

Tetanus Neonatorum Treated with Chlorpromazine, Tetanus Antiserum and Penicillin

BY

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In 1955 reports on the possible value of chlorpromazine (Largactil) in the treatment of tetanus neonatorum appeared from Central and East Africa (Gelfand, 1955, and Cole and Robertson, 1955). The former published a series of nine cases, all African neonates, who received 35 mg. chlorpromazine and 40,000 units of tetanus antiserum twice daily and 300,000 units penicillin once a day. After about six days the dosage of the drugs was gradually reduced. There were three recoveries. It was further suggested in this paper that chlorpromazine should be continued for as long as the spasms occurred, but that as soon as they ceased the chlorpromazine and antiserum should be tapered off or stopped. It was also observed in these cases that after the spasms ceased the spasticity remained often for a few weeks, affecting either the whole body or only the limbs. This sign is often present to a greater or lesser degree and the impression obtained when the



Fig. 1—Although the infant had recovered from the acute phase of the illness, he was left with a generalised stiffness which in itself is not serious. Should the infant be lifted, the impression gained is that one is handling a doll.

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infant is lifted up is that a doll is being held. I have tentatively called this "the doll sign" (Fig. 1).

Cole and Robertson of Tanganyika published their findings independently about the same time. Two of their patients were adults, but the third, a female infant who recovered, was 12 days old. She was given tetanus antiserum 10,000 units, penicillin 100,000 units, syrup of chloral half a drachm thrice daily and chlorpromazine 8 mg. intramuscularly at night. This regime was followed for four days, after which the chloral and penicillin were continued for a further few days.

MATERIAL

Since the publication of my paper I have treated a further 16 African neonates, all showing the typical features of tetanus neonatorum. The first sign of the disease is an inability to suck, followed very soon by the typical quivering or spasms. Another frequent sign mentioned by the mothers is constipation. As a rule a septic umbilicus is found. The characteristic quivering with stiffness appearing in a neonate is easily recognised, and by the time the infant is admitted to hospital little doubt remains as to the diagnosis.

The treatment adopted was follows: Each infant was given 35 mg. of Largactil morning and evening, 60,000 units A.T.S. once daily and 250,000 units penicillin twice daily. As soon as the sucking reflex had returned—often a sign of recovery—the A.T.S. was stopped, but the chlorpromazine continued for a day or two longer until the spasms had almost or completely ceased. The infant was fed with a teaspoon by its mother, who invariably insisted on remaining in hospital with her child. We found mothers very willing to help in this way and remarkably patient with the feeding.

RESULTS

From August, 1956, until the end of January, 1957, sixteen cases of tetanus neonatorum were admitted to hospital. Five died within a few hours of admission and were not included in the series. Of the 11 cases who survived for longer than a day in hospital, and therefore received the combined treatment of chlorpromazine, penicillin and tetanus antiserum, six died and the remaining were considered to have recovered. It was only possible to follow up two of the five cases for a month after discharge from hospital, as all trace of the other three was lost.

The results are summarised in Table I.

Table 1

Date	Hospital No.	Name	Age on Admission	Clinical Picture	Treatment	Result
19.11.56	3941	Estera (female)	7 days	Aged 6 days when inability to suck and spasms first appeared. Umbilicus infected.	Combined treatment for one day. Died 20.11.56.	Died
28.10.56	3899	Geteresi (female)	10 days	Was 8 days old when failure to suck began. Umbilical site septic.	Combined treatment for two days. Died 30.10.56.	Died
16.9.56	3687	Buky (male)	6 days	Septic umbilicus. Took ill on sixth day of life with inability to suck and spasms.	Combined treatment for one day. Died 17.9.56	Died
24.11.56	3966	Peter (male)	6 days	Started with spasms on sixth day of life. Umbilicus not septic.	Combined treatment for four days. Sucking on 28.11.56. Died 29.11.56.	Died
9.12.56	4041	Richard (male)	10 days	Took ill when 8 days old. First symptom mentioned was an inability to suck. Septic umbilicus.	Combined treatment for five days. No spasms, but still stiff even on discharge. Started to suck on third day of treatment.	Alive on discharge
28.11.56	3986	Bigane (male)	10 days	Started with stiffness on tenth day when baby admitted.	Combined treatment for five days. Treatment stopped 3.12.56. Discharged 8.12.56.	Alive on discharge
21.11.56	3950	Michael (male)	21 days	Began with stiffness and inability to suck when 19 days old.	Combined treatment for five days. Slow improvement. Alive on discharge, 2.12.56.	No record
23.1.57	4335	James (male)	7 days	Took ill at age of 6 days. First symptoms noticed were constipation and inability to suck. Then spasms appeared. Infected umbilical site.	Five days' treatment given, but penicillin continued thereafter for two more days. Discharged on 5.2.57 as cured, but "doll sign" still positive.	Alive on discharge
10.1.57	4256	Simon (male)	10 days	Took ill at age of 9 days. First started with spasms.	Combined treatment instituted. Died 12.1.57, two days after treatment begun.	Died
18.12.56	4087	Francisca (female)	9 days	Took ill when 6 days old. Spasms. Umbilicus clean.	Combined treatment instituted. After four days, sucking started again. Treatment given for 5 days. Died 24.12.56.	Died
18.12.56	4085	Mucrembo (male)	7 days	Became ill when 5 days old. Shivering, constipation. Umbilicus clean.	Combined treatment for 5 days, when sucking recommenced. Some stiffness when discharged on 27.12.56.	Alive on discharge

COMMENT

The earlier hope that chlorpromazine has a place in the treatment of tetanus neonatorum appears to be justified, as before it was used my results with diverse treatments were almost invariably disappointing and rarely was a recovery obtained. Patients treated previously with tetanus antiserum, penicillin and sedatives almost always died, whereas in the 11 cases reported now it would appear that the additional use of chlorpromazine has resulted in a cure of five. In undertaking the treatment of this disease it would have been preferable to have had a control series in which penicillin, tetanus antiserum and perhaps a sedative were given, but chlorpromazine withheld. I decided that in view of my past experiences of this disease I was not justified in denying any infant the drug.

It is difficult to explain the possible action of chlorpromazine in tetanus. I doubt if it is the depressant central action which the drug is alleged to possess. It may possibly be due rather to a local effect of chlorpromazine on voluntary muscle, for one of its properties is said to be

the production of hypotonia on muscles. (Quoted from *Largactil*, Pharmacology, May & Baker Ltd., page 17.)

SUMMARY

Out of eleven cases of tetanus neonatorum treated with chlorpromazine, tetanus antiserum and penicillin, five left hospital alive and without spasms. Two mothers brought their infants one month after discharge from hospital fully recovered. All trace of the remaining three infants has been lost. Since employing chlorpromazine some of the infants have recovered. The possible action of chlorpromazine in the disease is mentioned.

REFERENCES

- COLE, A. C. E. & ROBERTSON, D. H. H. (1955). *Lancet*, 2, 1063.
GELFAND, M. (1955). *C. Afr. J. Med.*, 1, 216.

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