The Use of Toxoid for the Prevention of Tetanus Neonatorum

Final Report of a Double-blind Controlled Field Trial *

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With a view to determining the effectiveness of a method for the control of tetanus neonatorum which would be independent of medical examination or care, a double-blind field trial covering 1618 women was conducted between 1961 and 1966 in a rural area of Colombia with an estimated existing tetanus neonatorum death rate of 11.6 per 100 births. The study group was given 1-3 injections of 1 ml of an aluminium-phosphate-adsorbed tetanus toxoid more than 6 weeks apart, and the control group a similar number of injections of an influenza-virus vaccine.

There was no statistically significant difference between those in the two groups given one injection. Those in the control group given 2 or 3 injections had a tetanus neonatorum death rate of 7.8 deaths per 100 births, and the corresponding subjects in the study group had none. This difference is unlikely to have occurred by chance.

In Northern Europe or in Canada, tetanus neonatorum is a curiosity which generally occurs in conjunction with a series of unusual circumstances, and results in an insignificant number of illnesses and deaths. As one approaches the tropics and subtropics, its importance changes. The number of illnesses and deaths increases; in some areas the mortality may be as high as 10% of births (Jelliffe, 1950; Earle & Mellon, 1958; Schofield, Tucker & Westbrook, 1961; Newell et al., 1964), exceeding that from all other causes of death in the first 28 days of life and becoming one of the dominating health problems. In between these two extremes, mortalities of the order of 1% of births are met with in certain large populations.

The areas with the highest rates are generally those with unsophisticated obstetrical services and only a small proportion of institutional deliveries. It appears probable that neonatal tetanus infection is directly related to birth practices influencing the contamination of the umbilical cord when it is cut or dressed at the time of the delivery.

A number of possible methods of preventing the disease have been proposed. They have ranged from the provision of obstetrical services to the protection of newborn babies with tetanus antitoxin or antibiotics. The introduction or improvement of services has advantages additional to the prevention of tetanus neonatorum, but it is clear that even minimal services are unlikely to reach many high-risk populations in the near future.

A number of investigators have considered other methods of prevention. Most work has been directed towards the passive protection of the baby. Broeck & Bauer (1923) and Nathan-Larrier, Ramon & Grasset (1927) described the passage of tetanus antitoxin across the placenta and suggested that this antitoxin might protect the baby. Later Schofield, Tucker & Westbrook (1961) showed, in a field trial in New Guinea, that two or three injections of 1 ml of CSL formolized tetanus toxoid given at 6-week intervals to pregnant women appeared to result in a dramatically lowered tetanus neonatorum rate.

For a method to be practical and economical in many communities, it must not only be effective and cheap to carry out, but it must also be able to be administered unselectively without the expense and organization needed for continuous detection of pregnancy. In the New Guinea study, facilities existed for prenatal care even though most of the deliveries were unsupervised. This is an exceptional situation: in most areas with high tetanus-neonatorum rates no organization exists for maternity services, and a method of prevention which requires the detection of women early in pregnancy is unworkable.

For these reasons we thought that it might be more practical to attempt to immunize women with tetanus toxoid on a population basis, in the hope that sufficiently high tetanus-toxoid levels might remain for the protection of babies resulting from subsequent pregnancies. For this to be economical, protection would need to be effective for periods of at least 3 to 5 years.

In order to test this possibility, a double-blind controlled field trial was started in Guachene, Departamento del Cauca, Colombia, in August 1961. A preliminary report of the trial was published in 1964 (Newell, Dueñas, LeBlanc & Garces, 1964) and the present report gives the final results after the completion of the trial in May 1966.

STUDY PLAN

The main object of the study was to compare the tetanus-neonatorum morbidity and mortality rates of infants born to women who had received 1 to 3 injections of an aluminium-adsorbed tetanus toxoid at different intervals of time prior to and during pregnancy with those of a similar group of infants whose mothers had not been immunized.

It was also hoped to measure serum levels of tetanus antitoxin in groups of mothers whose infants appeared to have different levels of protection to tetanus neonatorum, as demonstrated in the trial. This investigation could not be attempted until after the conclusion of the trial, and will not be reported on in this paper.

There appeared to be three major problems which could influence the design of the study; these will be discussed in turn.

