scratched conjunctiva. These areas not only provide a better soil than the intact epithelial surface for the multiplication of any staphylococci present but also aid localization of the organism.

Finally, I am convinced that satisfactory methods are available for reducing the number of viable staphylococci on the surfaces of the newborn, and it behoves us not to provide the circumstances to aid local increase of these organisms. I also believe that the presence of a moderate number of viable staphylococci on the newly born infant is not harmful and may even be desirable, as we know practically nothing concerning the early immunological responses of the newborn to the ubiquitous staphylococcus.

Summary

Certain aspects of an extensive bacteriological and clinical survey of staphylococcal infection occurring in the newborn are discussed.

The survey concerns 11,040 infants born in a 95-bed maternity unit between July, 1956, and December, 1960.

Changes in the conduct of this unit resulted in a reduction in minor staphylococcal disease in the newborn from 41.0% in 1956 to 4.7% in 1960. Staphylococcal skin disease itself was reduced from 30.8% to 1.3%.

The three principal factors responsible for the reduction were a restriction of " routine " nursing procedures, " rooming-in," and " dry washing " babies with phisohex.

Dry washing with phisohex is shown to be two and a half times more effective in reducing skin sepsis in hospital and for the first four weeks at home than a similar emulsion containing no hexachlorophane.

Of 10,401 infants followed for six months after birth only 0.3% were readmitted to hospital and 0.077% died as a direct result of staphylococcal disease. Both this morbidity and mortality bore a direct relationship to the occurrence of minor staphylococcal disease in the maternity unit.

The incidence of breast abscess in 9,291 mothers fell from 2.5% in 1956 to 0.6% in 1960.

Phage pattern 80/81 did not play a dominant part in the frequency of minor staphylococcal disease in the newborn in this hospital. The circumstances of the infection appeared more important that the strain of staphylococcus.

I am particularly indebted to Miss Joan Banks, bacteriologist of the Geelong and District Hospital, for much technical assistance and criticism. My thanks are due to the Committee of the Geelong and District Hospital for permitting and providing the facilities for the survey. The survey would not have been possible without the wholehearted support of the medical practitioners in Geelong and surrounding district, who all fully co-operated and allowed complete access to their private and public patients and records.

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NEONATAL TETANUS IN NEW GUINEA

EFFECT OF ACTIVE IMMUNIZATION IN PREGNANCY

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Tetanus of the newborn is most likely to occur where midwifery is absent or is performed by untrained people. Therefore reliable figures for the incidence of the disease are usually not available from the countries where they are likely to be highest—the underdeveloped regions of the tropics. Axnick and Alexander (1957), in the United States, found the highest incidence, 34.3 cases per 100,000 live births, among the non-white population of Florida. This contrasts with estimates of " from 5 to 10% " for part of Haiti by Earle and Mellon (1958) and about 11% for the Guachene district of Colombia (Dr. K. W. Newell, 1961, personal communication). The disease is common in Nigeria (Jelliffe, 1950; Tompkins, 1958); and Stahlie (1960) estimated that it caused at least 38% of neonatal deaths in Thailand.

In the Maprik area of the Sepik District, New Guinea, we found that the disease was very common, although it seldom came to the notice of doctors. Women during childbirth and the first one to two weeks of the puerperium are secluded as " unclean " in " menstrual houses " where no man dare visit them. It is thought that if he became " contaminated " by such women his yams, one of the staple crops and an important prestige symbol in the local Abelam people's culture, would fail

to grow. As all the medical and aid-post orderlies are Abelam men, with interests in family gardens where yams are grown, it is not surprising that they bring very few cases of any neonatal or puerperal disease into the hospital. Also, the people have little faith in the power of the hospital to cure serious illness. The women recognize the symptoms of neonatal tetanus and know it has invariably been fatal in the past.

