SEVERE HYPOPLASTIC ANAEMIA IN ASSOCIATION WITH TABES DORSALIS: REPORT OF A CASE IN WHICH RECOVERY FROM THE ANAEMIA FOLLOWED ADMINISTRATION OF PENICILLIN.

ALEXANDER BROWN, M.D., F.R.C.P.Ed., F.R.F.P.S.G.
and L. J. DAVIS, M.D., F.R.C.P., F.R.F.P.S.G.
from the University Department of Medicine, Royal Infirmary, Glasgow.

On the rare occasions when syphilis has caused severe anaemia, widespread visceral or skeletal lesions of the tertiary stage have usually been present. This short paper describes the case of a middle-aged woman who developed a severe hypoplastic anaemia, which was found to be associated with tabes dorsalis. The anaemia proved refractory to various forms of haematinic treatment, and during administration of penicillin progressed to almost complete aplasia as judged by sternal marrow examination. Penicillin was then discontinued and gradually haematological recovery took place.

CASE REPORT.

Mrs. E. T., a variety artiste, aged 48, was admitted to hospital on 5th January, 1948, with a two years' history of progressive dyspnoea on exertion which, six months before admission to hospital, had become so marked that she had been confined to bed. These symptoms had been associated with increasing pallor. On further inquiry it was discovered that for nine years she had suffered from lightning pains typical of tabes dorsalis. She had never received antiluetic treatment, or any therapeutic substance apart from ferrous sulphate.

Clinical examination. She was well-nourished but unduly pale. The tip of the spleen was felt on deep inspiration. Evidence of neurological disturbance comprised Argyll-Robertson pupils, absence of tendon reflexes, defective deep pressure pain sense and vibration sense in the lower limbs. There was no other abnormal clinical finding.

Laboratory investigations. The blood Wassermann reaction was negative but the cerebro-spinal fluid gave a positive Wassermann reaction and a paretic colloidal gold reaction (5555432100). Gastric analysis revealed achlorhydria, but hydrochloric acid was secreted in response to histamine. Plasma proteins and blood urea estimations yielded normal figures. X-ray examination of the skeleton revealed nothing abnormal. No urobilinogen was demonstrated in the urine.

Haematological findings. Blood examination revealed a severe macrocytic anaemia associated with anisocytosis, slight leucopenia, moderate eosinophilia and slight increase in monocytes (R.B.C. 0.83 million/cu.mm.; Hb. 24%, W.B.C. 4,400/cu.mm.; neutrophil polymorphs 54%, eosinophils 12%, basophils 4%, myelocytes 2%, lymphocytes 12%, monocytes 11%, smear cells 5%). There was no increase in reticulocytes (<1%). In smears of bone marrow obtained by sternal puncture the appearance was one of hypoplasia, fat being present in excessive amounts (Fig. 2). Red cell precursors were not numerous, but were essentially normoblastic in type. The most numerous cells were myelocytes, many of which had ill-defined granules.

Treatment and subsequent progress (Fig. 1). During the first month in hospital the patient received a blood transfusion of three pints, and, on essentially empirical grounds, oral and parenteral liver extracts and later folic acid, were given. By the

end of the fourth week the red cell count had fallen by half a million from the post-transfusion level. The red cell count was now 1.49 million per cu.mm. ; and although the patient's general condition was fairly good, it was apparent that erythropoiesis was still depressed.

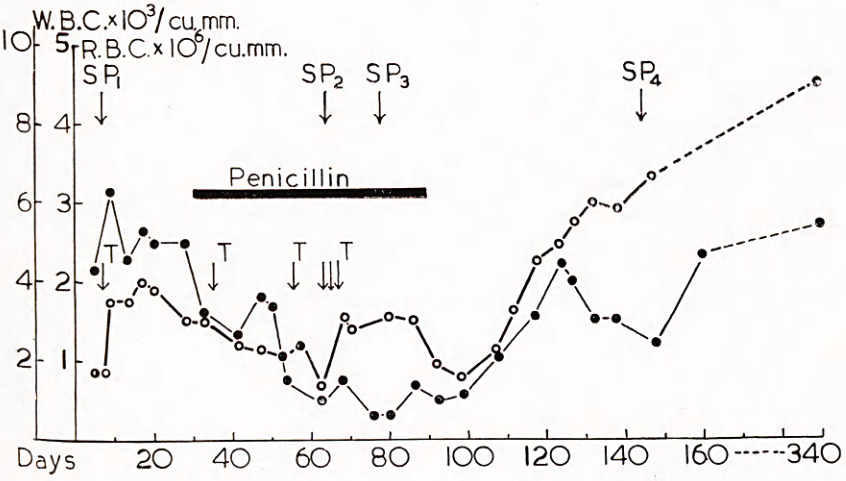

Fig. 1. The haematological findings in relation to treatment.

