other side-effect encountered was tinnitus in one patient; this and other aural disturbances have been described as rare complications of other amino-uracil derivatives.

No toxic effects were observed following the use of amisometradine. In the American reports quoted, skin reactions were rare, and leucopenia was described in one case.

The diuresis produced by aminometradine is accompanied by excretion of sodium and chloride in approximately equal amounts, with a small increase in potassium loss (Platts and Hanley, 1956). A similar loss of electrolytes accompanied by diuresis follows the administration of amisometradine to dogs (Van Arman *et al.*, 1957), and this is presumed to occur in man. The precise mode of action on the kidney is not yet known.

Summary

The effect of amisometradine (rolicton), a new oral diuretic, has been tested in 20 patients with heart failure.

In doses of 400 mg. three times daily over a period of two consecutive days it was found to have 40% of the diuretic potency of 2 ml. of mersalyl intramuscularly.

The drug was relatively free from side-effects, in respect of both gastro-intestinal tolerance and toxic reactions.

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TETANUS IN NIGERIA

REVIEW OF 100 CASES TREATED IN IBADAN

BY

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Tetanus is the third most common cause of admission to the adult medical wards of University College Hospital, Ibadan, being exceeded in frequency only by lobar pneumonia and pulmonary tuberculosis. It is by far the most frequent cause of death in these wards. Of 79 tetanus patients admitted during 1955, 43 died, representing 6% of all admissions and 21% of all deaths in the medical wards. The corresponding figures for 1954 were 77 admissions with 44 deaths. The incidence of tetanus in Nigeria is not known, but from the above figures and the fact that the category of adult, which in this hospital includes anyone over the age of 8 years, probably comprises half the total population (600,000), there are at least 80 cases a year in a population of 300,000. This gives an annual incidence of 26.6 per 100,000, with a mortality of 14.6 per 100,000. In England and Wales in 1951 (Registrar-General, 1953) 81 deaths were attributed to tetanus, a mortality of 0.2 per 100,000; and Hampton (1954), in a review of tetanus in the United States of America from 1947 to 1951, found an annual mortality of 0.2 per 100,000. To what extent the above approximation for Ibadan is applicable to Nigeria as a whole is unknown.

There have been few reports on tetanus from Nigeria. Jeliffe *et al.* (1950) described five cases (three fatal) of puerperal tetanus, drew attention to many factors present in domiciliary midwifery in Nigeria which encourage tetanus, and stressed the need for adequate prophylaxis at parturition for both mother and child. Jeliffe (1950) described 25 cases of neonatal tetanus with only one survival, and again drew attention to the many opportunities of contamination by tetanus spores in the poorer Nigerian home.

The purpose of the present article is to show from observations on 100 cases of tetanus the nature of the disease in a tropical area where the incidence is high, with reference to aetiology, factors influencing prognosis, course of the disease, and response to treatments used. A method of approach to the problem that tetanus presents in such an area is suggested.

Material and Methods

The material under review consists of 100 consecutive adult cases of tetanus treated at University College Hospital, Ibadan, from February, 1954, to May, 1955. Of the 100 cases, 19 occurred between February and May, 1954, and were treated by other members of the staff of the medical unit, while the remaining 81 were treated by me. The data pertaining to the first 19 cases were obtained from the case records.

The following scheme for recording observations was used in the 81 cases which I treated. (1) All patients were personally examined as soon as possible, usually within an hour after admission. (2) A history was taken so far as was possible from the patient, supplemented as necessary by further details from the relatives. (3) After initial examination and assessment, treatment was begun. (4) Records by nursing staff were kept on a specially designed tetanus progress sheet (see Chart). Observations by the medical staff were recorded on the clinical notes. Observations to be entered on the tetanus progress sheet were made when the sedative drugs were given, so that the patient was disturbed as little as possible. Thus the frequency of recorded observations increased with the frequency of administration of sedatives, which was usually in direct proportion to the severity of the case.