Spontaneous changes in tetanus neonatorum incidence

It was thought probable that relatively minor changes in birth practices could alter the risk of neonatal tetanus infection. It was also thought that these changes could be very local, and could take place over relatively short periods of time. Two adjacent areas can have markedly different tetanus rates, and the arrival or departure of a group of local midwives can result in major changes in incidence. The comparison of the results in a treated with those in an untreated village over a 5-year period might therefore give major difficulties in interpretation. For the same reasons, a comparison within a single area of the incidence prior to immunization with that after immunization might be uninterpretable. To avoid these possibilities of error, it was decided that the trial would have to be a comparison, within one area, between two groups of infants whose mothers had been randomly allocated to a study and a control group.

Diagnosis

The differential diagnosis of tetanus neonatorum presents few difficulties (Trowell & Jelliffe, 1958). It was decided that four criteria would be used for the definition of the disease, in conjunction with direct observation and medical records when possible. These criteria were:

(a) the child should cry and suck normally during the first 2 days after birth;

(b) the first symptom would be a failure to suck during the first 3-10 days after birth;

(c) risus sardonicus should be present; and

(d) the mother should be able to demonstrate the typical spasms of the infant (flexion of the arms, clenched fists, extension of the legs, plantar flexion of the toes).

It was recognized that direct observation and/or medical records might only rarely be available in the field. The diagnosis would therefore often need to be made, using the above criteria, by direct questioning of the mother. If the immunization status of the mother was known, this could result in bias on the part of both the mothers and the field workers. To avoid this, the study was designed to be double-blind with the immunization history of the women unknown and unavailable to the women, the field workers and the investigators.

The field area

It was necessary to select a field area which was clearly defined; where sufficient persons and tetanus neonatorum cases existed to demonstrate a difference between groups which was unlikely to have occurred by chance more than 1 in 20 times if the method

employed was 50% or more effective; and where there was little likelihood of change in obstetrical services in the following five years.

The Corregimiento of Guachene in the Departamento del Cauca, 45 km south-east of Cali, Colombia, was chosen as it appeared to have all these characteristics. The area is a rural administrative unit, at an altitude of 1200 m, defined on three sides by rivers, and measuring approximately 7 km × 14 km. It has a small town of 1400 persons and a total estimated population of 8000-9000 persons. The population is largely of the Negro ethnic group. Because of an unbridged river, Guachene is cut off from the capital of the Municipio and has no local medical services. The area is served by local unregistered midwives without formal training, but has no nurse or doctor. No immediate changes in medical services were proposed. Malaria control by house spraying, and smallpox vaccination, had been carried out by visiting teams but no tetanus toxoid had been used in the area. Most of the people live scattered on the partly cleared forest near to their smallholdings and to their coffee and cacao trees. There were three medium-sized sugar plantations and a few large mixed farms in the area.

Births were not registered in Guachene at the start of the study (1961) but deaths were registered locally in the township. A review of the deaths registered in 1960 suggested that some deaths in the first 2 days of life might not have been registered, but no other records were available for confirmation. The number of deaths registered in 1960 as tetanus neonatorum was 37 and all but one occurred between the 3rd and the 16th days of life. With an estimated number of births of 320 per year, the estimated tetanus neonatorum mortality rate for that year was 11.6 per 100 births.

Tetanus neonatorum was well known in the area; it was called by a local name (*el mal de los siete dias*— the illness of the seventh day); the usual age of onset was recognized, and the main symptoms could be described.

The nature of the trial was explained to the local community leaders and a statement made that the trial would not result in additional medical services at that time. The trial was accepted and supported by the offer of an empty room in the medical centre as a field office.

THE STUDY

The study commenced with the survey and registration of all women between the ages of 13 and 45 years who could be contacted; the formation of a pregnancy register kept up to date by continuous survey; the encouragement of birth and death registration; and the regular visiting of the families of all known or suspected newborn children (at birth, at suspected tetanus illness, at death, and/or at 30 days after birth) to complete birth registration, and to record and distinguish between tetanus and non-tetanus deaths in the first 30 days of life. In this pre-immunization phase, 15 tetanus neonatorum deaths occurred among 136 newborn children of women who later volunteered to enter the study (tetanus neonatorum mortality rate of 11.0 per 100 births).

In the immunization phase, all registered women were allotted a code number according to their order of ascertainment. These code numbers had previously been divided by means of random sampling numbers into two groups, A and B. Women who were registered, but who refused any immunization, were placed in group C.