The people say that spirits kill the baby because the mother has failed to perform correctly certain rituals during pregnancy and childbirth. Therefore the mothers dislike public discussion of the causes of neonatal death, and all attempts so far have failed to persuade them to alter their present method of dealing with the umbilical cord. The mother cuts the cord 1 in. (2.5 cm.) or less from the abdominal wall; it is never tied. In the past she would always have used a sliver of sago bark, but now she uses a steel trade-knife or an old razor-blade. These are not cleaned or sterilized in any way and no dressing is put on the cord. The child lies after birth on a dirty piece of soft bark, and the cut cord can easily become contaminated by dust from the floor of the hut or by the mother's faeces expressed during childbirth, as well as by the knife and her fingers.

Until these habits can be altered some simple method of preventing neonatal tetanus is needed. The most obvious is to try to confer a passive immunity upon the infant. Although Trowell and Jelliffe (1958) considered the active immunization of women during pregnancy to be usually impracticable, we found that it would be within the capabilities of the medical services in many rural areas of New Guinea, where scientific domiciliary midwifery does not yet exist. The W.H.O. (1950) suggested that an experiment be made to determine whether such a procedure would prevent neonatal tetanus.

Nicol *et al.* (1960) have shown that the tetanus antibody level in the newborn baby's cord blood is quite high after immunization of the mother, and Katitch (1960) has presented evidence that after inoculation with toxoid pregnant women have antibody levels nearly twice as high as those who are not pregnant. Many other investigations have been made to discover the effect of tetanus toxoid injections on antibody titres in the blood. In brief, one injection produces little antibody; two produce a titre that may fall greatly after six months; the third produces a further rise in titre within two weeks, and a significant titre is sustained for at least six years; a single booster injection, if given within this period, produces another rapid rise and prolongs the period of responsiveness for another six years or more. There is considerable individual variation in antibody responses after the second and subsequent injections.

Methods

The first necessity was to obtain from histories a rough estimate of the incidence of the disease. Stahlie (1960), in Thailand, found that "in cases of neonatal tetanus such a classical description is often supplied by the mothers that the diagnosis seems beyond doubt."

History-taking Survey

Histories were obtained from women in 12 villages around Maprik. It was found that old women's memories about the deaths of their babies long ago are hazy; therefore only the histories of babies born since 1945 were considered for this survey. This year is well remembered, as it was then that the fighting occurred in which Australian troops ended the Japanese occupation of the Maprik subdistrict. The history of each woman was taken by one of us (F. D. S.) privately because of their shame, already mentioned, about infant deaths.

No leading questions were asked of the mothers and care was taken to show no more apparent interest in descriptions of neonatal tetanus than in those of other causes of neonatal death. The following five criteria in the histories were all regarded as essential to a retrospective diagnosis of neonatal tetanus: (*a*) the child must have cried and sucked normally for at least the first two days after birth; (*b*) the first symptom noticed had to be a failure to suck appearing between the third and tenth days inclusive (the incubation period was always very short, as in Jelliffe's cases in Nigeria); (*c*) When asked about the appearance of the infant's face the mother had to imitate the risus sardonicus; (*d*) when asked to demonstrate what happened to the infant's limbs the mother had to imitate the spasms with flexion of the arms and clenched fists; and (*e*) the baby must have died before the end of the fourteenth day after birth.

Immunization Experiment

Fortnightly maternal and child welfare clinics were started by one of us (V. M. T.) in 25 villages around Maprik in September, 1959, and by G. R. W. in 27 villages around the mission at Wingei, 13 miles to the east, in February, 1960. Attendance soon reached 95% of the women registered. All sick infants in the Maprik area were brought by the sister, or by their mothers, to Maprik Hospital for a doctor's diagnosis. In the Wingei area all infants were seen, and the diagnoses made, by the sister alone. However, she had seen cases of the disease previously at Maprik Hospital, and this condition cannot be confused clinically with any other. Trowell and Jelliffe (1958) think that neonatal tetanus has no valid differential diagnosis. Therefore, in these circumstances, there was no need for a "blind" trial. Ten villages in the Wosera area, between the two areas served by the sisters' clinics, were covered by F. D. S. and a responsible medical orderly. Here infants who fell sick between our visits were taken by their mothers to the hospital or to a qualified nursing sister at a near-by mission.