General Management and Treatment

When available a special nurse was detailed for each patient, and the bed was placed against the wall in a corner of the ward. Special attention was paid to oral toilet. If possible, patients were given fluids orally and such food as they could take. Drinking was made easier for those with severe trismus by the use of straws. Before May, 1954, the oral fluid intake was supplemented if necessary by the

UNIVERSITY COLLEGE HOSPITAL, IBADAN. Tetanus Progress Chart.

Surname						First Name(s)				Number		
						FLUIDS				URINE		
Date and Time	Temperature	Pulse	Respiration	Spasms	Opisthotonos	Oral	Sub-cutaneous	Intra-venous	Sedation	Output	Chlorides	Haematocrit

rectal route. This proved unsatisfactory, and the following routine was adopted in the 81 cases treated after this date. In severe cases all specimens, and in milder cases daily specimens, of urine were tested for chloride content by Fantus's method. If it was 3 g. per 100 ml. or over the patient was considered to be adequately hydrated. If under 3 g. but over 1 g. per 100 ml. 2 pints (1,140 ml.) of normal saline was given intravenously, and if less than 1 g. per 100 ml. 3 pints (1,700 ml.) was given. The saline was infused rapidly, the first pint (570 ml.) in 20 minutes and the second in 40 minutes, the 2 pints thus taking one hour to give. In those requiring more than 2 pints the rate of infusion was slower. Intermittent infusions of short duration were employed, as careful attention could then be given during the process. Continuous intravenous infusions were not well tolerated. Although solid food was given where practicable, it was felt that patients could survive the major part of their illness on a low calorie intake. Intragastric intubation was attempted as a means of giving fluids, but the passage of the tube sometimes caused severe laryngeal spasm and the method was abandoned.

Penicillin.—All cases were given 300,000 units of procaine penicillin daily intramuscularly as a prophylactic measure against chest infection and in many cases as part of the treatment of the wound. This was continued for 24 hours after the cessation of clonic spasms unless required for further treatment of the wound or complications. It was stopped earlier only if some complication occurred requiring the use of a broad-spectrum antibiotic.

Treatment of Wound.—This was carried out as indicated for the particular wound irrespective of the occurrence of tetanus. Radical excision of tissue was done in one case which followed osteomyelitis of the radius and ulna. In this case the limb was amputated.

Antitetanic Serum.—In 77 cases 100,000 I.U. of antiserum was given as soon as the diagnosis was made (50,000 I.U. intravenously and 50,000 I.U. intramuscularly). Two patients, one of whom was treated entirely as an out-patient, were given 3,000 I.U. of antiserum only. The remaining 21 were not given antiserum; these were not selected, but occurred after it had been decided to stop giving antiserum for a trial period. The cases are fairly evenly distributed as regards their severity.

Sedative Treatment.—In 76 cases paraldehyde, 4–6 ml., and sodium amylobarbitone, 3¼ gr. (0.24 g.), were given intramuscularly in alternate doses. The interval between the doses varied from two to six hours, depending on the condition of the patient. Sedation was aimed at reducing reflex spasms and opisthotonos as much as possible without depressing respiration unduly. In 18 cases chlorpromazine, 15–25 mg. intramuscularly, and sodium amylobarbitone, 3¼ gr. (0.24 g.) intramuscularly, were given simultaneously. The interval between doses varied from three to six hours according to the condition of the patient. Two cases were given chlorpromazine alone for a short time in divided doses up to a total of 300 mg. daily. It did not appear to be controlling the spasms satisfactorily and was therefore abandoned. These two cases are included in the category under which the main part of their treatment was carried out.

Muscle Relaxants.—One patient who died was treated with intravenous thiopentone, gallamine triethiodide, and intermittent positive-pressure respiration, which was performed by means of a manually operated bellows. Four fatal cases were treated with mephenesin given intravenously at a rate which reduced spasms but did not necessitate the use of artificial respiration. It was given in normal saline or 6% glucose in distilled water solution, 3 g. to 1 pint (570 ml.), at a rate of from 0.3 to 1 g. an hour. These cases, which were all severe, became a great problem as regards their fluid balance, since they required up to 25 g. of mephenesin daily and it was felt that it might be dangerous to give more concentrated solutions. All specimens of urine passed by these patients were tested spectroscopically for the presence of haemoglobin and all were negative (Hewer and Woolmer, 1947; Pugh and Enderby, 1947; Murray Parkes, 1954; Docherty, 1955). Mephenesin was used orally (Adriani and Kerr, 1955) in doses up to 9 g. daily in convalescent cases in an attempt to accelerate the rate of reduction of residual stiffness, but as no definite benefit was observed it was abandoned.

