

*Case 16.*—A man aged 42 had had a dragging left leg and slightly ataxic gait for six years. He was found to have left ankle clonus, brisk reflexes, and bilateral extensor responses. Tubarine in doses of 20 mg. and 30 mg. produced severe side-effects, blurring of vision, and drunkenness, great ataxia, but no objective improvement in gait. The drug was discontinued at patient's own request.

*Case 17.*—A woman aged 44 had had disseminated sclerosis for 10 years. Brisk tendon reflexes, bilateral extensor plantar responses, and spastic paraplegia were present. She was able to walk a few steps, but had not been out of her house for three years. Tubarine in 30-mg. doses did not give any relief but made the patient giddy and more ataxic.

### Discussion

While we are in agreement with previous authors that curare temporarily diminishes the tone in spastic muscle without producing general paralysis, we have not been able to substantiate Schlesinger's claim that curare in oil has overcome the disadvantages of the drug in aqueous solution, nor have we been impressed with it as a therapeutic agent in our series of patients.

*Side-effects.*—Troublesome symptoms occurred in 10 of our 17 cases (so severe in two that the drug had to be discontinued), but we found, as West did with aqueous curare, that a tolerance usually developed on continued administration.

*Length of Action.*—In general the relaxation of muscle tone was apparent in 10 minutes, maximal in 20–30 minutes, began to wear off in an hour, and was completely absent in 24 hours. This action is no longer than that of aqueous curare, although, as with that drug (West, 1932; Harvey and Masland, 1941), some of our patients thought that relief lasted several days.

We have no satisfactory explanation to offer for the temporary reversal of plantar responses noted in Case 7 and merely record it as a matter of interest.

*Therapeutic Value.*—Reviewing our 17 cases, we find that in 11 the treatment either produced no improvement (7) or the patients were actually worse (4). The reason for definite deterioration appears to be that curare by lessening spasticity sometimes unmasks previously concealed posterior column loss. Turning to the cases in which improvement was noted, the only remarkable success was in Case 1. Here curare in oil was of no use until it was reinforced with quinine, but the combination of the drugs resulted in cessation of the flexion spasms, which did not return when the drugs were stopped a month later. (It may be worthy of note that all cases in which favourable results were reported by Schlesinger were traumatic in origin.) In the remainder of our cases which were thought to be improved the benefit was slight and usually only apparent to the patient. It was very difficult to assess minor fluctuations in muscular power, and interrogation of patients showed that there was considerable natural variability: thus hot weather and previous exercise both resulted in temporary improvement. Another factor which had to be borne in mind, particularly in dealing with disseminated sclerosis, was natural remission (Case 13). Even more important was the psychological aspect of the treatment. Most of our patients had been chronically ill for long periods, and when fresh hope was engendered by the new drug, intensive physiotherapy, and the encouragement of being a centre of interest once more, there was a natural tendency to think the treatment was doing good.

Bearing all these factors in mind, we do not feel that the improvement noted in six of our cases can with any certainty be attributed to tubarine, particularly as 11 showed no benefit whatever. In our opinion, therefore, curare in oil is not the hoped-for advance in reducing spasticity in

neurological disease, and we do not feel that our results justify the expense of the treatment, at any rate so far as adults are concerned. We have not used the drug in children, but it seems likely that the same disadvantages would obtain, and a recent communication (Collis, 1947) on the subject of reablement in Little's disease makes no mention of its use. Further investigation is necessary to see whether a combination of drugs is any more successful.

### Summary

The value of curare in oil in reducing spasticity of pyramidal type in 17 cases of neurological disease has been investigated.

In our opinion the drug has not proved superior to aqueous curare, and has been of little use in the rehabilitation of our patients.

Our thanks are due to Dr. H. S. Pemberton and Dr. Leslie Cunningham for help in providing some of the cases, and to Messrs. Burroughs Wellcome and Co. for the initial supply of tubarine.