These arrangements meant that a continuous belt of 62 villages extending from 5 miles west to 18 miles east of Maprik was covered in this experiment. We are confident that, from the beginning of the investigation, no case of neonatal tetanus in these villages escaped our observation. In four cases only, an infant was born alive and died rapidly before being seen. In these cases careful histories were taken from the mother and close female relatives; none suggested neonatal tetanus.

Control Group.—This was formed in two ways: (1) In the three areas 86 infants were born alive to mothers who had received no injections; at their first attendance they had come too late for immunization to be completed before delivery. (2) A shortage of toxoid developed owing to an unpredictable administrative error beyond our control. Many of the courses of injections were interrupted, and as a result 74 women received only one injection before delivery.

In some societies a group of women who first attended antenatal clinics late in pregnancy might be less conscientious, and therefore have less hygienic methods of dealing with the umbilical cord, than a group who

came earlier. However, up to the time of writing, no Abelam women show the slightest sign of modifying the standard method handed down by their ancestors. In these circumstances the infant's risk of contracting neonatal tetanus would not be related to the time at which his mother first attended the clinics.

Inoculated Groups.—Group 2 consists of 234 infants whose mothers were so advanced in pregnancy when first seen that they were given only two injections of tetanus toxoid before delivery. Group 3 consists of 175 infants whose mothers were given all three injections before delivery.

Toxoid, Dosage, and Intervals Between Injections.—Miller *et al.* (1949) produced evidence that alum-precipitated toxoid (A.P.T.) or aluminium hydroxide adsorbed toxoid (A.H.A.T.) may have advantages for primary immunization, but Weiner *et al.* (1955) have shown that, as a booster injection, fluid toxoid produces a better antibody response. For the sake of simplicity, and because it is the stock preparation available in this territory, fluid formalinized tetanus toxoid (Commonwealth Serum Laboratories, Melbourne) has been used throughout this experiment. The first inoculation of 1 ml. was given as early in pregnancy as possible. The second, 1 ml., was given six weeks after the first. The third inoculation, 1 ml., was given in the last trimester, not less than six weeks and not more than six months after the second. (In those cases where there was not time to complete the course before delivery it was completed afterwards.)

Two Parts of the Experiment.—For nine months from September, 1959, the results in groups 2 and 3 combined were compared with the results in the control group. The difference in the incidences of neonatal tetanus had become statistically significant at the 5% level by June, 1960. After June, therefore, it was thought ethically unjustified intentionally to withhold injections from any woman who could be immunized before delivery. The experiment was continued in order to compare the results of two injections with those of three.

Results

History-taking Survey.—Among the histories of 3,017 live births since 1945 there were 184 neonatal deaths the descriptions of which fitted the diagnostic criteria for neonatal tetanus. This gives a death rate of 61 per 1,000 live births since 1945. This figure must be taken as a conservative estimate in view of the strictness of the criteria used and the cultural factors already described.

The Immunization Experiment.—There were no complaints of reactions to the inoculations, which, like all injections, are popular among these people. All the infants recorded, except those who died of neonatal tetanus, were alive two weeks after birth—that is, all stillbirths and deaths in the first two weeks of life, except tetanus deaths, have been excluded from the figures. The sister in Wingei has been able to assist personally at 12 of the births in the menstrual huts. These infants have not been included; nor have two infants born in Maprik Hospital. It is not known whether the administration of antibiotics reduces the incidence of neonatal tetanus. Therefore those babies who had received antibiotics in the first two weeks of life, for diseases other than diagnosed neonatal tetanus, have also been excluded. The infants excluded for all these reasons were evenly distributed among the three groups (see Table II).

