A STUDY OF TETANUS MORTALITY

By A. L. Gwee and Y. K. Lee

(Department of Clinical Medicine University of Singapore)

In 1960, a survey of Tetanus cases in Singapore was made with the hope of finding out possible "black" areas where the disease was more, so that a limited local campaign for active immunisation may be considered (Gwee and Nadarajah 1960). The survey showed on the contrary no such tendency thereby indicating that a general active immunisation campaign was the only answer to the problem here as in other parts of the world. A surprising finding coming out of the survey was that tetanus mortality had risen in the 3-year period 1957 - 1959 although the case- incidence, population and economic statistics had remained much the same, and the professional care as far as specialist number went was in fact better and better! This has led to the speculation whether the therapeutic regimes adopted might have exerted an adverse effect on the survival chances of tetanus cases. Hence, a team was formed in 1961 to study all the cases of tentanus in the 3-year period retrospectively with the specific object of elucidating the reason for this disturbing trend of tentanus mortality, so that remedial measures if necessary could be adopted.

Personnel was drawn from Surgical, Medical and Paediatric units in the General Hospital as cases of tetanus were admitted into General Hospital alone in that period. All cases with open injury would be received by Surgical Units, whereas all cases without obvious injury would go to the Medical units excepting neonatal and those below the age of 10, which were treated by the paediatricians. A fixed schedule was drawn up so as to permit easy comparison and also with the expressed intention to detect if possible any likely undesirable trend in therapeutics.

It was felt that a rising mortality could be due to many reasons amongst which the following might be enumerated :

1. Difference in the affected cases such as age difference. A greater number of cases in the neonatal group would naturally increase the mortality and the converse would also be true.
2. Difference in the severity of injury. The more the injury with greater contamination, the risk would be expected to increase.
3. Difference in the therapy. A regime less or more effectual would conceivably alter the mortality figure.

There was no change in the population structure or socio-economic activity in that 3 year period, and it seemed to one of the team (Gwee, A.L) that the first two reasons were unlikely to be the causes. However, in therapy, it was found that owing to the rapid increase of trained specialists, most of them had a period of post-graduate training overseas, the views regarding management have been diverse and hence many differing policies were in fact operating simultaneously. Amongst these, the one at greatest dispute was the use of lytic cocktail — a mixture of chlorpromazine, pethidine and phenergan given as an intravenous drip. This regime has been reported favourably by many workers (Kochhar 1961, Spence 1961, Wright and Adams 1960, Shanker and Meherotra 1959), but the therapy required much more nursing care than was usually available locally at that time, and there were some who were apprehensive that an effective regime if not adequately administered could be equally effective in an adverse manner.

At the same time, it was found that a very popular sedative, namely, paraldehyde, was not up to the required standard of pharmacologic purity. The climatic and storage conditions were such locally that it would appear impossible to prevent deterioration. It must be pointed out that locally paraldehyde has been in use for many years and in many other conditions besides tetanus. Although no definite figures were available, all clinicians locally were cognisant of the comparative safety of its use, and in fact amongst the thousands of times it has been employed, only one instance occurred where the death of a case in status epilepticus might be contributed to paraldehyde. However, in spite of consistent clinical observation of its safety, the drug was regarded as suspect, and toxicity studies were made by the Department of Pharmacology, the result of which is reported elsewhere in this issue (Yeoh 1962). Also special attention was paid to the exhibition of paraldehyde in the period under study in order that any adverse trend might not be overlooked.

Locally, it was uniformly accepted that the use of anti-tetanic serum was theoretically sound and in practice given. However, it is recognised that serum can give rise to complications some of which are fatal (Toogood 1960). It was felt that in fatal anaphylaxis, the result of intravenous therapy would most likely be dramatic and evident, and if serum reaction has played a part in contributing to a rising mortality, then an adverse trend may be detectable in cases given serum intravenously.

Finally, Periston-N was used in a limited scale at that time with conflicting results. Some were sanguine (Yeoh 1960) whereas others were dubious. The survey accordingly included this to determine if possible its real benefits.

Method :

If, for a series of 100 cases, a regime is adopted, so that each consecutive case will either be given a particular drug or not given, then given that the drug itself has a certain lethal risk (A) and the disease has an innate mortality rate (B), then the result may be represented as follows :—

Total Death = innate mortality of the disease plus lethal risk of the drug.
= A + B.

Total Living = 100 — (A+B).

If the lethal risk of the drug is 100%, i.e., it kills every patient who receives it, then amongst the living cases, none would have received the drug, i.e., percentage of cases receiving the drug would be zero in living cases. If the innate mortality of the disease is nil, then the cases amongst the death receiving the drug would be 100%, and amongst the living cases 0%.

If however, the lethal risk is not complete, say 10%, and the innate mortality is 20%, then the following situation applies :—

100 cases
50 not receiving drug (I)
50 receiving drug (II).

Assuming fair scatter in the distribution :

(I) 50 cases not receiving drug would have 10 deaths (20%).

(II) 50 cases receiving drug would have 10-15 deaths (20-30%, average 25%) as it is theoretically possible that a case may be amongst the innately mortal group, and also fatally reacting to the drug,
and living (70-80%, average 75%).
Hence, total living cases would be 40 + (35-40) = 75-80, of which 35-40 would have received the drug, i.e., 46-50% and total dead cases would be 10 + (10-15) = 20-25% of which 10-15 would have received the drug, i.e., 50-60%.
In other words, increase risk is shown in a higher figure in dead cases.

Thus, by comparing the groups receiving drugs, it may be possible to detect an increase risk in a particular therapy.