Any woman who agreed to accept immunization was injected intramuscularly with 1 ml of a preparation bearing the same group letter (i.e., A or B) as her registration card. One vaccine was a 10 LF commercial aluminium-phosphate-adsorbed tetanus toxoid and the other a polyvalent influenza-virus vaccine. The preparations were indistinguishable in appearance and packaging (apart from the colour of the label; see below), and were precoded by a person unconnected with the study. Neither the women nor the field workers knew which preparation was tetanus toxoid at any time during the trial. Three injections were offered to each woman with a minimum interval of 6 weeks between injections.

All groups (A, B, and C) were followed until May 1966 by the methods described for the pre-immunization phase. All births and deaths and all tetanus illnesses in the first 30 days of life were related to the code number, group and immunization status of the mothers at the time of their delivery by means of master cards.

Early in the immunization phase it was recognized by both the field workers and the volunteer women that one preparation with a label of one colour was slightly more painful for a few minutes after injection than was the other. No other reactions were observed. The use of a colour code in addition to the marking of the group on the preparation bottles proved to be an error, as it allowed a second decision to be made by some of the volunteers after their acceptance. A greater number of women refused in

TABLE 1

REGISTERED WOMEN BY GROUP AND IMMUNIZATION STATUS

Group	Number of registered women	Number of women given:		
		1 Injection	2 injections	3 injections
Control	846	272	144	430
Study	772	255	145	372
Non-immunized	1 158	0	0	0
Total	2 776	527	289	802

one group than in the other. At the conclusion of the study, the control group contained 10% more women than the study group.

The number of women and the number of injections given are shown in Table 1 and some of the characteristics of all three groups are tabulated in Table 2. Women in the control group were (on the average) one year older than in the study group. The women in these two groups had had a similar number of deliveries at registration and after the first injection, but the control-group women had a higher birth rate between registration and first injection, and a similar birth rate following first injection. (Group C were younger, of lower parity, and had fewer registered births during the study period.) While these differences may indicate variations which occurred by chance, or by a selective refusal which was not similar in the two groups, it is probable that women who, by their registration

number, would have been in the study group but refused included a greater proportion who recently had been pregnant and who were older.

These differences could be related to the expectancy of a woman having a liveborn child who could die of tetanus, and thus could have introduced a bias into group comparisons. However, the main study indicated that the age of the mother appeared to be unrelated to the risk of a newborn child having tetanus neonatorum, and that the differences were of such a minor order that it is improbable that they could explain the differences in tetanus neonatorum rates between the groups which were observed later.

RESULTS

Births

Between 17 August 1961 and 15 May 1966, there were 1888 recorded deliveries in the study population, resulting in 1919 registered live births (study group 625, control group 693, group C 601). This gave birth rates of 80.9 (study group), 81.9 (control group) and 51.9 (group C) births per 100 registered women. In addition, there were 145 recorded foetal losses (stillbirths and abortions) distributed at the rate of 9.6 (study group), 7.8 (control group), and 5.8 (group C) per 100 registered women.

The 1888 deliveries included 32 sets of twin births (one twin was stillborn) with 11 sets in the study group, 12 in the control group and 9 in group C. One of the twins died from tetanus neonatorum and one had non-fatal tetanus neonatorum, but the related twin in each case was unaffected. Of the 63 live twins, 9 died in the neonatal period from non-tetanus causes. As some of the twin births were

TABLE 2

SOME CHARACTERISTICS OF THE THREE GROUPS OF WOMEN

Group	Year of birth (mean)				Parity (mean)		Births			
	Total	With 1 injection	With 2 injections	With 3 injections	At registration	At end of study	Between registration and first injection		After first injection	
							No.	%	No.	%
Control	1936.3	1936.0	1937.2	1936.2	2.9	3.8	76	9.0	617	72.9
Study	1937.5	1937.6	1937.2	1937.5	2.8	3.6	60	7.8	565	73.1
Non-immunized	1938.7 [a]	—	—	—	2.3	2.9	—	—	—	—

[a] Year of birth unknown for 13 women.

clumped together in time, and as the twin deaths comprised 9% of all non-tetanus deaths, deaths related to twinning distorted the non-tetanus death rates in some groups in limited periods of the study.

Non-tetanus deaths

During the entire study, 102 non-tetanus deaths occurred in registered newborn children in the first 30 days of life (33 in the study group, 33 in the controls, and 36 in group C). Their age at death is given in Table 3. Of these, 59% died in the first 7 days and 23% in less than 24 hours after birth. No accurate data on the causes of death are available. The non-tetanus death rate per 100 births in the period from first injection to the end of the trial was 5.3 in the study group and 4.5 in the control group.

