The reactions of the patient's serum and cells during and after the disease are described.

The presence of a heat-stable auto-agglutinin and auto-haemolysin and an auto-agglutininogen is demonstrated.

The presence of an autohaemolysinogen is suggested.

Changes in the granulocytes are reported and their aetiological significance is indicated.

I wish to thank Dr. J. W. Macfarlane for permission to publish this report, and Dr. George Will, resident physician, for his help in the investigation of the case.

BIBLIOGRAPHY

(For a full list of reported cases of haemolytic anaemia the reader is referred to Dameshek and Schwartz's review—*Medicine*, 1940, **19**, 231.)

- Brulé, M. (1909). *Thèse Paris*.
 — (1909). *Sem. méd.*, B. Aires, **29**, 47.
 Chauffard, M. A. (1907). *Ibid.*, **27**, 25.
 — (1912). *Rev. gén. Clin. Thérap.*, **26**, 199.
 — Troisier, J., and Vincent, C. S. (1908). *Sem. méd.*, B. Aires, **28**, 345.
 Dameshek, W., and Schwartz, S. O. (1938). *Amer. J. med. Sci.*, **196**, 769.
 — (1940). *Medicine*, **19**, 231.
 Donath, J., and Landsteiner, K. (1905). *Z. klin. Med.*, **58**, 173.
 Giordano, A. S., and Blum, L. L. (1937). *Amer. J. med. Sci.*, **194**, 311.
 Greenwald, H. M. (1938). *Ibid.*, **196**, 179.
 Hayem, G. (1898). *Presse méd.*, **1**, 121.
 Lederer, M. (1925). *Amer. J. med. Sci.*, **170**, 500.
 Lieberman, L. von, and Fenyvessy, B. von (1911). *Jhrb. Immunforsch.*, **7**, 2.
 Mendell, T. H., Meranze, D. R., and Meranze, T. (1936). *Amer. J. med. Sci.*, **192**, 316.
 Minkowski, O. (1900). *Ver. Kongr. inn. Med.*, **18**, 316.
 Paterson, W. H., and Smith, G. S. (1936). *Lancet*, **2**, 1096.
 Roth, O. (1912). *Dtsch. Arch. klin. Med.*, **106**, 137.
 Troisier, J. (1910). *Thèse Paris*.
 Widall, F., Abrami, P., and Brulé, M. (1907). *Presse méd.*, **15**, 641.

TYPHUS FEVER IN GREAT BRITAIN

BY

ALAN P. AGNEW, M.B., M.R.C.P.Ed.

Physician, E.M.S., Scotland

AND

W. B. KYLES, M.B.

Consulting Clinical Pathologist, E.M.S., Scotland

Typhus fever is rare in this country, and in everyday practice is seldom considered in the differential diagnosis of pyrexia of uncertain origin. This might have unfortunate consequences at the present time when numbers of people are arriving here having travelled under conditions of war from districts where the disease is endemic or epidemic. The following report of a single case is therefore of topical interest and may serve as a useful reminder that typhus fever may make an unexpected appearance.

Case History

The patient, a man aged 24, was one of 19 men admitted to hospital on the evening of Jan. 5, 1944, from sick quarters on board ship. They had embarked on Dec. 20, 1943, from an area in which typhus was prevalent and all had been taken ill on the voyage. "Influenza" had been prevalent, and a number of the men, including the patient, had acute respiratory infections. The only available history of the case was as follows: Dec. 31: complained of headache, cough, and general muscular pains; temperature 102°. Jan. 1: progress satisfactory. Jan. 2: temperature, pulse, and respirations normal. Jan. 3: temperature 99°. Jan. 4: T. 101.2°; P. 80; R. 20. Diagnosis—bronchitis.

On admission the patient looked toxic and complained of severe headache, sore throat, and cough. He had a sharp rigor, and collapsed before being put to bed. On examination he was flushed; there were muco-pus in the nose and throat, definite bronchitis, slight general adenitis, and slight neck rigidity. There were healed scars of desert sores on both hands. No abnormality was found in any of the other systems. Temperature 103°; pulse 84; respirations 22. The subsequent course of events may be briefly summarized:

Jan. 6.—Temperature range, 100.4° to 103.4°; pulse 100; respirations 30. Patient flushed; conjunctivae injected; tongue dry and coated; non-adherent exudate on throat; slight adenitis; bronchitis less marked. Throat swab negative for *C. diphtheriae*, haemolytic streptococci, and Vincent's organisms. Leucocytes 12,800 per c.mm.—neutrophils 62%. No malaria parasites seen in film.