Effect of One Injection.—There were eight cases of neonatal tetanus among 86 infants with uninoculated mothers and eight among 74 whose mothers had received only one injection. As expected, therefore, one injection had no apparent effect on the incidence of the disease and the inclusion of these cases in group 1 appears justified.

First Part of Experiment.—As already stated, by the beginning of June, 1960, statistical evidence of the protective effect was available. The figures were: group 1, 11 cases among 127 infants (8.7%); groups 2 and 3 combined, 3 cases among 149 infants (2.0%). The standard error of the difference is 2.75.

Second Part of Experiment.—The figures in Table I are those for 17 months, September, 1959, to January, 1961, inclusive. The standard errors of the differences between the three groups are: groups 1 and 2, 2.7; groups 2 and 3, 1.3. Therefore even two fluid formalinized tetanus toxoid injections in pregnancy, given six weeks apart, appear to have conferred a statistically significant degree of protection on the infants after birth, lowering the expected incidence of neonatal tetanus by two-thirds. The effect of a third injection, given six weeks or more after the second, was significantly better than that of two.

TABLE I.—*Incidence of Neonatal Tetanus (N.T.) in Relation to Number of Injections of Tetanus Toxoid Previously Given During Pregnancy*

Group of Villages	Group 1. No Injection or 1 Injection		Group 2. 2 Injections		Group 3. 3 Injections	
	No. of Infants	No. Cases of N.T.	No. of Infants	No. Cases of N.T.	No. of Infants	No. Cases of N.T.
Maprik ..	79	7	84	2	38	0
Wingei ..	57	7	108	5	69	1
Wosera ..	24	2	42	1	68	0
Totals ..	160	16	234	8	175	1
N.T. % ..		10·0		3·42		0·57

The one infant in group 3 who developed neonatal tetanus was born three days after his mother's third injection. In this case probably there had not been time for the maternal antibody titre to have risen to its maximum. Bigler (1951) found that, in response to a booster injection, the rise in titre starts only between the third and fifth days.

If it is assumed that an infant born less than one week after his mother's last injection might have received little benefit from that injection, it is important to know how many infants in this category have been included in groups 2 and 3. There were 10 such infants (including one case of neonatal tetanus) in group 2 and six (including one case of neonatal tetanus) in group 3.

The distribution of the infants excluded from Table I is shown in Table II. Current investigations show that, excluding neonatal tetanus deaths, the neonatal mortality from other causes is about 200 per 1,000 live births except in the small minority of 52 villages where the clinics are now operating. Therefore the observed incidence of neonatal tetanus of 16 out of 160 in this investigation represents approximately 80 per 1,000 live births in the absence of the clinics.

In all the cases death occurred before the fourteenth day of life in spite of treatment, and in the eight cases where the mother had been given two injections the incubation period did not appear to be longer than the average.

TABLE II.—*Distribution of and Causes for Exclusion of Infants from Table I*

Cause	Area	Group 1	Group 2	Group 3
Assisted delivery	Maprik	1	—	1
	Wingei	3	5	4
	Wosera	—	—	—
Died before observed	Maprik	—	—	—
	Wingei	—	—	—
	Wosera	2	1	1
Death observed (not tetanus)	Maprik	3	4	2
	Wingei	2	4	2
	Wosera	—	2	3
Antibiotic administered; lived	Maprik	1	2	—
	Wingei	—	2	1
	Wosera	1	1	1
Stillbirths	Maprik	5	6	2
	Wingei	4	8	5
	Wosera	2	4	6

Discussion

From the figures given in Table I it is evident that the three areas were not completely comparable in all respects. There were most first attendances early in pregnancy in Wosera and least in Maprik. The incidence of the disease appears to have been higher in Wingei than in the other two areas, which appear to have had equal rates. For the first part of the experiment—September, 1959, to June, 1960—additions to each group occurred at a steady rate in all areas, but after June group 1 increased very slowly, and more Wingei and Wosera women than Maprik women came early enough to be given three injections.