T = Blood transfusion.
SP_1 = Sternal puncture which provided the bone marrow shown in Fig. 2.
SP_2 = Bone marrow shown in Figs. 3 & 6.
SP_3 = Bone marrow shown in Figs. 4 & 7.
SP_4 = Bone marrow shown in Fig. 5.

In view of the active syphilitic infection it was decided to commence penicillin therapy. This was given from the 31st day in a daily dose of 200,000 units. There was no immediate beneficial effect. Indeed she became more listless and weak. Red cell levels had to be maintained by repeated transfusion, and the number of white cells fell until by the 76th day there were only 600 per cu.mm. most of which were mononuclear (Fig. 1). Bone marrow examination on the 64th and 78th days revealed increasing hypoplasia and then almost complete aplasia respectively (Figs. 3 & 4). By the 89th day there was still no evidence of improvement and it was decided to stop the administration of penicillin. Within the next week there was some improvement in the patient's general condition : she felt stronger and her appetite returned. Haematological improvement was not noted until about a week later and from this time onwards there was gradual improvment in the anaemia. Bone marrow examination on the 146th day revealed no evidence of hypoplasia ; the picture was one of active regeneration (Fig. 5).

Improvement, both clinical and haematological, continued without interruption thereafter, and the patient was discharged from hospital on 29th May, 1948, five months after admission. She has been seen at intervals during the succeeding two years and during this time she has been in good health. Further courses of penicillin treatment were given in December, 1948, and in September, 1949. Her C.S.F. Wassermann reaction remained weakly positive and the colloidal gold reaction continued to be of the paretic type. She still shows Argyll-Robertson pupils and absent knee jerks but she has been without symptoms and has lived an active life. Blood examinations carried out at intervals since the patient was discharged from hospital have not revealed any tendency to haematological relapse.

DISCUSSION.

Syphilis is rarely associated with severe anaemia. In a series of 4,800 patients with syphilis, only 25 had blood haemoglobin concentrations under 55 per cent (Foucar & Stokes, 1921). When anaemia does

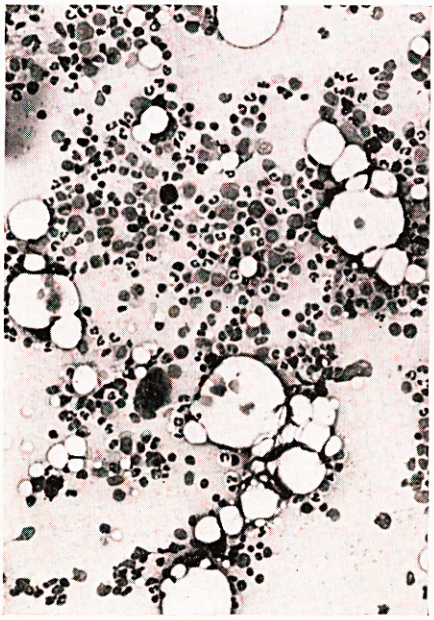

Fig. 2. Bone marrow smear prior to all treatment (10th day). × 300.

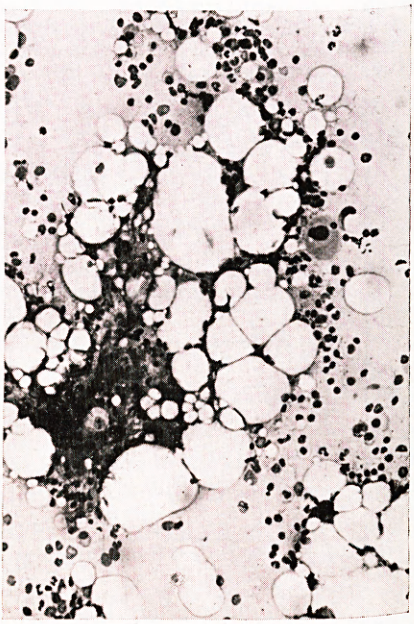

Fig. 3. Bone marrow smear after nearly five weeks' treatment with penicillin (64th day). × 300.

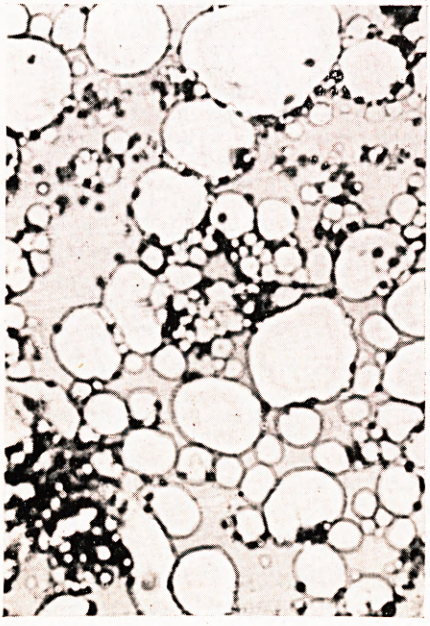

Fig. 4. Bone marrow smear five days before penicilin was discontinued (78th day). × 300.