Tetanus cases and deaths

During the same period, 115 cases of tetanus neonatorum occurred in newborn registered children. Of these children, 109 died (case-fatality rate 95%). As the local treatment available was largely non-specific, this case-fatality rate could be considered to indicate the risks of an untreated tetanus neonatorum illness in a population of these racial, nutritional and social characteristics. Of the non-fatal tetanus illnesses, 3 occurred in the control group and 3 in group C. None was in the study group. The dates of onset of the illness were similar to those recorded for the fatal cases. One of the group-C children with a tetanus illness died on the 30th day of life from non-tetanus causes.

The age at onset and death of the 109 children who died from tetanus neonatorum is given in Table 3. The age at onset was distributed around the 6th and 7th days (mean 6.3 days); 1 child was less than 3 days old at onset (2 days), and 3 were more than 10 days old (2 were 11 days old and 1 was 12 days). These children did not thus fulfil all the four study criteria, but were registered as having tetanus neonatorum on other evidence. The ages at death were more widely distributed than the ages of onset and ranged from 3 to 19 days (mean 9.4 days). The interval between onset and death varied from 1 to 14 days but was frequently 2 or 3 days. No gross differences in the number of days of illness was apparent in children from the three groups.

Of the tetanus neonatorum deaths, 52 were in males and 57 in females.

The number and rate of births, tetanus deaths and non-tetanus deaths varied markedly from month to month throughout the study but there

TABLE 3

AGE AT ONSET AND DEATH OF ALL CHILDREN REGISTERED AS DYING FROM TETANUS NEONATORUM, AND AGE AT DEATH OF ALL REGISTERED NON-TETANUS DEATHS IN THE FIRST 30 DAYS
(ALL GROUPS)

| Days after birth | Tetanus | | Non-tetanus day of death |
	Day of onset	Day of death	
0	0	0	23
1	0	0	11
2	1	0	10
3	9	1	6
4	13	1	3
5	13	4	3
6	26	6	1
7	18	22	3
8	14	14	3
9	6	19	2
10	5	9	1
11	2	8	1
12	1	10	4
13	0	5	2
14	0	2	3
15	0	0	4
16	0	4	2
17	0	1	1
18	0	1	0
19	0	2	2
20-30	0	0	17
Unknown	1	0	0
Total	109	109	102

was no regular pattern. When the results for the whole 4½-year study period were examined by month, the differences were found not to be significant.

The age of the mother, her parity, and the birth order of the infants showed no relationship to the tetanus neonatorum death rates. No socio-economic classification of registered women was recorded.

During the study, 63 registered women died (5 per 1000 women per year). Of these, 22 were in the study group, 19 in the controls, and 22 in group C. None was known to have died from tetanus.

TABLE 4

BIRTHS, TETANUS AND NON-TETANUS DEATHS DURING STUDY PERIOD BY TYPE OF DELIVERY
(ALL GROUPS)

Delivery	Number of births	Tetanus Neonatorum deaths		Non-tetanus deaths in the first 30 days	
		No.	%	No.	%
By doctors, nurses or in hospital	75	0	0	1	1.3
By relatives [a]	109	3	2.8	6	5.5
By mother herself	139	6	4.3	5	3.6
By midwives who delivered 20 or more births during study period	843	38	4.5	46	5.5
By midwives who delivered 10-19 births in study period	221	14	6.3	10	4.5
By midwives who delivered 9 or less births in study period	284	20	7.0	9	3.2
Total	1 671	81	4.8	77	4.6

[a] Excluding those relatives who were midwives.

Effect of birth attendant

It is thought that the risks of a child receiving a tetanus neonatorum infection may be related to the methods employed in cutting and dressing the umbilical cord. The methods employed in Guachene are unknown, but the birth attendants have been classified and the tetanus and non-tetanus death rates calculated for the deliveries conducted by each group are given in Table 4. The rates in this table are from all groups and thus include some women who had been immunized with tetanus toxoid. They are therefore minimum rates and should only be used for comparison purposes.

No tetanus deaths occurred in any child delivered in hospital or whose delivery was conducted by a doctor or a nurse. The tetanus death rate was 2.8 per 100 births in babies delivered by relatives, was greater after delivery by the mother herself and births managed by " frequent " midwives participating in many deliveries, and was greatest (7.0 per 100 births) following deliveries made by " amateur " midwives involved in few deliveries. The highest rate was in babies delivered by a blind midwife; 8 tetanus deaths and 2 non-tetanus deaths occurred in the 32 babies she delivered—tetanus death rate 25 per 100 births (all groups) or 35 per 100 births from unimmunized women.