### REFERENCES

- Bennett, A. E. (1941). *Amer. J. med. Sci.*, **202**, 102.  
 Bremer, F. (1927). *C. r. Soc. Biol.*, **96**, 704; **97**, 895.  
 — (1928). *Ibid.*, **99**, 624.  
 — (1931). *Ibid.*, **107**, 253.  
 Burman, M. S. (1940). *J. Pharmacol.*, **69**, 143.  
 Collis, Eirene (1947). *Lancet*, **2**, 239.  
 Denhoff, E., and Bradley, C. (1942). *New Engl. J. Med.*, **226**, 411.  
 Hartridge, H., and West, R. (1931). *Brain*, **54**, 312.  
 Harvey, A. M. (1939). *J. Physiol.*, **95**, 45.  
 — and Masland, R. L. (1941). *J. Pharmacol.*, **73**, 304.  
*Lancet* (1946). **2**, 355.  
 Schlesinger, E. B. (1946). *Arch. Neurol. Psychiat.*, Chicago, **55**, 530.  
 West, R. (1932). *Proc. roy. Soc. Med.*, **25**, 1107.

## LOUSE-BORNE RELAPSING FEVER IN PERSIA

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An epidemic of a recurrent fever occurred in Abadan between November, 1945, and June, 1946—1,087 cases being admitted to the isolation hospital. We intend to show that this was in fact an epidemic of louse-borne relapsing fever, and to give an account of its symptomatology and the results of treatment with arsenicals.

In reviewing the available literature no report has been found of louse-borne relapsing fever in Persia. Current textbooks do not mention the disease as occurring there, although Rogers and Megaw (1944) say it is common in most parts of India. The present epidemic was undoubtedly part of the widespread epidemics described in the Mediterranean and North Africa during 1943–5—e.g., Algeria (Grenouilleau, 1946), Morocco (Sicault, 1944), Cairo (Wolman, Omar, and Abu-Taleb, 1945), and Abyssinia (Charters, 1945); and reviewed by Stuart (1945), who also mentions Tunisia, France, Greece, Rumania, and Turkey.

The tick-borne disease is found all over the Middle East and Central Asia—namely, Cyprus (Wood and Dixon, 1945), Palestine (Adler, Theodor, and Schieber, 1937), Azerbaijan (Popow and Achundow, 1936), Persia (Delpy and Rafyi, 1939), Caucasus (Maruashvili, 1945), Afghanistan (Avanessov, 1938), Kazakhstan (Andreev, 1944), and Tashkent (Kassirsky, 1933)—but it has, of course, different characteristics from louse-borne relapsing fever.

### The Epidemic

The first case was detected in the first week of November, 1945; other cases followed quickly, and 50 to 60 were being admitted weekly in January. The epidemic followed closely the degree of coldness of the weather as shown by the average minimum daily temperature until the end of January, 1946, when the active measures taken by the Health Department, who began disinfecting the population with D.D.T. on a big scale, caused a considerable drop in the incidence of the disease, although the minimum temperature remained about 45° F. (7.2° C.) until the end of February. As soon as the general temperature began to rise the epidemic quickly declined; it was no longer necessary for the poorer classes to crowd into houses for shelter, and the heat of the sun soon killed off the lice carried in their clothes. The critical temperature was reached at the end of May, with an average daily minimum of 80° F. (26.7° C.), an average maximum shade temperature of 105° F. (40.6° C.), and an average maximum sun temperature of 150° F. (65.5° C.). The last case was admitted on June 24.

It is interesting to compare Chart 1 with Chart 2, which is compiled from statistics of the typhus epidemic here in the