Jan. 7.—T. 102° to 103°; P. 110; R. 30 to 40. Patient drowsy, restless, and irritable; increased neck rigidity; respirations irregular; more intense bronchitis but no definite bronchopneumonia; moderate

albuminuria; hearing impaired; slight injection of both tympanic membranes.

Jan. 8.—T. 101° to 102°; P. 110; R. 40 to 50. General condition deteriorating; meningism; respiration of Cheyne-Stokes type; more definite evidence of bronchopneumonia. Urine: albuminuria, occasional granular casts. Blood: leucocytes 13,000 per c.mm.—neutrophils 90%. Cerebrospinal fluid: clear, pressure 220 mm. H₂O; protein 30 mg. per 100 ml., chlorides 690 mg. per 100 ml., sugar 65 mg. per 100 ml.; no organisms seen. Widal test—compatible with previous T.A.B. inoculation.

Jan. 9.—T. 99.4° to 105°; P. 120; R. 40 to 50. General condition unchanged. A sparse macular rash, comprising some 20 spots in all, on the flanks and anterior aspects of the shoulders was seen for the first time. The macules were 2 to 3 mm. in diameter, dusky red in colour, and did not entirely fade on pressure.

Jan. 10.—T. 101° to 102°; P. 120 to 130; R. 40 to 50. General condition and rash unchanged. More definite evidence of bronchopneumonia. Weil-Felix reaction reported positive.

Jan. 11–13.—T. 99° to 101°; P. 100 to 110; R. 40. Patient much quieter but still very drowsy; sleep disturbed by occupational dreams; appreciable loss of flesh.

Jan. 14–15.—T. 97° to 99°; P. 80 to 90; R. 30 to 40. Progressive improvement.

Jan. 17.—T. normal; P. 80; R. 20.

The subsequent course was uneventful apart from a voracious appetite.

Treatment was symptomatic except for 12 g. of sulphapyridine given between Jan. 7 and 9. Liberal amounts of bland fluids, glucose, and sodium chloride were given throughout the illness. Oxygen and cardiac stimulants were not required.

Weil-Felix Reactions.—Blood sera were examined on three occasions; the following titres were obtained:

Date	Type OX 19	Type OX 2	Type OX K
10/1/44	1 : 4,000	1 : 125	1 : 25
15/1/44	1 : 12,800	1 : 400	1 : 25
21/2/44	1 : 6,400	1 : 400	1 : 25

The maximal titre, 12,800 v. OX 19, thus occurred about the end of the second week of illness, as is usual in epidemic typhus. Five weeks later, when last estimated, this titre was 6,400. No significant reaction was obtained against *B. proteus* OX K. No antityphus vaccine has been given. *B. proteus* suspensions used were supplied by the Standards Laboratory (M.R.C.), Oxford, agglutinability being standard throughout.

Discussion

The incubation period of typhus fever is rarely less than 8 days; it is usually 8 to 13 days, but may be 20 days or even longer (Rogers and Megaw, 1942). Though infection might have occurred on board ship, it probably took place before embarkation on Dec. 20, either from a louse-bite or from infected formites. A third possible source was by droplet infection (Pole and Bensted, 1943). Presumably forms frustes and abortive and ambulant cases occur in typhus as in other fevers.

The rash appears on the fourth or fifth day. It was not seen in this case until Jan. 9, which suggests that the first day of the invasion period was Jan. 4 or 5. By this reckoning the earlier fever may have been due to a prodromal state (Harries and Mitman, 1940) or to "influenza," which, as stated above, was prevalent. On the other hand, the high-titre positive Weil-Felix reaction on Jan. 10 favours an onset as early as Dec. 31.

Diagnosis was rendered difficult by the reported normal temperature on Jan. 2, by the apparent delay in appearance of the rash and its scanty indefinite character, and by the absence of disproportionate tachycardia in the early stages. Other misleading features were the presence of membrane in the throat and the adenopathy. The decisive stages in reaching a correct diagnosis were: first, the recognition of typhus fever as a possible cause of the illness; secondly, the appearance of the rash; and, thirdly, the positive Weil-Felix test. The fact that the rash does not always appear renders the first of these all-important.