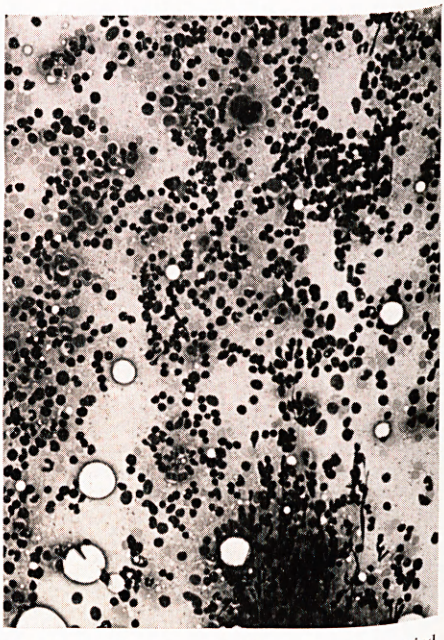

Fig. 5. Bone marrow smear in the recovery period (145th day). × 300.

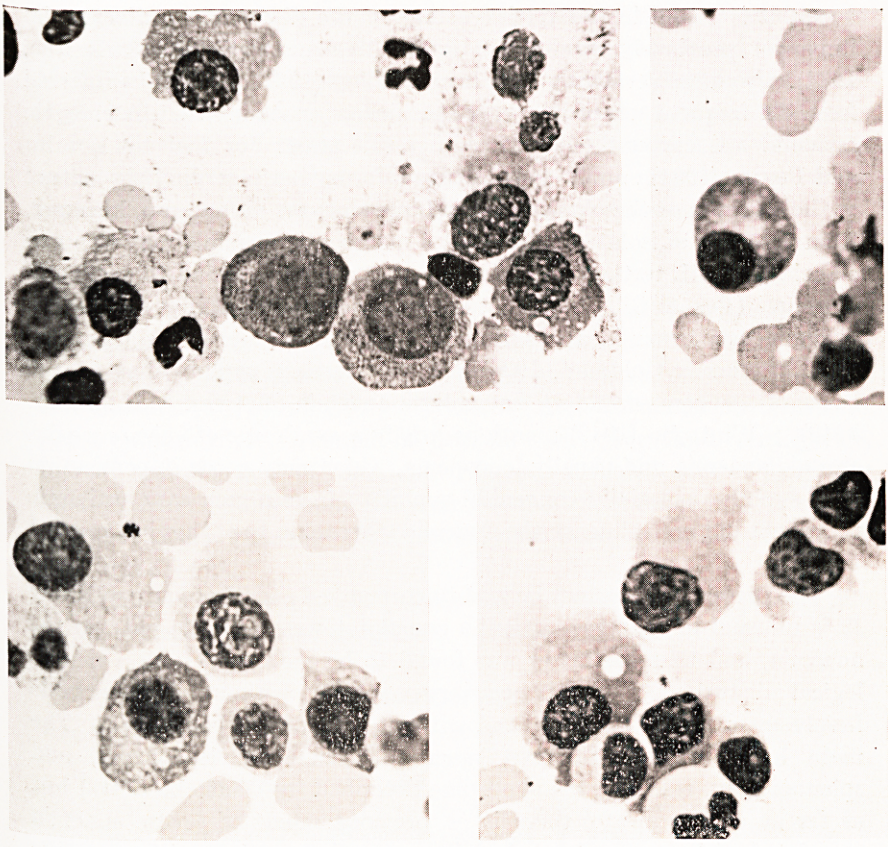

Fig. 6. Examples of plasma cells seen in the second marrow (Fig. 3). × 800.