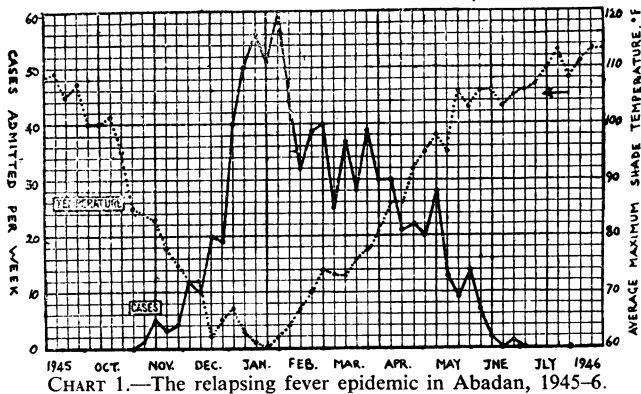


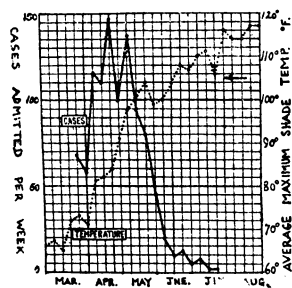
CHART 1.—The relapsing fever epidemic in Abadan, 1945-6.

winter of 1943, the critical temperatures for the termination of the epidemics being almost identical.

The disease was first diagnosed by one of us (I.S.S.) when *Spirochaeta recurrentis* was found on routine examination of blood slides from the out-patient department. Suspecting

the vector to be the louse, the next 50 cases were examined; 36 of these were found to be infested with *Pediculus humanus*. The lice were crushed in saline and examined under dark-ground illumination. The *Sp. recurrentis* was demonstrated in six lice. The dark-ground microscopical examination of a drop of blood under a cover-slip was found to be the quickest way

CHART 2.—The typhus epidemic in Abadan, 1943.



of diagnosing the disease; but as it was not possible to exclude concomitant malaria by this method routine diagnosis was made by staining a blood smear with Leishman's stain.

The following reasons do not fulfil all Koch's postulates, but they convincingly demonstrate that the relapsing fever was in fact louse-borne: (1) The Health Department has never found any tick focus in Abadan, and is of the opinion that there are no human ticks in the town. (2) Of the patients admitted to the isolation hospital 87.85% were found to be infested with lice. (3) *Sp. recurrentis* was demonstrated in lice taken from the bodies of patients.

(4) The epidemic form of the disease and its relationship to the average temperature are characteristic of a louse-borne disease. Comparison with the previous epidemic of typhus is very significant. (5) The drop in the weekly admissions following the mass disinfection of the populace with D.D.T. powder.

### Symptomatology

The last 214 male cases admitted to the isolation hospital were examined clinically by one of us (R.I.B.). (Very few women were admitted. The proportion was 19 men to one woman. This is certainly not a true figure for the incidence of the disease, but an indication that women were unwilling to apply for treatment.) All these cases were diagnosed by positive blood smears at the out-patient department before admission to the isolation hospital.

No account is given here of the preventive work carried out by our Health Department. All the cases came from the labouring and unemployed class of the community. The great majority were young adults, the age incidence being: under 8 years, 1 case; 8-15 years, 9 cases; 15-30 years, 117; over 30 years, 87.

**Onset.**—All these patients could recall the day on which the attack started; most of them could fix the time within a few hours. The attack began with a splitting frontal headache, which very soon was followed by a high fever and in many cases a rigor. The fever was maintained for an average of 4 to 5 days.

**Course.**—During the initial attack the temperature was usually raised to 103° or 104° F. (39.4° or 40° C.) and remained at this height until the crisis, when it fell to normal within a few hours. At this time the patient sweated profusely and was often weak and exhausted. During the next few days he quickly regained his strength and demanded to be discharged from hospital. The period of apyrexia lasted about nine days, although it was found that the most constant time-relationship was from the day of onset to the day of relapse—an average period of 14 days. During the relapse the patient's temperature was raised to 102°-103° F. (38.9°-39.4° C.) for about two days.

**Symptoms.**—During the initial fever patients complained of headache and pain in the back. Percussion over the lower thoracic and upper lumbar spine revealed tenderness, and the muscles of the arms and legs were also painful and tender to deep pressure. Anorexia was common, and some complained of epigastric pain after taking food. Vomiting was frequent; the bowels were usually constipated. Epistaxis was not uncommon; a non-haemorrhagic herpes febrilis occurred in a small number of cases. Many patients complained of a cough. During the apyrexial period all symptoms abated and the patient was quite well unless he had respiratory trouble.