Pethidine.—This was used, both orally and intramuscularly, in the later stages of the disease for the treatment of muscular pain and cramp, and was extremely effective.

Physiotherapy.—This was begun as soon as clonic spasms had definitely ceased. It was continued in all cases until discharge from hospital, and, in as many cases as would attend, until all stiffness had gone.

Post-mortem Examination.—This was carried out on only one case. This patient had been treated by complete muscular relaxation with intermittent positive-pressure respiration, and the cause of death was bronchopneumonia.

Analysis of Clinical Material

The series comprised 56 male and 44 female patients: 30 males and 26 females died, the overall mortality being 56%. There is no statistically significant difference in the mortality of the various age groups (Table I).

As no attempt to culture *Cl. tetani* from wounds was made, owing to technical difficulties, the decision on the portal of entry of the organism was made on the history and clinical examination (Table II). The cases following lower-limb injury, which form the largest group, are further subdivided (Table III). The chronic non-specific ulcers had been present for one year in one case, three months in another, and for an average of 14 days in the remainder, except for one case of unknown duration. Guinea-worm infestation is a common cause of ulceration; it occurred in 11 cases (10 in the lower limb and one in the arm).

It is felt that most of these cases in which no causative injury was found probably followed minor foot injuries which had healed before admission. The post-partum cases comprised 18 puerperal cases and 2 following abortion. The five post-operative cases were in hospital at the onset of the disease, and, although treatment was begun within three hours of the onset, all five patients died. Two of the cases occurred at a time when the sterilizing equipment was found to be faulty.

TABLE I.—*Age and Mortality*

Age Group	Lived	Died	Total	Mortality
Under 10	Nil	1	1	100%
10–19	11	9	20	45%
20–29	15	21	36	58%
30–39	9	16	25	64%
40–49	8	8	16	50%
50 and over	1	1	2	50%

TABLE II.—*Portal of Entry of Cl. tetani*

Portal of Entry	Lived	Died	Total	Mortality
Lower limb injury	17	22	39	56%
Post-partum	8	12	20	60%
Post-operative	Nil	5	5	100%
Upper-limb injury	3	1	4	25%
Head and neck injury	1	2	3	66·6%
Otitis media	1	Nil	1	Nil
Vaccination sore	1	,,	1	,,
Penile sore	1	,,	1	,,
Not known	12	14	26	54%

TABLE III.—*Types of Injury of Lower Limb Followed by Tetanus*

Type of Injury	Lived	Died	Total	Mortality
Lacerations	6	10	16	63%
Chronic non-specific ulcers	6	4	10	40%
Guinea-worm sore	4	6	10	60%
Chigger flea sore	1	2	3	66·6%

Native applications to sores, including those following vaccination against smallpox, include earth and animal excreta, and must often be responsible for the occurrence of tetanus.

The relation of incubation period to mortality is shown in Table IV. The cases were grouped into those having an incubation period of nine days and over and those having an incubation period of less than nine days, as this division gave the nearest to a significant difference in the mortality ($\chi^2=2.803$, $P=0.09$). Cases in which the causative injury occurred more than one month before the onset of symptoms are not included in Table IV, as the patients' estimate of time intervals of over one month tended to be extremely inaccurate.

Table V shows the relation of period of onset to mortality. The period of onset, which is defined as the time elapsing between the onset of the first symptom and the first generalized spasm, if less than 48 hours indicates a bad prognosis (Cole, 1940; Knott and Cole, 1952). It is usually more accurately measured than the incubation period, as the two events involved occur at a reasonably short time interval and are of such a nature that they are likely to impress the patient or his relatives. There is a significant difference in the mortality of the above groups ($\chi^2=11.38$, $P<0.01$).