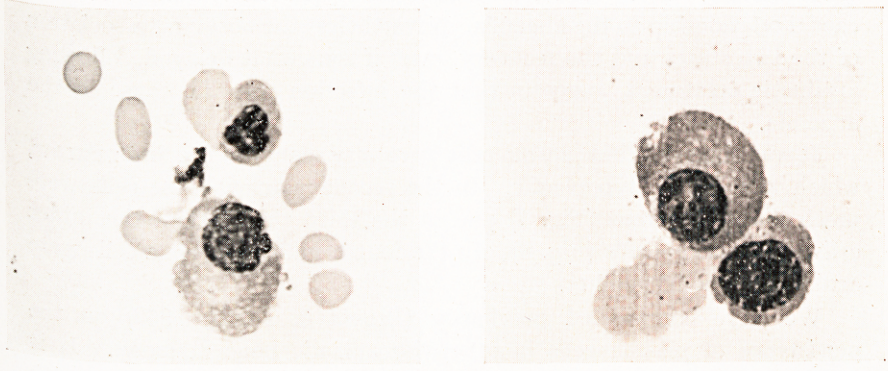

Fig. 7. Plasma cells in the markedly hypoplastic marrow of Fig. 4. × 800.

occur, it is found in the tertiary stage of the disease, in patients who have not previously received antiluetic treatment (Rosahn & Pearce, 1934). From the review by Foucar and Stokes (1921) it might be inferred from the frequent use of the term ' pernicious anaemia ' that macrocytic anaemia was encountered, but neither this paper nor that by Rosahn and Pearce (1934) supply any definite information regarding the nature of the anaemia or the changes in the bone marrow. It appears, however, from accounts of isolated cases, that a macrocytic anaemia may occur in association with tertiary syphilis, and that it may respond to antiluetic measures (Box & Gill, 1936). It is also evident that severe macrocytic anaemia may occur in association with extensive gummatous lesions of bone (Tauber & Goldman, 1935) and that tertiary syphilis may be the cause of a severe secondary haemolytic anaemia (Gatman & Hamilton, 1949). Wintrobe (1942) mentions briefly a syndrome of splenomegaly, chronic anaemia and usually leucopenia, which may occur in connection with syphilis, especially congenital syphilis. In one such case antiluetic treatment did not influence the anaemia whereas in the other it appeared to do so.

The present case cannot be said to correspond exactly to any of these. It is unusual in that the patient's complaint was referable only to the anaemia, and that the latter was found to be associated with a neurological disturbance of late tertiary syphilis, without demonstrable involvement of the skeleton, and without evidence of haemolysis. The main haematological features, macrocytic anaemia, leucopenia, and splenomegaly, resemble the syndrome described by Wintrobe (1942) but as far as we are aware, there is no previous report of severe anaemia associated with marrow hypoplasia occurring in a patient with an active luetic infection.

The mechanism of production of the anaemia in this patient is not quite certain. It is conceivable that the syphilitic infection bore no causal relationship to the anaemia. Nevertheless the observed association of the two states and the recovery, even if somewhat delayed, following antiluetic treatment, suggests that the infection was the cause of the anaemia.

It was observed that plasma cells were very scanty in the first marrow, which was mildly hypoplastic. In the second marrow these cells were much more numerous (Fig. 7) and in the third the most of the intact cells were plasma cells (Fig. 8). In the fourth marrow plasma cells were again very few in number.

We have commented previously (Brown & Davis, 1950) on the persistence of plasma cells in otherwise aplastic bone marrows. It is difficult to assess the apparent increase in these cells in marrows with varying degrees of cellularity, especially in small specimens obtained by aspiration. The impression has been gained, however, that an absolute

increase in plasma cells may occur in hypoplastic states, in addition to the many conditions in which such an increase has been found (Fadem & McBirnie, 1950). The significance of the plasma cells remains to be elucidated. They seem to be unusually resistant to toxic substances which adversely affect the other marrow cells (Brown & Davis, 1950), and occasionally appearances suggest that they may be capable of participating in the regenerative phase if recovery occurs.

SUMMARY.

A case is described in which severe macrocytic anaemia occurred in association with tabes dorsalis. The bone marrow obtained by sternal puncture was normoblastic in type, but the picture was one of hypoplasia. The anaemia proved refractory to various forms of haematinic treatment given empyrically. A course of penicillin was given and, during this, further examination of the bone marrow revealed almost complete aplasia. After completion of this course of treatment progressive haematological recovery occurred. This recovery has been maintained during the past three years.

Attention is drawn to the prominence and persistence of plasma cells in the otherwise almost completely aplastic marrow.

REFERENCES.

Box, C. R. & Gill, A. M. (1936). *Lancet.* **1** : 24
Brown, A. & Davis, L. J. (1950). *Glasg. med. J.* **31** : 93
Fadem, R. S. & McBirnie, J. E. (1950). *Blood.* **5** : 191
Foucar, H. O. & Stokes, J. H. (1921). *Amer. J. med. Sci.* **162** : 633
Gatman, M. & Hamilton, L. (1949). *J. clin. Path.* **2** : 225
Rosahn, P. D. & Pearce, L. (1934). *Amer. J. med. Sci.* **187** : 88
Tauber, E. B. & Goldman, L. (1935). *Amer. J. Syph.* **19** : 339
Wintrobe, M. M. (1942). *Clinical Hematology.* London : Kimpton