SOUTH AFRICAN TYPHUS

By ADRIANUS PIJPER, M.D. and HELEN DAU

From the Authors' private laboratory, Pretoria, South Africa

(With 2 Figures in the Text)

Purpose of paper

This is:

(1) To describe a recent outbreak of typhus-like disease in Pretoria.

(2) To show how this outbreak fits into the general scheme of typhus-like diseases in South Africa, as outlined by us (1934).

(3) To review the literature of southern Africa on typhus-like diseases in the light of our own observations.

The Pretoria outbreak

One or two cases of "sporadic" or "mild" typhus occur in Pretoria every year. At the end of the particularly wet summer 1933–4, however, so many cases occurred within a few weeks that one could justifiably speak of an outbreak. Most cases were very mild, many probably never reached a doctor and so the exact number of cases remains unknown. Personally we know of about forty cases.

All cases showed a characteristic papular rash, extending over palms of hands and soles of feet. Most patients had little fever, many refused to go to bed, but others went through a period of continuous fever extending over 12–14 days, as illustrated in Curves 1 and 2 (in all our curves the disease is called sporadic typhus). A few cases were severely ill, with all the symptoms of classical typhus.

In no instance did one case follow another in one and the same household, and careful investigation by the local medical officer of health, Dr F. A. Donnolly, failed to find any evidence of the infection being carried by any conceivable means from one case to another. The cases occurred quite irregularly all over the town and suburbs.

The social position of practically all sufferers allowed to lice being excluded as vectors. They were all people in good circumstances, and the standard of personal cleanliness in South Africa amongst such people is very high.

We have no information as to the occurrence of the outbreak amongst the native and coloured population, and all our remarks refer to white people only.

It is perhaps not superfluous to point out that no cases of tick-bite fever were included in this series of cases.

Thanks to the help of our local colleagues and the local health authorities, we had an opportunity in most cases of firmly establishing a diagnosis of

typhus-like disease by means of agglutination-tests. We used O-strains only, kindly supplied by Dr Felix of the Lister Institute. The results of our Weil-Felix rections are given in Table I.

Table I. *Weil-Felix reactions of "sporadic" or "mild" typhus in Pretoria.*

Patient	X 19	X 2	X Kingsbury	Patient	X 19	X 2	X Kingsbury
1	160	320	20	**17**	0	10	0
2	80	160	160	**18**	10	20	10
3	80	40	0	**19**	20	20	160
4	160	320	10	**20**	0	20	20
5	20	0	0	**21**	10	80	80
6	10	10	40	**22**	20	80	10
7	0	20	20	**23**	80	40	20
8	10	0	10	**24**	40	40	80
9	40	20	0	**25**	40	80	80
10	1280	40	1280	**26**	1280	1280	60
11	20	40	0	**27**	1280	1280	10
12	20	40	0	**28**	20	80	40
13	20	40	10	**29**	20	160	80
14	20	80	40	**30**	40	160	10
15	10	0	20	**31**	160	320	40
16	20	20	20				

All cases were tested after the appearance of the rash, which usually seemed to appear on the fifth day of illness. As a rule the titre was higher the later the blood was taken. Table I shows that most cases gave significant reactions, and some of them more than that. On the whole X 19 and X 2 reacted better than X Kingsbury, but this was not always the case. The most striking feature however of the table is that X 2 reacted at least as well as X 19, a phenomenon which has not been recorded before in any comparable form of typhus-like disease (Felix, 1933*a*).

EXPERIMENTAL INVESTIGATION OF OUTBREAK

Transmission of the virus to animals was attempted by us from one of the severe cases. Injection of 5 c.c. of the patient's blood intraperitoneally into a guinea-pig resulted in fever, illustrated by Curve 3. The virus has since been passaged from guinea-pig to guinea-pig by means of intraperitoneal injections of emulsified brain. Curve 4 is a seventh passage. These guinea-pigs showed occasional swelling of testicles, and some redness of the tunica, but Rickettsia-like structures were hard to find. They also showed a swollen spleen, swollen adrenals, a clean peritoneal cavity without evidence of secondary infection, and a hyperaemic brain with occasional "nodules."