In the treatment of tetanus in Singapore, the previous survey has shown the disturbing tendency that mortality has increased. It was noted in the analysis of these cases that therapeutic regimens had altered. Although it is within the bounds of probability that more toxic cases were coming in, that resistance to tetanus was falling, or that tetanus bacillus was increasing its potency, the more likely explanation would appear that the therapeutic regimens adopted might have contributed towards increasing mortality.

Accordingly, four specific therapeutic measures were singled out as being under suspect, for reasons to be discussed later, and analysis on the preceding method was made to see if a specific adverse trend could be detected.

It can be readily seen that with no freak distribution and a constant disease mortality, the increase in the drug risk can be appreciated by comparing the figures of cases receiving a drug between living and dead cases.

At the same time, other information was regarding age, distribution, site of entry, length of incubation and severity of the disease. These would help to establish that there was no real change in the patient-status or disease severity to affect the ultimate mortality figure.

Also it might yield information of value in the consideration of future management of tetanus cases.

Medical Unit II, under Professor E. S. Monteiro, Department of Clinical Medicine, participated in the Survey, and the following was an analysis based on the 3 year period of tetanus cases in the Unit.

RESULTS

A total of 61 cases occurred in the 3 years, and the results were tabulated :
(Table I, II, III, IVa, V & VI.)

TABLE I.

	CASES	DEATHS	
1957	19	4	= 21.1%
1958	17	9	= 52.9%
1959	25	11	= 39.3%
	61	24	

TABLE II.

AGE	DIED	ALIVE
10-19	2	14
20-29	4	10
30-39	6	4
40-49	4	4
50-59	4	2
60+above	4	3
	24	37

M : F : : 15 : 9.

TABLE III.

Days on which death occurred.

Less than 24 hours	2	
1st day	8	
2nd day	6	
3rd day	—	87.5%
4th day	3	
5th day	2	
6th day	—	
7th day	—	
8th day	2	
9th day	—	
10th day	1	
11th day	—	
12th day	—	
13th day	—	
14th day	—	

TABLE IVa.

DEAD Total number of cases: 24

ATS i/v (exclude unknown route)	16
Cocktail (exclude i/v Largactil or Phenergan or pethidine only)	14
Paraldehyde (include oral)	20
Periston-N	6
Incubation below 7 days	7
Incubation 7 days and above (include unknown)	17
Peripheral sites of entry (limbs only)	11
Central sites (including umbilicus)	4
Generalised spasms	21
Localised spasms	3
Pyrexia	1
Spasm	3
Asphaxia	1
Anaphylactic shock after ATS	0
Cardiac Failure	1

NOTE: 1. Unknown cause of death omitted.
2. Where paraldehyde and cocktail, etc. were given more than one entry is made.
3. Where site of entry is unknown entry is omitted.

TABLE IVb.

ALIVE.

Total number of cases: 37

ATS i/v (exclude unknown route)	20
Cocktail (exclude i/v Largactil or Phenergan or Pethidine only)	10
Paraldehyde (include oral)	27
Periston-N	9
Incubation below 7 days	5
Incubation 7 days and above (include unknown)	32
Peripheral sites of entry (limbs only)	18
Central sites (including umbilicus)	5
Generalised spasms	28
Localised spasms	9

TABLE V.

Comparison of the 2 Series.

	DEAD	ALIVE
ATS i/v	16/24 = 66.7%	20/37 = 54.1%
Cocktail	14/24 = 58.3%	10/37 = 27.0%
Paraldehyde	20/24 = 83.3%	27/37 = 73.0%
Periston — N	6/24 = 25 %	9/37 = 24.3%
General spasms	21/24 = 87.5%	28/37 = 75.7%
Local spasms	3/24 = 12.5%	9/37 = 24.3%
Incubation < 7 days	7/24 = 29.2%	5/37 = 13.5%
Incubation 7 days & more	17/24 = 70.8%	32/37 = 86.5%
Peripheral-entry	11/24 = 45.8%	18/37 = 48.6%
Central-entry	4/24 = 16.7%	5/37 = 13.5%

TABLE VI.

	Dead	Alive
Total	4	5
Umbilicus	0	0
Uterus (abortion)	4	3
Ear	0	2
Others	0	0

DISCUSSION

Table I showed a marked increase of mortality for 1958 and 1959, a period where lytic cocktails were used in the Unit. The age group (Table II) seemed to suggest that the best outlook was in the younger age (10-29), and that mortality became higher as age advanced. Most of the mortality occurred within the first 7 days (87.5%) which would suggest that the needed care in looking after a case of tetanus to tide it over the danger period was quite short, and also that any aggressive therapy should not really be contemplated after that period, as the prognosis of the case would appear to be quite good as it was, and no undue risk required to be considered in the way of therapy.

A study of the subsequent Tables III a, b and IV showed that although there did not seem to be any definite favourable or adverse trend in the giving of serum intravenously, administration of paraldehyde or Periston-N, the use of lytic cocktail was disturbing in that the figure was significantly higher amongst the dead (58.3%) against 27.0% in living (Table V).

Similarly, although there did not seem to be any suggestion that the site of entry or the presence of general spasm made much difference one way or the other, but an incubation under 7 days would be a serious thing, and presence of local spasms only, a favourable omen. It is heartening to find that the cases of central entry cases (Criminal abortion) fared better than expected (3 out of 7 survival 42.8%).

SUMMARY

A retrospective survey of tetanus cases was carried out for a restricted period, and the material of a particular Unit was analysed and reported.

It is believed that the use of lytic cocktail under the local conditions was likely to be a risky procedure, and that paraldehyde, in spite of its unsatisfactory pharmacological status, was quite safe for therapeutic purposes.

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