the safety of the patient; second, the comfort of the patient; third, the efficiency of the anesthetic agent; fourth, control, avoiding anesthetics which cannot be withdrawn with the first appearance of danger; fifth, the simplicity and general adaptability of the method; sixth, after-effects on blood tissues and viscera; seventh, complications, vomiting, etc., and eighth, effects on immunity against pus organisms, pneumococci, etc.

This study is based on the special interest devoted to this subject in my own clinic by myself and assistants, Drs. Isabella C. Herb, Hamburger and Ewing, Evarts Graham, B. F. Davis, and F. B. McCarty, on pieces of laboratory research which we have carried on, on observations made in the clinics of others both in this country and abroad, and from a study of the literature. The last ten years have been very active ones in the field of anesthesia. New and better means of local anesthesia have been introduced. The use of nitrous oxid has been gradually extended, especially in this country. Complicated apparatus, mixtures and sequences have been widely employed. The use of scopolamin and morphin and various substitutes for morphin, pantopon, narcophin, etc., have been given an extended trial. The intralaryngeal method has been developed by Meltzer and Auer. Spinal anesthesia, nerve blocking, and intravenous and rectal anesthesia have enthusiastic supporters, and have been employed in large series of cases. We have during this period seen in this country the gradual development of the trained anesthetist as a member of the surgical team. So much work has been done that it would seem that we have at hand enough evidence to determine what are the best and safest anesthetics, and in what particular fields each should be employed. Such an analysis would necessarily cover a very wide field, and in this brief paper it will be possible to present simply the essential facts of this study of each of the agents and the methods.

I began this study with the intention of securing for my own clinic methods of anesthesia which would cover fully the entire surgical field, which would be the safest, most efficient, the most satisfactory to both

patient and surgeon, the simplest and least complicated. I desired also to find anesthetics which could be adopted and employed by medical men generally, as my clinic is a teaching clinic for medical students, and part of their instruction is the giving of anesthetics. From this standpoint I have analyzed the following:

1. Chloroform.
2. Ether.
3. Nitrous oxid gas.
4. Scopolamin and morphin.
5. Spinal anesthesia.
6. Blocking.
7. Infiltration.
8. Intravenous, general and local.
9. Intrarectal.
10. Intratracheal.
11. Intrapharyngeal.
12. Mixtures.
13. Sequences.
14. Anociassociation.

In each instance we have analyzed these agents and methods from the standpoint of:

1. Safety.
2. Comfort.
3. Efficiency.
4. Control.
5. Simplicity and general adaptability.
6. After-effects on blood and tissues and viscera.
7. Complications, vomiting, etc. Paresis of bladder and bowels.
8. Effect on immunity to pus organisms, pneumococcus, etc.

As a result of this study I submit the following brief summary:

CHLOROFORM BY INHALATION, OPEN DROP METHOD

1. Safety: The most dangerous of all inhalation anesthetics. Deaths from one in 1,000 to one in 3,000 on the operating table.

2. Comfort: A most agreeable anesthetic to the patient.

3. Efficiency: The most efficient anesthetic. Anesthesia and relaxation profound and complete.

4. Control: The anesthetic can at once be stopped on the appearance of danger signals, but the chloroform already in the system cannot be rapidly eliminated, and the effects persist for a considerable period. The margin between the required anesthetic dose and the toxic dose is too narrow for safety.

5. Simplicity and general adaptability: All that could be desired.

6. After-effects on blood tissues and viscera: Reduces hemoglobin. Produces often what is now generally recognized as late chloroform poisoning with fatty degeneration of liver, kidneys and muscle tissue which is usually fatal.

7. Complications: Vomiting in about one third of the cases. Lung complications and nephritis in a small percentage.

8. Effects on immunity: Reduces resistance against pus organisms, pneumococcus, etc.

Conclusion.—Because of its efficiency, comfort and simplicity it has probably been employed more generally the world over than any other anesthetic, possibly more than all other anesthetics combined. And yet the time has come when chloroform in spite of its many advantages should be absolutely and finally discarded because of the huge mortality attending its use