Injection of brain and other organs from infected guinea-pigs into the peritoneal cavity of rabbits, the procedure introduced by Felix (1933), produced agglutinins for the X-strains. The rise in titre in such animals is exemplified in Curve 5.

We further found that the virus protected guinea-pigs against itself. An example is given in Curves 6, 7 and 8. Curve 6 is an ordinary passage. After having shown a normal temperature for 6 weeks, the animal was reinfected with brain emulsion. It showed no rise in temperature (Curve 7), whilst a fresh

animal, having received exactly the same dose, showed a typical curve (Curve 8).

We further undertook cross-immunity experiments in guinea-pigs. Our laboratory possesses two strains of tick-bite fever, and one strain of louse-borne typhus from Basutoland where louse-typhus frequently occurs. Through access to a sick traveller from Basutoland who arrived in Pretoria, we fortunately were able to start a strain of louse-typhus in guinea-pigs. Louse-typhus does not occur in or around Pretoria. Our two strains of tick-bite fever are of local origin. These three strains had been kept going in our laboratory in guinea-pigs for many months. Details about them have been given elsewhere

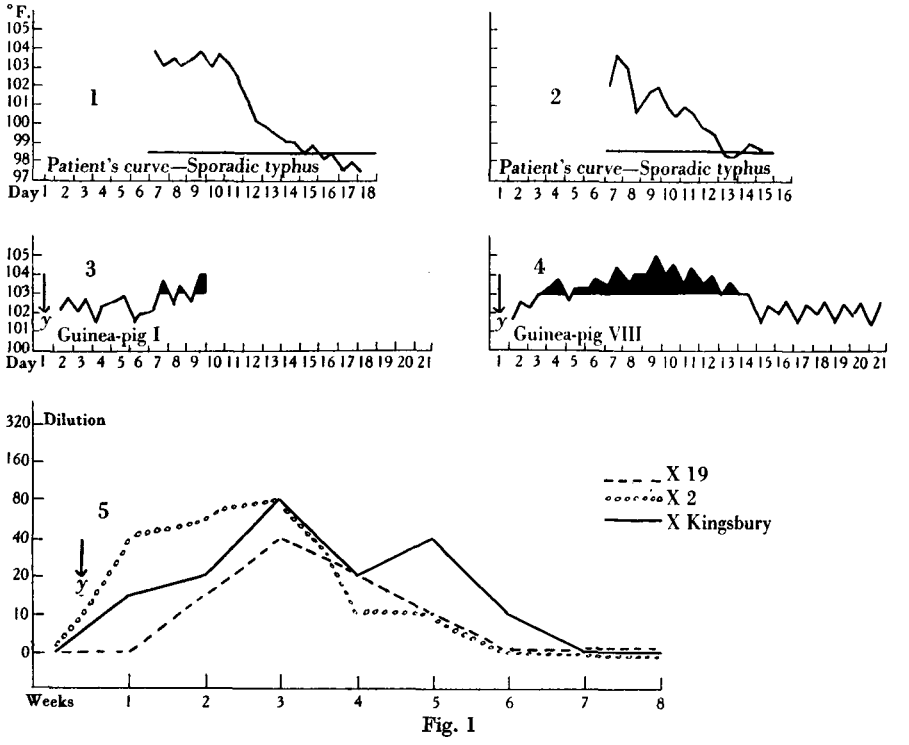

Fig. 1

(Pijper and Dau, 1934). That tick-bite fever is a typhus-like disease has been demonstrated by us on previous occasions (Troup and Pijper, 1931; Pijper and Dau, 1930–33; Pijper, 1934).

These cross-immunity experiments gave uniform results. Examples are given in Curves 9–20. The experiments were undertaken in the usual way, by first infecting an animal intraperitoneally with brain emulsion, noting its temperature curve, letting it have an undisturbed period, free from fever, for at least 6 weeks, and then infecting it again, intraperitoneally, with a big dose of some other typhus-like virus, an identical dose of this virus being given to a fresh animal. Thus Curves 9, 10 and 11 illustrate that the new virus immunises

against tick-bite fever. Curves 12, 13 and 14 show that it does not immunise against our epidemic (louse-) typhus. Curves 15, 16 and 17 show that tick-bite fever does not immunise against the new virus, and Curves 18, 19 and 20 show