The cases in group 1 were mostly seen in the wetter season, September, 1959, to May, 1960. Tompkins (1958) found a lower rate of admission to hospital in the wet season than in the dry. If his observation reflects a truly lower incidence of neonatal tetanus in the wet months the figures for the first part of this experiment represent accurately the incidence in the rainy season, but the figures for group 1 in Table I may be slightly lower than the true incidence for a whole year.

Stillbirth rates (Table II) did not differ appreciably in the three groups, but it is possible, in spite of this, that premature delivery might have been commoner, because of the way they were selected, among women given one injection than among those given two or three. It is not known whether minor degrees of prematurity predispose to clinical neonatal tetanus.

These unmeasured variables, some of which might have exerted an effect on the figures one way, others the opposite way, are not important enough to invalidate the conclusion that the procedure used is practicable and effective in greatly reducing the incidence of neonatal tetanus in a tropical community where antenatal clinics are in operation. (Up to May, 1961, there had been 15 additions to group 2 and 45 additions to group 3, without any further cases of neonatal tetanus, since the experiment ended in February, 1961.) In effect the infant is given antitetanus serum by his mother. His immunity, though adequate for the first few weeks of life, will be only temporary, and he will need active immunization later as much as other children.

Though seldom seen in hospital, the disease has been found in many parts of New Guinea. An exception is the Okapa area of the Eastern Highlands. There, although other forms of tetanus are common, neonatal tetanus has been carefully looked for and not found (Dr. A. J. Gray, 1960, personal communication). It may be significant that there the custom is to cut the cord about 6 in. (15 cm.) from the abdominal wall.

As 100 ampoules of the tetanus toxoid cost £A.5 9s. 3d., the primary maternal immunization is not expensive. It is intended, as a future investigation, to give immunized women only 1 ml. in the last trimester of each subsequent pregnancy, unless more than six years have elapsed between pregnancies.

Further work is needed to determine whether primary immunization during pregnancy with A.P.T. or A.H.A.T. might produce better results than with fluid toxoid, especially in areas where only two injections are possible before delivery. However, our experience was that, once their confidence in the clinics had been gained, most of the pregnant women started to attend early enough to allow them to be given all three injections before delivery.

Another scheme, for areas where antenatal clinics have not yet been established, would be to immunize the whole female population aged 12 to 45 years by six-yearly injections in their villages and to use governmental influence to encourage one attendance at the local hospital, for the booster inoculation, in the last trimester of each pregnancy.

The greatest difficulty in underdeveloped countries is to ensure that the three primary injections are given to all the women at the correct intervals. This difficulty would be overcome if an adjuvant could be added to the toxoid which allowed the antigen to be absorbed so slowly that only one injection achieved primary immunization. (The single booster doses in subsequent pregnancies would be of plain formalinized toxoid.) With such an adjuvant world-wide control of the disease would be practicable.

Tetanus acquired from wounds is much less common in the Sepik District than the neonatal variety, and its prognosis is quite good if the patient reaches hospital. Puerperal tetanus is particularly likely to occur where neonatal tetanus is common. We saw four very severe cases in 18 months, and many from outside the clinic areas may not have reached us. Therefore, in countries where neonatal tetanus is common, pregnant women who will have no skilled help during childbirth should have the first claim for immunization both for their own and for their infants' sakes.

Summary

Neonatal tetanus is common among the Abelam people, Sepik District, New Guinea, who have no trained attendants during childbirth. A history-taking survey suggested an incidence of 61 cases per 1,000 live births; direct observations showed an incidence of approximately 80 per 1,000 live births.

Women were actively immunized with three injections of fluid formalinized tetanus toxoid during pregnancy, the third inoculation always being given in the last trimester. It has been shown that their infants were provided with substantial protection against the risk of neonatal tetanus. It is presumed that in these circumstances the foetus received transplacentally enough maternal antibody to protect the infant against clinical tetanus before the umbilicus healed.

In cases where there had not been time to give more than two injections before delivery the neonates were still protected to a statistically significant degree, the incidence being reduced by two-thirds. In future, women who have been fully immunized less than six years previously will be given only one booster injection of

fluid toxoid in the last trimester of subsequent pregnancies.