The incubation period and period of onset are related to mortality in Table VI. In 19 cases the sum of the incubation period and the period of onset was less than the seven days of Knott and Cole (1952). Only 13 of these patients died, giving a mortality of 68%.

TABLE IV.—*Relation of Incubation Period to Mortality. Assessable in 64 Cases*

Incubation Period	Lived	Died	Total	Mortality
Under 9 days	13	28	41	68%
9 days and over	13	10	23	43%

TABLE V.—*Relation of Period of Onset to Mortality. Assessable in 88 Cases*

Period of Onset	Lived	Died	Total	Mortality
0–48 hours	20	45	65	69%
Over 48 hours	16	7	23	30%

TABLE VI.—*Incubation Period and Period of Onset Related to Mortality. Assessable in 60 Cases*

Incubation Period	Period of Onset	Lived	Died	Total	Mortality
Under 9 days	0–48 hours ..	6	23	29	79%
	Over 48 ,, ..	4	5	9	56%
9 days and over	0–48 ,, ..	7	10	17	59%
	Over 48 ,, ..	5	Nil	5	Nil

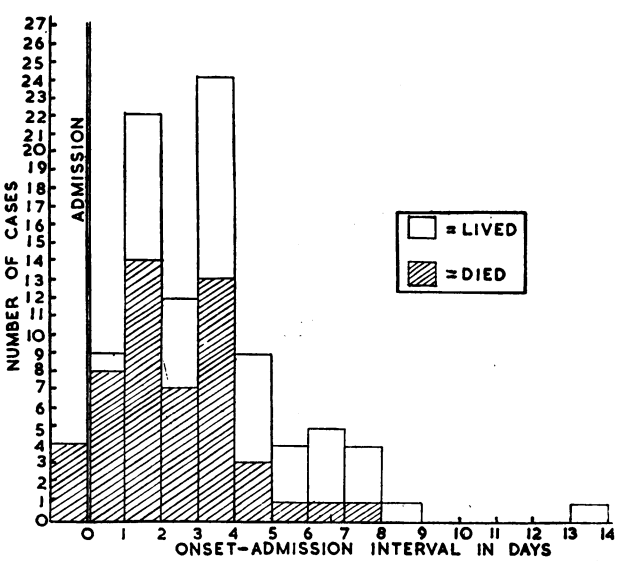

FIG. 1.—Onset-admission interval, showing mortality. Assessable in only 95 cases.

The high mortality among the cases treated early in the disease (Fig. 1) can be partly explained by the fact that severe cases were, on the whole, brought for treatment earlier than milder cases. It would not appear that early treatment, of the type used here, affects the mortality greatly in severe cases.

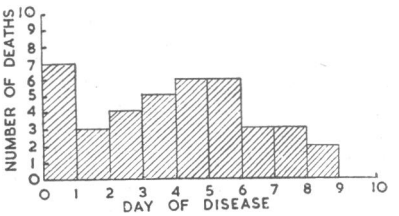

FIG. 2.—Duration of disease in fatal cases, omitting cases in which complications or treatment may have directly caused death, the duration of disease was assessable in 39 cases.

The average interval from onset to death in 39 cases was 4.5 days (Fig. 2). The duration of treatment in these fatal cases is shown in Fig. 3. The high mortality in the first three days after admission can be explained by reference to Figs. 1 and 2. Although the largest single number of deaths occurred on the first day of the disease, many of the cases were not seen until the disease was far advanced.

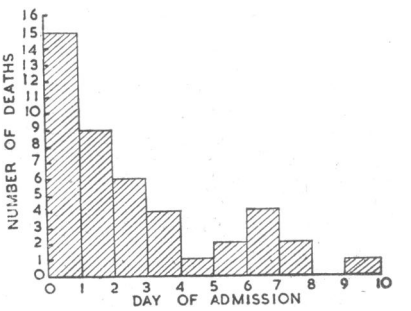

FIG. 3.—Duration of treatment in fatal cases, omitting cases in which complications or treatment may have directly caused death.

The temperatures given in Table VIII are the highest recorded on the patients at any time.