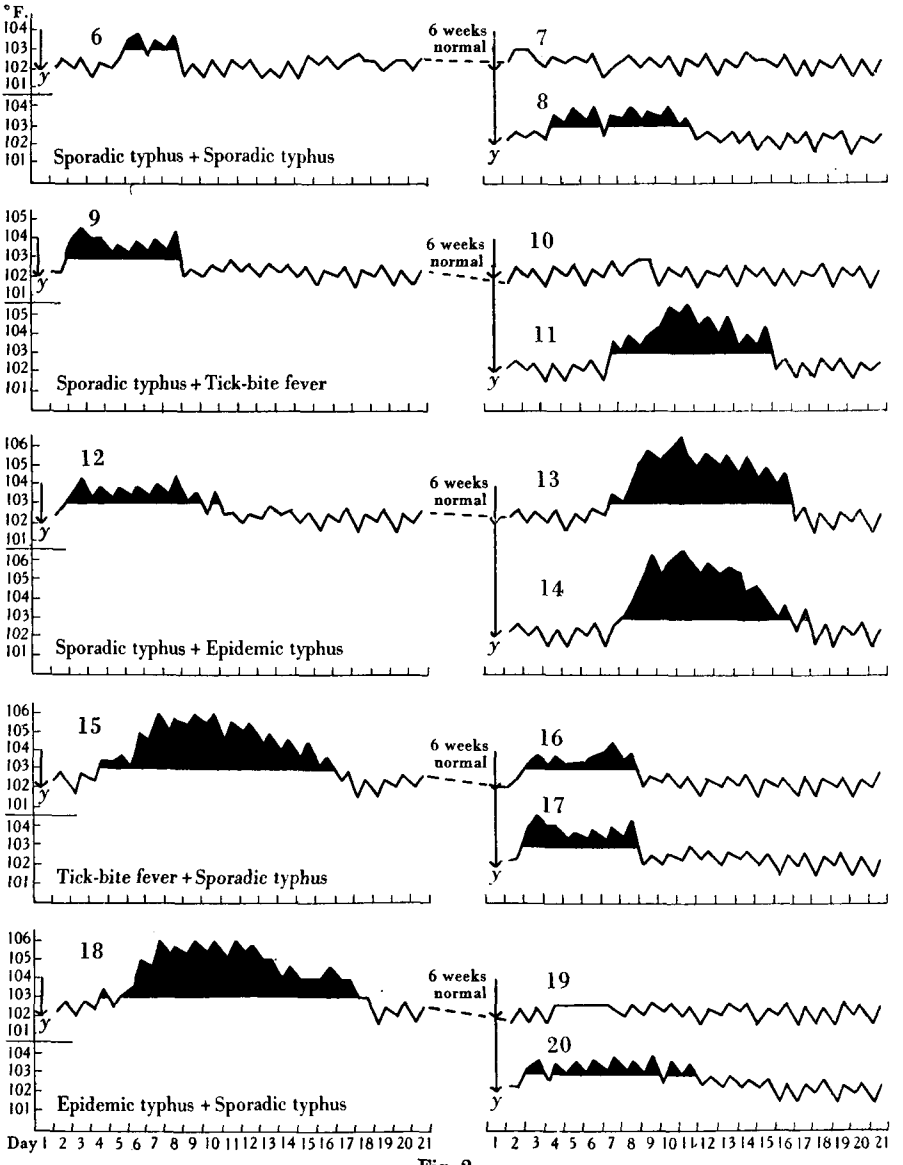

Fig. 2

that epidemic (louse-) typhus does immunise against the new virus. Both our strains of tick-bite fever behaved in exactly the same manner.

The results of these cross-immunity experiments may be summed up by saying that this new virus from the Pretoria outbreak has properties which place

it between that of tick-bite fever and that of our South African epidemic (louse-) typhus.

The results confirm a previous single observation of ours, where we had succeeded in producing fever in a guinea-pig by means of an injection of blood from a single sporadic case of typhus in Pretoria, and found that this animal was not protected against a subsequent infection with epidemic (louse-) typhus (Pijper and Dau, 1934). At that time no further experiments could be undertaken with that strain of virus.