### Physical Examination

The patient was usually seen on the third or fourth day of the disease, and presented the appearance of a high fever. No rash was seen in the majority of cases, but a few had definite petechial rash on the trunk only; in these the Weickel-Felix reaction showed only a slight agglutination with OXK—e.g., 1/25 +, 1/50 ±. A number of cases were jaundiced; these were classified as: +, conjunctival coloration; ++, skin coloration; +++, marked skin coloration. The colour was easily demonstrated in the serum of many cases in which the Wassermann test was carried out. Nine cases had a marked jaundice, and this was found to be a bad prognostic sign; two of these cases were fatal (see below). The spleen showed all degrees of enlargement—down to the umbilicus; the liver was sometimes enlarged and often tender. No change was found in the cardiovascular system,

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but minor respiratory complications were very common. The reflexes were normal, and there were no significant signs.

Incidence of Symptoms			
Fever .. .. .	98.07%	Epistaxis .. .. .	14.02%
Headache .. .. .	90.65%	Anorexia .. .. .	92.52%
Backache .. .. .	77.57%	Vomiting .. .. .	56.07%
Pains in limbs .. .. .	71.50%	Constipation (2-6 days) .. .. .	51.40%
Incidence of Signs			
Jaundice .. .. .	9.81%	Enlarged spleen (1-4 fingers) .. .. .	76.63%
Herpes .. .. .	7.48%		
Rash .. .. .	3.22%		

#### Complications

Respiratory complications were by far the commonest. Minor respiratory complications occurred in 49.07%, and major respiratory complications in 11.21%—a total of 60.28% with pulmonary disturbances varying from a "cough" to bronchopneumonia. The most usual symptom was a characteristic dry irritative tracheitis which often went on to a bronchitis. These cases were classified as minor complications. Sulphonamide treatment was given in 10.75% of the major complications. Bronchopneumonia was treated as a major complication.

There was a non-specific arthritis in four cases (1.87%)—two in the knee and two in the shoulder. These were treated with kaolin poultices. Perisplenitis due to the size of the spleen occurred in two cases (0.94%); these were successfully treated with repeated subcutaneous injections of adrenaline.

Complications in the central nervous system were found in three cases (1.40%).

*Mental Cases.*—Two patients developed obsessions that the other patients in the ward were plotting against them and wanting to kill them; both had to be put under restraint. One managed to escape in spite of being under careful guard and committed suicide; the other eventually recovered completely.

*Case of Transverse Myelitis.*—This was a very interesting case of a lesion of the spinal cord almost certainly due to relapsing fever. The patient was admitted to the isolation hospital on March 31, 1946, as an ordinary proved case of relapsing fever and given 0.45 g. of N.A.B. He developed a cough and bronchitis, for which he was treated with a full course (five days) of sulphonamides. He did not have a relapse. About 10 days after admission he complained of pain over the lumbar spine; this was more severe than the backache described by other patients and was not relieved by sedatives. After 15 days he was found to be developing a spastic paralysis in both legs and soon he was unable to walk. On examination the knee-jerks were R. + + +, L. + +, and the ankle-jerks were normal, Babinski's sign was positive, and the abdominal reflexes were exaggerated. There was some skin hypersensitivity around the lower abdomen. He was now transferred to the general hospital. The Wassermann reaction was negative. Spinal puncture unfortunately was unsuccessful owing to the rigidity of the back. The patient was examined by a surgeon, who could find no evidence of injury or disease of the vertebra. A radiograph of the spine revealed no abnormality. He was discharged from the hospital on June 25. He was then able to walk very precariously with a pair of crutches and was invalided as permanently unfit. On Aug. 7 he returned to the hospital applying for a certificate of fitness for re-employment; he was examined and found to be without any residual disability. This case was almost certainly a myelitis due to the relapsing-fever spirochaete; it was a pity the case could not be proved by lumbar puncture.

In view of the research carried out recently by French workers into the neurotropic character of the louse-borne *Sp. recurrentis* in rats, it is interesting to note that the central nervous system is affected more than other systems in the human body. Of our patients 90.65% complained of headache and 77.57% of severe backache in the thoracic and upper lumbar regions—i.e., over the spinal cord. Two cases suffered severe mental derangement, one resulting in death. One case of myelitis was almost certainly due to *Sp. recurrentis*.