The methods of sedative and relaxant treatment are related to mortality in Table VIII. Table IX shows the mortality in those given and those not given antiserum; Table X shows the mortality in the "antiserum" and "non-antiserum" cases with the period of onset. There is no statistically significant differences in the mortality of those

TABLE VII.—*Maximum Temperature Related to Mortality*

Temperature Range	Lived	Died	Total	Mortality
98·4° F. (36·9° C.) ..	8	3	11	27%
98·5° F.–(37° C.–) ..	7	5	12	42%
101° F.–(38·3° C.–) ..	11	11	22	50%
102° F.–(38·9° C.–) ..	6	8	14	57%
103° F.–(39·4° C.–) ..	8	11	19	58%
104° F.–(40° C.–)	2	9	11	82%
105° F.–(40·6° C.–) ..	2	7	9	78%
106° F. (41·1° C.) and over	Nil	2	2	100%

TABLE VIII.—*Methods of Sedative and Relaxant Treatment Related to Mortality*

Drugs Employed	Lived	Died	Total	Mortality
Paraldehyde and sodium amylobarbitone	37	40	77	52%
Chlorpromazine and sodium amylobarbitone	6	11	17	65%
Intravenous mephenesin ..	Nil	4	4	100%
Thiopentone and gallamine	,,	1	1	100%
None	1	Nil	1	Nil

TABLE IX.—*"Antiserum" and "Non-Antiserum" Cases, With Mortality*

Antiserum	Lived	Died	Total	Mortality
Given	35	39	74	53%
Not given	7	12	19	63%

Two cases which did not have a standard dose of A.T.S. and five cases treated by relaxants have been omitted.

who were given antiserum and those who were not. The two cases which had only 3,000 I.U. of antiserum have been omitted from Tables IX and X.

TABLE X.—*"Antiserum" and "Non-Antiserum" Cases, With Period of Onset and Mortality*

Anti-serum	Period of Onset	Lived	Died	Total	Mortality
Given	0–48 hours ..	17	32	49	65%
	Over 48 ,, ..	15	4	19	21%
Not given	0–48 ,, ..	3	9	12	75%
	Over 48 ,, ..	1	2	3	67%

Assessment was made in 83 cases only; two cases which did not have a standard dose of A.T.S. and five cases which were treated by relaxants being omitted.

Complications

There were four clinically definable cases of bronchopneumonia (all fatal), and one further case was discovered at necropsy. In no other case was clinical evidence of chest infection found, although it is probable that many cases had some degree of such infection.

Four male cases had retention of urine which persisted into the later stages of the disease. They were treated in the acute stage by catheterization twice daily and in the convalescent stage by intramuscular injections of carbachol. Two of these patients and three female patients, all of whom had been catheterized, developed urinary infections. They were treated initially with sulphadimidine, 1 g. eight-hourly. Four of them did not respond and were given chloramphenicol, 500 mg. six-hourly. Two of the females died, apparently as a direct result of their urinary infection.

There were two cases of spinal fracture, but as both patients had received injuries which could have caused the fractures, it is not possible to be certain whether these were due to or only aggravated by tetanus. One had an "opera-hat" fracture of T. 4–T. 10; the other had a compression fracture of L. 1. Both patients had plaster jackets applied in the convalescent period and both had a good result.

One patient died following a severe hyperpyrexial reaction to an intravenous infusion. Three patients sustained severe lacerations of the tongue through biting during spasms. In each case the tongue was almost severed. One male patient, in whom the causative injury was in the right forearm, continued to have localized spasms of the muscles of the forearm for a total of 58 days from the onset of spasms, and for 32 days after the cessation of generalized spasms (Millard, 1954).

One patient was 36 weeks pregnant at the onset of the disease. She was admitted on the seventh day, having had generalized spasms for five days. She gave birth to a live child eight hours after admission. Generalized spasms continued throughout the labour and continued until the 11th day after admission. The child was healthy and at no time showed signs of tetanus. Both mother and child were well when discharged from hospital 30 days after admission.

Observations on Fatal Cases

If we omit cases which had a known complication that may have contributed to death, and those which were treated with relaxant drugs, there remain 47 patients who died apparently as a direct result of tetanus, four of whom had periods of onset of over 48 hours. Two of these were old by Nigerian standards—48 and 55 years—and, as they died on the eighth and ninth day of the disease respectively, exhaustion and age may have been largely responsible. In the remaining 45 cases the only consistent feature is that they all had generalized reflex spasms which continued until death. All except three cases had a pyrexia at some time.