There was no regular pattern of non-tetanus death rates by birth attendant although babies delivered by " frequent " midwives and relatives appeared to have the highest rates.

Comparison between study and control groups

The tetanus neonatorum death rate per 100 births in the 3 groups for the total period of the study was 2.2 (study group), 7.9 (control group) and 6.7 (group C). The rates after registration but prior to the first injection were 8.3 (study group) and 13.1 (control group). The difference between these last two figures is less than the standard error and could well have occurred by chance.

After 1 injection. A comparison of the results for the women in the study and control groups who had only one injection by interval between the injection and birth is shown in Table 5. The registered birth rate in the two groups was similar. Apparent differences were present in the tetanus and non-tetanus death rates at different periods, but these differences were less than twice the standard error and could have been due to chance. Thus the apparent decrease in the tetanus death rate at 4-24 months following injection (1.8 per 100 births in the study group, compared with 5.7 per 100 births in the control group) cannot definitely be attributed to the

TABLE 5

BIRTHS, TETANUS AND NON-TETANUS MORTALITY RATES IN THE STUDY AND CONTROL GROUPS AFTER ONLY ONE INJECTION

Interval from injection to birth (months)	Births	Tetanus mortality		Non-tetanus mortality	
		No.	%	No.	%
Control group					
0-3	67	9 [a]	13.4	3	4.5
4-12	68	6	8.8	1	1.5
13-24	54	1	1.9	0	0
25-36	44	2	4.5	3	6.8
37-54	37	1	2.7	2	5.4
Total	270	19	7.0	9	3.3
Study group					
0-3	37	2	5.4	2	5.4
4-12	63	2	3.2	2	3.2
13-24	47	0	0	5	10.6
25-36	32	2	6.3	6	18.8
37-54	45	3	6.7	1	2.2
Total	224	9	4.0	16	7.1

[a] There was also 1 non-fatal tetanus neonatorum case in this period.

TABLE 6

BIRTHS, TETANUS AND NON-TETANUS MORTALITY RATES IN THE STUDY AND CONTROL GROUPS AFTER TWO OR THREE INJECTIONS

Interval from injection to birth (months)	Births	Tetanus mortality		Non-tetanus mortality	
		No.	%	No.	%
Control group					
0-3	44	2	4.5	2	4.5
4-12	80	7 [a]	8.8	5	6.3
13-24	109	10	9.2	5	4.6
25-36	83	6	7.2	3	3.6
37-54	31	2	6.5	4	12.9
Total	347	27	7.8 [b]	19	5.5
Study group					
0-3	58	0	0	1	1.7
4-12	88	0	0	7	8.0
13-24	98	0	0	4	4.1
25-36	74	0	0	2	2.7
37-54	23	0	0	0	0
Total	341	0	0 [b]	14	4.1

[a] There was also 1 non-fatal tetanus neonatorum case in this period.
[b] The difference between the tetanus mortalities in the control and study groups is more than 5 times the standard error.

women's immunization with tetanus toxoid but may have been due to chance factors.

The difference in the number of non-tetanus deaths (16 in the study group and 9 in the control group) could also have been due to chance. However, as this difference could indicate selection factors within the two groups of women, or differential diagnosis biases, these death records were reviewed in detail. The 1-injection portion of the study group contained 3 sets of twins and that of the control group none. Of the 6 twins involved, 5 died within 24 hours and thus could not have died from tetanus neonatorum. In addition, the study group had 4 other deaths which occurred in the first 48 hours after birth; 2 of the deaths related to prematurity and 2 to babies with gross malformation. The control group had 1 death related to prematurity and 1 related to gross malformation. None of these 6 women had any injection during her pregnancy and these occurrences were thus unconnected with any substances given. These differences between the

groups do not indicate any bias in selection or in diagnosis.

After 2 or 3 injections. A similar comparison between the study and control groups following 2 and 3 injections is given in Table 6. No differences could be shown between women who had 2 and those who had 3 injections, and the results are presented together. It can be seen that this control group had tetanus neonatorum rates similar to those for the control group with 1 injection. However, the babies of study-group mothers who had been immunized with tetanus toxoid had no recorded tetanus illness or death during the entire study period of more than 4 years. The observed differences in tetanus neonatorum rates between the study and control groups is greater than 5 times the standard error and is unlikely to have occurred by chance. The non-tetanus mortality was similar for the two groups.