Precautionary measures taken in hospital included the shaving of the patient and the disinfection of his clothing and that of the other men from the same ship. Contacts were quarantined, and were inspected for lice on two occasions at an interval of seven days. No lice, bites, or scratches were found on the patient or on any of the contacts. Pathological specimens, especially blood, were carefully handled. In view of the possibility of droplet infection all attendants were masked and gowned. Typhus vaccine was not given to contacts or attendants in view of the time necessary to establish immunity and also because of possible undesirable effects if administered during the incubation period.

None of the other patients developed a positive Weil-Felix reaction. No secondary cases occurred locally or, so far as is known,

elsewhere in the country. This may be regarded as fortunate in view of the wide dispersal of other passengers and the crew of the ship.

Summary

A case of typhus fever occurring in this country is described.

The importance of including typhus fever in the differential diagnosis of pyrexia of uncertain origin is stressed.

We are indebted to the Department of Health for permission to publish this report.

REFERENCES

- Harries, E. H. R., and Mitman, M. (1940). *Clinical Practice in Infectious Diseases*, p. 410, Livingstone, Edinburgh.
 Poole, L. T., and Bensted, H. J. (1943). *Med. Annual*, p. 368, Wright, Bristol.
 Rogers, Sir L., and Megaw, Sir J. W. D. (1942). *Tropical Medicine*, p. 193, Churchill, London.

TETANUS AFTER HEAD INJURY IN AN IMMUNIZED SUBJECT

BY

WALPOLE LEWIN, M.S., F.R.C.S.

Captain, R.A.M.C.

(From a Military Hospital for Head Injuries)

At a time when the results of active immunization against tetanus are coming under review, the following case seems worthy of record. Five days after a penetrating head injury the patient developed tetanus and died, despite the fact that he had received active immunization and the standard 3,000 units of A.T.S. one hour after the accident. The source of the infection and the clinical picture presented, in combination with the results of a severe brain injury and a meningitis, are also of interest.

Case History

A pilot aged 23 was involved in an aeroplane accident on April 10, 1943. He was landing a bomber and crashed into another aeroplane which was on the runway. His head was thrown forwards on to the control panel and he lost consciousness. The aircraft were jammed together but were little damaged; the pilot remained in his seat. He had multiple facial wounds, which were cleansed and sutured at the station, 3,000 units of A.T.S. being given one hour after the accident. Tetanus toxoid had been given on Feb. 16 and Feb. 20, 1940, but none since, so far as could be ascertained from the documents.

On admission, 18 hours after the accident, the patient was severely confused and had a slow bounding pulse of 48 a minute. Numerous small sutured wounds were present on the face, but just below the left eye was a punctured wound 1/4 in. in diameter, and a probe passed in about 1 in. encountered jagged bone edges. There was severe bruising around both eyes and moderate swelling of the face. The left eye was a little proptosed, with subconjunctival haemorrhages and chemosis; there was also a partial third and a complete sixth nerve palsy. The tone of the right arm and leg was slightly increased, and the right plantar response was extensor. There was no neck rigidity, and Kernig's sign was negative.

A radiograph of the skull showed that a large foreign body had entered through the left cheek and was lying intracranially. From its position it appeared that it had passed through the frontal lobe and must be lying very close to, or actually in, the frontal horn of the left ventricle.

Treatment.—Immediate operation was performed by Major P. B. Ascroft under pentothal anaesthesia. The entry wound in the left cheek was enlarged and numerous small bony fragments and wood splinters were removed. The large foreign body was seen at the bottom of the wound, and was easily removed with forceps. It proved to be a rectangular piece of wood 10 by 0.8 by 0.8 cm., painted on three sides. Bleeding ceased spontaneously and the wound was left open, a gauze drain impregnated with sulphamilamide powder being inserted. Culture from the wound grew *Staph. albus* aerobically and anaerobically. Sulphathiazole was given intravenously and later by mouth, a blood concentration of 9 mg. per 100 c.cm. being reached. Three days after operation the temperature rose to 100° F. and the patient developed a little neck rigidity and a positive Kernig sign. Lumbar puncture showed a C.S.F. pressure of 290 mm., with 128,000 red cells and 3,600 white cells (66% polymorphs) per c.mm. The disproportionate number of white cells, with the polymorphonuclear preponderance, indicated a meningitis, although the culture was sterile. The following day the neck rigidity increased and the patient developed attacks of fine tremors in both legs lasting for a few minutes at a time; the C.S.F. now grew *Staph. albus* on culture. Sulphadiazine was substituted for sulphathiazole, as he did not seem to be responding to the latter.