An investigation is needed to determine whether, for primary immunization, alum-precipitated toxoid or aluminium hydroxide adsorbed toxoid might give better results than fluid toxoid, particularly in circumstances where only two injections are possible before delivery. There is a great need for a toxoid preparation containing an adjuvant which would enable primary immunization to be achieved with only one injection.

No reactions to the toxoid injections were noticed and, for the results achieved, the cost was not high. In countries where neonatal tetanus is common women can often be given inoculations during pregnancy although the medical services cannot yet provide them with domiciliary midwifery. It is thought that in such circumstances they have the best claim of any section of the civilian population to routine tetanus immunization.

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CHLORPROMAZINE IN TETANUS

BY

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In recent years there have been many reports on the value of chlorpromazine in the management of tetanus. Most of them were based on trials conducted on a small number of patients, and one could not be certain that the conclusions reached were applicable to all cases. This study was undertaken to determine the response of a large series of tetanus patients to treatment with chlorpromazine.

The major prognostic criteria governing the ultimate outcome of tetanus are the length of the incubation period and the interval between the onset of trismus and generalized spasms. The results of any investigation are obviously influenced by the proportion of milder and graver forms of the disease included in the study. The incubation period was not thought to be a suitable standard from which the severity of the disease could be gauged, because the history of the injury might not be accurately given, the time of the injury might not have been the time of infection, and there might even have been no history of injury at all. On the other hand, the interval between the onset of trismus and generalized spasms was regarded as a reliable index of the severity of the disease, as one could expect patients to be accurate about the actual time of onset of the disease.

Method and Material

The cases of tetanus admitted to the wards of the department of clinical surgery, Medical College, Amritsar, were divided at random into two groups without reference to the severity of the disease. The patients in group A were given paraldehyde (4–6 ml.) by intramuscular injection six-hourly, and the patients in group B were given chlorpromazine (50 mg.) in a similar manner. Neonatal cases were excluded from the investigation. All patients were also put on a standard treatment, which consisted of the following measures: (1) They were isolated in dark, quiet surroundings and given intramuscular injections of soluble phenobarbitone, 2–3 gr. (130–200 mg.), every six hours. (2) After a test dose, an intravenous injection of 100,000 units of antitetanic serum was given. (3) Injections of crystalline penicillin were administered, and those patients with pulmonary complications received streptomycin as well. (4) The portal of infection was treated surgically. (5) Nutrition was maintained on fluid diet, given by mouth or, if necessary, intravenously.

The results are shown in the accompanying table.

Table of Results

Interval Between Trismus and Generalized Spasms	No. Treated	Cured	
		No.	%
Group A (Paraldehyde Group)			
0–48 hours	58	30	51·7
More than 48 hours ..	31	26	83·9
Group B (Chlorpromazine Group)			
0–48 hours	54	28	51·9
More than 48 hours ..	27	23	85·2

Discussion

Chlorpromazine is a phenothiazine derivative which acts mainly on the formatio reticularis, abolishing excitement and lowering muscle tonus. At the same time it potentiates the action of other sedatives. Because of these properties chlorpromazine has been used by various workers in the management of tetanus.

In the present study, spasms were more rapidly controlled by chlorpromazine than by paraldehyde, and a good deal of muscle tonus remained in patients treated with the latter. Of the 89 cases in group A, 58 were of the severe type, and 30 (51.7%) of these patients survived. Among the 31 patients who had less severe tetanus, 26 (83.9%) survived. Group B contained 81 cases, 54 of them being of the severe type. Among these there were 28 (51.9%) survivors, compared with the 23 (85.2%) survivors among the 27 patients with a milder type of tetanus.

It is obvious that there is no significant difference in the ultimate results obtained in the two groups.

Summary

A clinical trial was conducted on 170 cases of tetanus in order to assess the comparative value of paraldehyde