If the rates for all recorded deaths (tetanus and non-tetanus) for the two groups are compared, the observed difference is more than 4 times the standard error. If the two groups of women and children were similar in other relevant respects, then it is probable that the differences in the mortality experienced were related to the administration of 2 or 3 injections of tetanus toxoid.

DISCUSSION AND CONCLUSIONS

Tetanus neonatorum is a disease of importance in much of the tropical and subtropical world. The case-fatality rate may be as high as 95 % in untreated children and it can be the dominating cause of death in the first month of life.

The evidence that infection is related to birth practices is reinforced by the findings in this study that the tetanus neonatorum rates varied markedly with the attendant who assisted with the delivery of the baby.

While it is accepted that the prevention of tetanus neonatorum can result from the improvement of obstetrical services and delivery practices, and that the active immunization of pregnant women may be a cheap and efficient method of prevention where antenatal services exist and pregnancy can be ascertained at an early stage, both of these methods have practical and economic disadvantages.

This study has demonstrated that in an area of rural Colombia where the tetanus neonatorum rate was high, a third possible community method of prevention is practicable and effective. The immunization of a group of volunteer women with 2 (or 3) intramuscular injections of 1 ml of aluminium-phosphate-adsorbed tetanus toxoid resulted in the complete absence of tetanus neonatorum from their babies born in subsequent pregnancies, for a period of more than four years. If the results of this study are valid and are applicable to other populations, then a method exists by which populations of newborn babies can be protected without the difficulty and expense of individual detection.

As this protection appears to last for more than 4 years, this method could be used in conjunction with other disease-control campaigns such as those designed for smallpox vaccinations.

A disadvantage of this method is the need for two injections spaced at greater than 6-week intervals. However, until an effective single-injection preparation is developed, this disadvantage could be overcome by the administration of a single injection of tetanus toxoid to all females from the age of 10 years and over (or at all ages) at 5-year intervals. This would result in community protection by the second injection. Such a method would appear to be cheap and practicable and clearly justified in high-risk areas, now.

ACKNOWLEDGEMENTS

RÉSUMÉ

Une enquête a été menée de 1961 à 1966 dans une région rurale de Colombie où l'incidence du tétanos ombilical est particulièrement élevée et le taux de la mortalité due à cette affection évalué à 11,6 par 100 naissances. Son but était d'étudier l'efficacité de la vaccination antitétanique appliquée sans discrimination à toutes les femmes en âge de procréer.

Toutes les femmes âgées de 13 à 45 ans ont été enregistrées. Par la méthode du double anonymat, 772 d'entre elles ont reçu de l'anatoxine tétanique adsorbée sur phosphate d'aluminium, cependant qu'un groupe témoin de 846 femmes recevait une préparation de vaccin antigrippal. Trois injections de l'une ou l'autre préparation ont été effectuées, à intervalle d'au moins six semaines. Enfin un 3e groupe comptant 1158 femmes n'a été soumis à aucune vaccination.

Durant les cinq années de l'enquête, 115 cas de tétanos ombilical sont survenus entraînant le décès de 109 nouveau-nés, soit un taux de létalité de 95 %. Trois cas non mortels ont été observés dans le groupe témoin, trois dans le 3e groupe non immunisé, aucun dans le groupe vacciné à l'anatoxine. Le taux de la mortalité par tétanos parmi

les nouveau-nés a été de 2,2 par 100 naissances dans le groupe vacciné à l'anatoxine, de 7,9 dans le groupe témoin et de 6,7 dans le 3e groupe non vacciné. Lorsqu'une seule injection a été pratiquée, les taux de la mortalité ont été respectivement de 4,0% (9 décès) et de 7,0% (19 décès) dans le groupe vacciné à l'anatoxine et le groupe témoin. Lorsque l'immunisation a comporté deux ou trois injections, les taux de la mortalité par tétanos ombilical ont été de 7,8% dans le groupe témoin (27 décès) et de 0% dans le groupe vacciné à l'anatoxine (0 décès).

Ces résultats montrent l'intérêt prophylactique de la vaccination systématique des femmes en âge de procréer, qui semble conférer une protection effective pendant au moins quatre ans. Un désavantage de la méthode est de nécessiter l'administration de deux doses au moins d'anatoxine à intervalles de plus de six semaines. En attendant que l'on dispose d'une préparation active à dose unique, il semble que l'injection d'une dose d'anatoxine à toutes les femmes âgées de 10 ans et plus, répétée tous les cinq ans, puisse assurer une protection satisfaisante de la collectivité dès la seconde injection.

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