#### Deaths

The death rate among all the cases of relapsing fever admitted during the epidemic was 1.11%. In the series of 214 cases specially studied, five (2.34%) deaths occurred—one from an unrelated disease (infected amoebic abscess), two from bronchopneumonia complicating the relapsing fever, and two from relapsing fever.

#### Treatment

The 214 cases under special study were divided into two groups for the purpose of treatment. Group 1, consisting of 97 patients, were treated with an injection of 0.45 g. of N.A.B. intravenously immediately on admission—11 (11.34%) suffered one relapse and no case relapsed a second time.

As we were very short of N.A.B. at this time and the epidemic appeared to be mild we decided not to give the drug on admission, but to wait, as some authorities recommend, until the case relapsed. There were 117 cases in group 2; 75 (64.10%) of them relapsed. As soon as the relapse was detected they were given 0.45 g. of N.A.B. Not only did this save the use of the drug in 35.9% of cases—those that did not relapse—but it demonstrated how effective the N.A.B. treatment had been in group 1, when only 11.34% of cases relapsed.

All the cases in group 1 which relapsed received a further 0.45 g. of N.A.B.; none relapsed a second time. In group 2 only one case relapsed a second time, and was treated with a further 0.45 g. of N.A.B.—thus demonstrating that the drug is more effective when used later in the disease.

Few reactions followed the injections of N.A.B.; sometimes the patient's temperature would be raised for 24 hours. No definite time interval was detected between giving the injection and the crisis.

Another interesting point emerged during the course of treating the two groups: nine patients developed a marked jaundice. Three of these did not receive N.A.B. on admission, as it was thought that it would be dangerous to give arsenic to patients whose liver was already damaged; it was also believed that a dangerous crisis might be provoked. However, two of these three died. The remaining six received N.A.B. on admission and none of them died.

#### Summary

An epidemic of louse-borne relapsing fever, believed to be the first reported in Persia, is described.

A detailed clinical description, demonstrating the mildness of the epidemic and the low death rate, is given.

The effect of treatment with N.A.B. is quantitatively assessed.

We wish to thank the Health Department for co-operation in this report, and in particular Mr. C. Brooking, chief health inspector, for the graph of the typhus epidemic, 1943. This paper is submitted by permission of the chief medical officer, Anglo-Iranian Oil Co., Abadan.

#### REFERENCES

- Adler, S., Theodor, O., and Schieber, H. (1937). *Ann. trop. Med. Parasit.*, **31**, 25.  
 Andreev (1944). *Med. Parasitol.*, Moscow, **13**, 53.  
 Avanesov, G. A. (1938). *Ibid.*, **7**, 88.  
 Charters, A. D. (1945). *E. Afr. med. J.*, **22**, 308.  
 Delpy, L., and Rafyi, A. (1939). *Ann. Parasit. Humaine comparée*, **17**, 45.  
 Grenoilleau, G. (1946). *Bull. Acad. Med.*, **130**, 144.  
 Kassirsky, J. A. (1933). *Arch. Schiffs- u. Tropenhyg.*, **37**, 380.  
 Maruashvili, G. M. (1945). *Med. Parasitol.*, Moscow, **14**, 24.  
 Popow, P. P., and Achundow, I. (1936). *Arch. Schiffs- u. Tropenhyg.*, **40**, 289.  
 Rogers, Sir L., and Megaw, Sir J. W. O. (1944). *Tropical Medicine*, p. 98. London.  
 Sicault, G. (1944). *Bull. Inst. Hyg. Maroc.*, **2**, 5.  
 Stuart, G. (1945). *Epidem. Inform. Bull. UNRRA*, **1**, 453.  
 Wolman, M., Omar, M., and Abu-Taleb, M. (1945). *Lancet*, **2**, 775.  
 Wood, R. C., and Dixon, K. C. (1945). *British Medical Journal*, **2**, 526.