We now wish to recall some older investigations of ours, where we found a typhus-like virus in rats caught in the town of Potchefstroom, Transvaal (Pijper and Dau, 1933*a*). This virus we kept going in guinea-pigs and rabbits for a sufficiently long time to study its behaviour as regards cross-immunity, agglutinin production, etc. (Pijper and Dau, 1934). This strain in every respect behaved exactly like the strain from the Pretoria outbreak we have described here. The rat and human strains must therefore be regarded as identical. It follows that this Pretoria outbreak, and also the sporadic cases occurring in Pretoria from time to time, are due to a virus from rats, conveyed to man by means of rat-fleas. The particularly wet summer 1933–4 would naturally favour the development of a particularly large number of rat-fleas and thus give rise to the unusually large number of cases.

Quite recently Rhodes (private communication) found an apparently typhus-like virus in rats from the Cape; this would show that the infection of rats is not confined to the Transvaal.

The three South African typhus-like viruses

Our work has established that in South Africa there are three viruses belonging to the typhus-group. One is tick-bite fever, the second is louse-typhus, which occurs endemically and epidemically, and the third is a virus which occurs in rats and which we have now also found in man, where it produces sporadic cases, with an occasional larger outbreak.

Tick-bite fever resembles fièvre boutonneuse, but the two diseases cannot be regarded as identical. Tick-bite fever has nothing to do with dogs, nor with dog-ticks, its agglutination reactions are different, its duration is shorter, it can much more easily be transferred to guinea-pigs, it is a much milder disease, and at least half the cases show nothing more than a tick-bite and swollen glands with a little fever, without a rash, a "forme fruste" which does not exist in fièvre boutonneuse. Clinically it is of course quite different from Rocky Mountains Spotted Fever, moreover, immune-serum from this disease, kindly supplied to us by Dr R. R. Parker, of the Montana Laboratory, did not protect our animals against even small doses of virus and immune-serum from our animals failed to protect against the American disease (Parker, 1933). Tick-bite fever therefore is a disease *sui generis*.

In other parts of the world there seems to exist at least a certain amount of cross-immunity between local flea-typhus and louse-typhus. We have found

with absolute regularity that although our louse-typhus always protects animals against our flea-typhus, our flea-typhus gave no immunity against our louse-typhus. The immune-serum from Rocky Mountains Spotted Fever, mentioned above, gave no protection in our animals against even small doses of either of our viruses.

We have already commented on the important serological difference between South African flea-typhus and similar diseases in other parts of the world: our flea-typhus agglutinates X 2 at least as well as X 19. It can therefore not be identified with these otherwise somewhat similar diseases.

Lastly there is the position of South African louse-typhus. Here again we have found important serological differences. In South Africa it has been a common complaint for many years that the Weil-Felix reaction never gave those impressive quantitative results the reports from other parts of the world would lead one to expect. South African workers had to be satisfied with hundredfold

Table II. *Weil-Felix reactions of South African louse-typhus.*

Patient	X 19	X 2	X Kingsbury	Remarks
1	160	640	20	Native, 7th day
2	640	1280	80	Native, convalescent
3	320	160	40	Native, convalescent
4	5120	2560	640	Native, 5th day(?)
5	640	640	160	Native
6	20	80	40	Native
7	160	40	320	Native, mild case
8	20	20	10	Native, early
9	20	40	0	White man, early
10	20	80	80	White man, same as **9**
11	160	320	10	Native, early
12	40	160	0	Native, late
13	640	320	160	Native, convalescent
14	800	800	0	White man, late
15	400	400	40	White man, late
16	80	160	40	Native
17	40	40	20	Native

dilutions where oversea reports spoke of thousandfold dilutions. To this quantitative difference we can now add a much more trenchant distinction. It has not been customary in South Africa in the Weil-Felix test to use anything else but X 19 strains. When we applied strains of X 19, X 2 and X Kingsbury to our first two cases, we found that X 19 and X 2 were agglutinated about equally well (Pijper and Dau, 1934). We have recently been able, thanks to the kindness of Dr H. H. Schulz, of the Whites Cement Factory in the Orange Free State, who supplied us with serums from his cases of louse-typhus, to confirm these findings on a somewhat larger scale. Table II gives the results of these tests. It is quite evident that X 2 is agglutinated at least as well as X 19, and also that the titres on the whole are considerably lower than they would have been in cases of European louse-typhus.