On April 15 his mental condition was a little improved, but the tremors in his legs continued, and now affected his left arm. Since the accident the patient had only been able to open his mouth a little, owing to his facial injuries; but now the nurse noticed that it was becoming more difficult for him to open it to drink. In the evening he had a typical generalized tetanic spasm lasting about a minute and accompanied by marked neck retraction and cyanosis. Following this the tremors in his legs were more pronounced, his jaw remained very stiff, and his neck was thrown right back. The C.S.F. contained 2,400 white cells (60% polymorphs) per c.mm. and was sterile on culture. Tetanus was diagnosed, and 100,000 units of A.T.S. were given intravenously. A small dose of rectal avertin was employed to control the tremors, which were now almost continuous. His condition, however, deteriorated rapidly, the respirations mounting and the temperature rising to 105° F. He became comatose, and as this deepened so the neck rigidity passed off. He died in the early hours of April 16, six days after the accident.

Necropsy.—A well-built young man. Facial wounds over left maxilla, right zygoma, and right side of chin. Bruising of skin from chin to clavicles. Track, containing blood-clot and a few flakes of white paint, leading from wound in left cheek along ventro-lateral borders of maxillary antrum and left orbit, and thence by an opening, 2 by 1 cm., in lesser wing of sphenoid to enter inferior surface of left frontal lobe. Detachment by fracture of left anterior clinoid process. Left optic nerve intact. Left third, fourth, and sixth nerves not demonstrably injured, but lying at margin of perforation at anterior end of cavernous sinus. Cavernous sinus empty. Altered blood in sphenoidal air sinus. Purple gelatinous clot in left posterior ethmoidal air cells and left maxillary antrum. No significant changes in other organs.

Examination of the brain, after fixation, revealed slight purulent exudate in the leptomeninges at the base of the organ. On section the perforation in the left frontal lobe was continuous, with an ill-defined area, measuring 5 by 4 by 4 cm., of haemolytic softening which involved the ependyma of the left frontal horn and extended laterally to the island of Reil. A mass of clot, 2 cm. in diameter, occupied the centre of this area. The ventricular system contained fluid blood. The remainder of the brain was congested.

Microscopical Examination.—The site of laceration in the left frontal lobe showed extensive ill-defined necrosis, with haemorrhage, fibrin filaments, and uneven purulent infiltration extending into the white matter. The adjacent fringes of leptomeninges contained thrombosed vessels and showed early fibroblastic proliferation, but little cellular infiltration. A few Gram-positive and numerous morphologically similar Gram-negative bacilli, interpreted as *Cl. tetani*, were present in the necrotic tissue. Over the right Rolandic area the leptomeninges showed stages in phagocytosis of extravasated red corpuscles by large mononuclear cells, accompanied by a few lymphocytes. Chromatolysis and karyolysis affected some of the pyramidal cells. Similar meningitis, with a moderate amount of purulent exudate, was present over the midbrain and medulla oblongata. No organisms were observed in Weigert-Gram preparations. The aqueduct contained a little pus. The nervous tissue of the brain-stem at these levels was not affected, save for chromatolysis and "ischaemic" degeneration of occasional neurones.

Bacteriology.—Swab from depths of wound track grew *Cl. tetani*, *Staph. albus*, diphtheroids, and *B. subtilis*. Presence of tetanus confirmed by positive virulence test on guinea-pig. *Cl. tetani* also isolated from the left ventricular fluid.

Comment

The head is one of the less common sites for the development of tetanus. In the last war the French incidence was 4.7%, the German 4.2%, and the British 3.3%. In the present war, in the Middle East up to the end of 1942, none of the 18 cases reported by Boyd and MacLennan (1942) followed head wounds, and Eden (1943) and Ascroft (1943) encountered no instance in over 800 head wounds. Radley Smith (1942) reported 6 cases occurring in a London E.M.S. sector in the first two years of war; four of the cases had head wounds in addition to other injuries, but in only one was there a suggestion that the head wound may have been the source of infection, and no wound cultures were mentioned.

Diagnosis.—In the present case the association of the results of a severe brain injury with a meningitis and tetanus provided an interesting problem in differential diagnosis. The fine tremor observed in the early stages of the illness was similar to those seen in some cases of ventriculitis, and may have been connected with the presence of blood in the ventricle, as was found at necropsy. In addition to the major spasm, the diagnosis of tetanus in the presence of meningitis was helped by the increasing jaw stiffness at a time when the swelling of