Discussion

The main source of infection in tetanus is the soil (Boyd and Maclennan, 1942; Knott and Cole, 1952). It is therefore not surprising to find that in a country like Nigeria, where the population is largely unshod, the largest single group of cases followed injury of the lower limbs. If, as is probable, the cases in which no causative injury was found followed small healed injuries of the lower limbs, then more than half (65%) of the cases are attributable to this source. Apart from acute injuries, tetanus is a serious and by no means uncommon complication of any condition, such as guinea-worm infestation (Bryant and Fairman, 1940), which causes chronic ulceration.

The only other large aetiological group is made up of cases which followed childbirth and abortion. The mortality (60%) in these cases was not much higher than that of the series as a whole, and compares favourably with the 75–100% quoted by other writers (Sahiar, 1954; Adams and Morton, 1955).

The post-operative cases show the necessity for an absolutely efficient sterilizing technique, and the remainder of the cases demonstrate well the variety of portals of entry of infection in this disease.

Shackleton (1954) has drawn attention to the necessity for taking into account prognostic criteria before assessing the value of any method of treatment in tetanus. By using the period of onset and of incubation, as described by Cole (1940) and verified experimentally by Pillemer and Wartman (1947), and a practical modification of Shackleton's (1954) classification, it is possible to divide otherwise healthy cases of tetanus into two groups—namely, mild cases, which will recover, and severe cases, in which the issue is in doubt. Cases in which the incubation period is over nine days and the period of onset over 48 hours constitute the mild ones, and in such cases it is not justifiable to use methods of treatment which are in themselves hazardous, nor is it possible to assess the effect on mortality of any method of treatment. Severe cases are those in which the incubation period is under nine days and the period of onset less than 48 hours. It is by their effect on the mortality of these cases that new methods of treatment must be judged. It is clear from the above findings that no case of tetanus must be judged hopeless on prognostic criteria alone.

The use of muscle relaxants in the treatment of tetanus, implying as it usually does long periods of artificial respiration, and requiring skilled attention, is not a practical proposition in an area where the incidence is high and trained staff scarce. It is felt, however, that mephenesin, given intravenously as described above, could be used advantageously for short intervals to give periods of rest to patients who do not respond well to the more usual form of treatment. The central depressant drugs, which were used in most of these cases, continue to be the most practical means of treatment. There is no need for artificial respiration or for continuous supervision, and in many cases the patient can drink, and occasionally eat, normally. Chlorpromazine, while it prolonged the effect of sodium amylobarbitone, seemed to have no specific effect on the disease. It is now felt, in the light of further knowledge (Godman and Adriani, 1949; Forrester, 1954; Forbes and Auld, 1955; Galloway and Wilson, 1955), that if tracheotomy had been freely carried out in cases of the severe group and the usual means of sedation employed, the nursing problems would not have been overwhelmingly increased and the mortality would probably have been reduced.

While the prophylactic administration of small doses of tetanus antiserum at the time of injury has reduced both the incidence and the mortality of tetanus (Bruce, 1920; *History of the Great War*, 1922), the results of treating established tetanus with large doses of antiserum are inconclusive (Huntington *et al.*, 1937; Bryant and Fairman, 1940). The giving of antiserum can in itself be dangerous (Bruce, 1920), and sensitivity tests are often misleading (Moynihan, 1956). In the cases here reviewed the mortality was not significantly higher in those cases which had no antiserum, nor did the severity of the disease appear to be less in cases that were given antiserum early in its course. There appears to be no justification for assuming that the prompt administration of large doses of antiserum will immediately arrest the progress of tetanus, or, indeed, have any beneficial effect.

Although the mortality in tetanus is higher in patients who have a pyrexia, this is not a constant feature in those dying from the disease. Pyrexia is probably due in every case to some degree of chest infection. The only constant feature in those dying from tetanus appears to be the presence of reflex spasms, which continue until death.