The South African form of louse-typhus therefore cannot be regarded as identical with louse-typhus in other countries.

In the preceding paragraphs we have insisted upon the differences between

South African typhus-like viruses and those of other parts of the world, not merely for the theoretical interest which attaches to them. There also is a practical side to the matter. Prophylactic vaccines against "typhus" are being tried out in many countries. We wish to point out that an indiscriminate use of vaccines prepared from other than South African viruses is not likely to produce the desired effect in South Africa.

Other observations on typhus-like diseases in southern Africa

It seems to us that our work, which has allowed us to reach certain definite conclusions, can throw light on some other observations on typhus-like diseases in southern Africa, which have been published from time to time by various authors:

McNaught (1911) described an outbreak of what he thought closely resembled Brills disease in Potchefstroom. Although the possibility that this was, or at least partly was, tick-bite fever, cannot absolutely be excluded, we feel inclined to regard McNaught's outbreak as identical with our Pretoria outbreak. Our reasons for doing this are the clinical similarity, the fact that since McNaught's publication cases of this nature have been repeatedly described in Potchefstroom by Dickson (1912) and by Friel (1932) and lastly the fact that we actually obtained our strain of typhus-like virus from rats caught in Potchefstroom.

In recent years in South Africa the belief has often been expressed chiefly on clinical, but also epidemiological, grounds that not everything that was here labelled "typhus," was carried by lice and that it seemed likely that fleas sometimes played a part and caused a type of case that sometimes could be distinguished from real epidemic typhus. Scroggie (1931) and Gray (1931) made out a particularly good case for this belief. Our work has now supplied the experimental foundation.

Ross (1932) found a disease in South Rhodesia, which he thought belonged to the typhus group. From his own data there is no doubt but the disease he dealt with was tick-bite fever, the disease first described by Sant'Anna (1911) and Nuttall and named by the latter (1911), of which disease we had then already definitely established the typhus-like nature (Troup and Pijper, 1931; Pijper and Dau, 1930–3; Pijper, 1934).

Ross's paper established the fact that tick-bite fever, which has been seen as far south as Cape Town, extends as far north as South Rhodesia.

There is so far no evidence that tick-bite fever occurs in North Rhodesia. It certainly does occur in Mozambique, at least in its southern half, in and around Lorenzo Marques.

Hennessey (1934) published a series of experimental observations, made in Uganda, proving that typhus occurs which is conveyed by lice. The low titre for X 19 which he found in his patients makes it appear probable that this Uganda typhus is the same as louse-typhus in the Union of South Africa, but

as X 2 was not used and of course no cross-immunity experiments were undertaken, complete proof of this is lacking.

In Kenya the position is different. Gilks (1920, 1921) first described a typhus-like disease there. He was followed by Clearkin (1921), Anderson (1925), Jewell and Cormack (1930), Tonking (1932), and Roberts and Tonking (1933). Some of these authors speak of "tropical typhus." No thorough experiments were undertaken on this disease before the work of Roberts and Tonking. A striking feature of all these papers is that so often in the clinical description of the disease mention is made of a "tick-bite," although the authors generally do not ascribe any importance to this symptom. Hopkirk (personal communication), working in the same country, assured us that a tick-bite can be found in all cases. Roberts and Tonking (1933) have given experimental evidence that in infected surroundings the dog-tick *Rhipicephalus sanguineus* harbours a typhus-like virus, the exact nature of which so far remains unknown. Judging from what we have brought to light about tick-bite fever, the Kenya disease cannot be tick-bite fever. The tick is different, the duration of the fever is different (12–14 days instead of 10), the clinical symptoms also appear to be different, especially in so far as no mention is ever made of the curious "forme fruste," which is according to us (1934) such an important feature in tick-bite fever. Balfour (1925) has already suggested that the Kenya disease might easily be fièvre boutonneuse, and as far as we can see there is nothing to deny, and everything to support this view. Both fièvre boutonneuse and the Kenya fever are conveyed by *Rhip. sanguineus*, which has never been found associated with tick-bite fever.

SUMMARY AND CONCLUSIONS

From an outbreak of very mild "typhus-like disease" in Pretoria, which strongly resembled the cases of "sporadic" or "mild" typhus occasionally occurring in that town, a virus was isolated which was studied in guinea-pigs and rabbits, and was found to belong to the typhus-group.

This virus in cross-immunity experiments with virus of South African louse-typhus and South African tick-bite fever and also in other respects behaved exactly like the typhus-like virus the authors on a previous occasion isolated from rats in a South African town where cases of "mild" or "sporadic" typhus have been known to occur regularly for many years.

This constitutes evidence that South African "mild" or "sporadic" typhus comes from rats and is communicated to man by rat-fleas.

In southern Africa, therefore, one has to reckon with three typhus-like diseases: tick-bite fever, flea-typhus from rats, and louse-typhus. Tick-bite fever has a primary sore, the tick-bite, as a pathognomic symptom, the other two can only be differentiated satisfactorily from one another by cross-immunity tests.

Agglutination reactions and cross-immunity tests show that South African

louse-typhus and South African rat- or flea-typhus are not identical with similar diseases in other parts of the world.

Tick-bite fever is a mild typhus-like disease extending from the Cape to South Rhodesia.

The typhus-like disease of Kenya is not tick-bite fever, and seems to be identical with fièvre boutonneuse.

REFERENCES

ANDERSON, G. V. W. (1925). *Kenya Med. J.* **2**, 42.
BALFOUR, A. (1925). *Ibid.* **1**, 352.
CLEARKIN, P. A. (1921). *Ann. Report Kenya*, also (1925) *Kenya Med. J.* April.
DICKSON, I. D. (1912). *Thesis* submitted for M.D. Edinburgh University.
FELIX, A. (1933). *Trans. Roy. Soc. Trop. Med. Hyg.* **26**, 365.
—— (1933*a*). *Ibid.* **27**, 147.
FRIEL, R. (1932). *S. Afr. Med. J.* 10 Sept.
GILKS, J. L. (1920 and 1921). *Ann. Report Kenya.*
GRAY, F. C. (1931). *J. Med. Ass. S. Africa*, 26 Dec.
HENNESSEY, R. S. F. (1934). *E. Afr. Med. J.* **9**, 42.
JEWELL, N. P. and CORMACK, R. P. (1930). *J. Trop. Med. Hyg.* 301.
MCNAUGHT, J. G. (1911). *J. Roy. Army Med. Corps*, **16**, 505, 586 (see also *S. Afr. Med. Record*, 24 Dec. 1910).
NUTTALL, G. H. F. (1911). *Parasitology*, **4**, 89.
PARKER, R. R. (1933). *Public Health Reports, U.S. Treasury Dept.* Reprint 1569.
PIJPER, A. (1934). *S. Afr. Med. J.* **15**, 551.
PIJPER, A. and DAU, H. (1930). *J. Trop. Med. Hyg.* 93.
—— —— (1930). *Brit. J. exp. Path.* **11**, 287.
—— —— (1931). *Ibid.* **12**, 123.
—— —— (1932). *Ibid.* **13**, 33.
—— —— (1931). *J. Med. Ass. S. Africa.* 22 Aug.
—— —— (1933). *Ned. Tijdschr. v. Geneesk.* **77**, 2030.
—— —— (1933*a*). *S. Afr. Med. J.* 11 Nov.
—— —— (1934). *Ztrlbl. f. Bakt.* I Abt. Orig. (in press).
ROBERTS, J. I. and TONKING, H. D. (1933). *E. Afr. Med. J.* **9**, 310.
ROSS, G. R. (1932). *S. Afr. Med. J.* **6**, 453.
SANT'ANNA, J. F. (1911). *Parasitology*, **4**, 87.
SCROGGIE, F. H. (1931). *J. Med. Ass. S. Africa*, 26 Dec.
TONKING, H. D. (1932). *E. Afr. Med. J.* **6**.
TROUP, J. MACD. and PIJPER, A. (1931). *Lancet*, 28 Nov.

(*MS. received for publication* 12. XI. 1934.—Ed.)