In our present state of knowledge the greatest hope of reducing the mortality from tetanus in Nigeria lies in prevention. While it is important to instruct the public how to avoid infection, the most rapid and most certain method of prophylaxis is by immunization with tetanus toxoid (Hampton, 1954; Emmett and Breck, 1955). A primary immunizing course of two injections of toxoid at an interval of six weeks, followed by a booster dose, will confer a lifelong immunity in most cases (Peterson *et al.*, 1955; Moss *et al.*, 1955). Production of tetanus toxin from a contaminated wound will further increase the immunity (Peterson *et al.*, 1955). To immunize the whole population of Nigeria against tetanus is a formidable task, but this must be the aim. The following is a suggested approach to the problem. (1) All schoolchildren be given a primary immunizing course of tetanus toxoid and at least one booster dose during their school years. As schooling has recently become compulsory, this would prove a comprehensive measure. (2) All expectant mothers be given a primary immunizing course of tetanus toxoid during pregnancy followed by a booster dose at parturition. (As a corollary to this it is suggested that all newborn children be given a protective dose of antiserum at birth.) (3) The remainder of the population be offered immunization as soon as the above groups have been dealt with. This approach is aimed at reducing the incidence of tetanus and is at present the most promising means of reducing the mortality.

Summary

A review is made of 100 consecutive adult cases of tetanus treated at University College Hospital, Ibadan.

The problem that tetanus presents in Nigeria is discussed with reference to incidence and causative injuries.

The importance is shown of assessing prognosis before deciding the method of treatment to be used and in estimating the value of different types of treatment.

The methods of treatment used, and their suitability for an area where the incidence is high, are described.

The value of antitetanic serum in the treatment of established tetanus is questioned.

Reduction of the incidence of the disease by prophylactic immunization is suggested as the most effective means of reducing the mortality.

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MANAGEMENT OF SEVERE TETANUS

USE OF CHLORPROMAZINE IN TWO PATIENTS

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Many drugs and techniques have been employed in the search for a safe and effective method of controlling the convulsions of severe tetanus. The ideal agent should abolish spasms and provide adequate sedation without respiratory depression. Chloral hydrate, bromides, paraldehyde, magnesium sulphate, morphine, pethidine, bromethol, and various barbiturates have been used, but all have defects. More recently muscular relaxant drugs have been employed with or without anaesthetic agents and artificial respiration. While their use is logical, the full regime involves many hazards and has not been shown to lower the mortality. Some of the most convincing recent series (Forbes and Auld, 1955; Veronesi, 1956) have been managed by more conservative methods.

Following reports of the experimental and clinical control of the muscular spasms of tetanus with chlorpromazine, we determined to explore its possibilities as the mainstay of sedative and anticonvulsant therapy. This drug has been shown experimentally to have properties which make it likely to be of value in tetanus. It antagonizes some central convulsant drugs (Courvoisier *et al.*, 1953); in cats it inhibits motor activity induced by cortical stimulation and suppresses the postural responses which occur on stimulation of the cerebellar cortex and the reticular formation (Dasgupta and Werner, 1955); it abolishes local tetanus in rabbits (Hougs and Andersen, 1954; Kelly and Laurence, 1956). The injection of chlorpromazine in cats has been shown to prolong the action of relaxant drugs such as *d*-tubocurarine and mephenesin (Courvoisier *et al.*, 1953); further, it has a direct paralytic effect on skeletal muscle (Burn, 1954).

These qualities, together with its better-known central effects as a tranquillizing agent and sedative and in potentiating the effect of hypnotic and analgesic drugs, suggest that its use in tetanus is rational. There are relatively few clinical reports of its use in the disease. Most of those that have appeared describe it as a useful adjunct in therapy (Adriani and Kerr, 1955; Bodman *et al.*, 1955) or discuss its use in mild and moderate cases (Cole and Robertson, 1955). Others have considered it a failure (Andersen *et al.*, 1955). In all these instances the doses used were small.

Our approach to the problem has been more in line with that of Kelly and Laurence (1956). We had previously observed the effect of chlorpromazine in four patients with mild tetanus in whom it relieved muscular