histology, and, in addition, the viruses of some members of this group have antigens in common. Epidemics caused by this group of virus agents have occurred in hot weather, have sometimes chiefly affected young children, and have been associated with a clinical picture quite similar to our cases. In this group of encephalitis the histological lesions are often widely scattered throughout the central nervous system. Although the brain stem is perhaps the favourite location, the cerebral hemispheres, cerebellum, and spinal cord may all be involved; the white matter as well as the grey matter is affected; and there is more meningeal reaction than in encephalitis lethargica. In Japanese B encephalitis destruction of Purkinje cells in the cerebellum is a striking feature. In view of the restriction of the lesions to the grey matter in our two fatal cases, and of the absence of involvement of the cerebral cortex or cerebellum, it is impossible to regard the distribution of the lesions as at all characteristic of this group of infections; nevertheless, on histological grounds it is not impossible that our cases might belong to that group. The character of the lesions also is consistent with such a diagnosis, but again there is nothing distinctive about it. The Purkinje cells in our cases did not appear to be reduced in number, and although some of them showed apparent degenerative changes, similar changes can be seen in control sections of the cerebellum of children who did not die of encephalitis.

In this group of encephalitis the virus can often be isolated with relative ease by intracerebral inoculation of mice; the negative findings in this respect therefore are worth noting.

Summary and Conclusions

An outbreak of encephalitis is described; eight children were affected, with two deaths.

Clinically the pyramidal and extrapyramidal motor systems were predominantly affected, and lower motor neurone lesions (with one minor exception) did not occur.

The histology of the brains of the two fatal cases was consistent with poliomyelitis; on the other hand, the lesions in the spinal cords were not nearly so prominent as is the rule in poliomyelitis.

Poliomyelitis virus was recovered from the stools of one case, and from a pool of the faeces of three others.

In comparing the clinical, epidemiological, viral, and neurohistological findings in our cases with those of other known encephalitis, we conclude that this outbreak was either one of poliomyelitis with several most unusual features or was an example of some hitherto undescribed type of encephalitis. We slightly favour the former view.

Our thanks are due to Dr. F. O. MacCallum, Director of the Virus Research Laboratory of the Public Health Laboratory Service, and to Dr. N. B. Finter, of the Department of Pathology, Cambridge, for the virus studies; and to Mr. S. W. Patman for the photomicrographs.

REFERENCES

- Bodian, D. (1949). *Amer. J. Med.*, 6, 563.
 Buzzard, E. F., and Greenfield, J. G. (1919). *Brain*, 42, 305.
 Jennings, G. H., Hamilton-Paterson, J. L., and MacCallum, F. O. (1949). *British Medical Journal*, 2, 210.
 Kelleher, W. H., Bratton, A. B., and MacCallum, F. O. (1949). *Ibid.*, 2, 213.
 MacNalty, A. S. (1921). *Brit. J. exp. Path.*, 2, 141.
 Marinisco, G. (1918). *Rep. loc. Govt Bd publ. Hlth med. Subj.* (New Series). London. No. 121, p. 47.
 Medin, O. (1898). *Arch. Méd. Enf.*, 1, 257.
 Peabody, F. W., Draper, G., and Dochez, A. R. (1912). *Monogr. Rockefeller Inst. med. Res.*, No. 4.
 Perdrau, J. R. (1922). *Ministry of Health Rep. publ. Hlth med. Subj.* No. 11, p. 143. London.
 Strümpell, A. (1885). *Jb. Kinderheilk.*, 22, 173.
 Watson, G. A. (1920). *J. Neurol. Psychopath.*, 1, 34.
 Wyllie, W. G. (1948). *Proc. roy. Soc. Med.*, 41, 459.

HAEMOLYTIC ANAEMIA AND RETICULOSES

BY

D. R. C. WILLCOX, M.B., B.S.

(From the Department of Clinical Pathology, Guy's Hospital London)

[WITH SPECIAL PLATE]

Haemolytic anaemia associated with various neoplastic processes is a recognized but not a common clinical entity (Davidson, 1932; Waugh, 1936; Singer, 1940; Stats, Rosenthal, and Wasserman, 1947). In many of these cases the haemolytic picture is merely incidental to the malignant process. Lucey (1939) and Pollard (1948) have recorded single cases in which haemolytic anaemia presented, apparently of idiopathic type, and the neoplastic association was found only at necropsy. Both these were cases of carcinomatosis.

Four cases of haemolytic anaemia are recorded here. In two of them clinical evidence of malignant disease (lymphosarcoma and reticulum-cell sarcoma) first appeared several months after the onset of haemolytic anaemia. In another case reticulo-endothelial changes were found only at post-mortem examination. These cases appeared to illustrate some points of interest in the clinico-pathological picture, and also in the possible mechanism of production of this type of anaemia.

Case 1

An unmarried woman aged 40 had lived a healthy and active life. Menstruation had ceased 18 months previously. She complained of lassitude for five weeks, and of dyspnoea and palpitations for two weeks. The severity of her symptoms had increased rapidly up to the time of her admission to hospital.

On admission on June 14, 1949, she was slightly dyspnoeic at rest. The skin and mucous membranes were very pale and slightly icteric, as were the sclerae. The apex beat was just beyond the mid-clavicular line, and a blowing systolic murmur was heard in this area. Her temperature was 99.8° F. (37.7° C.), pulse 100, and respirations 22. There were no other abnormalities on physical examination. The spleen was not palpable.

Investigations.—Urine: excess of urobilin, no bilirubin, no haemoglobin. Blood: haemoglobin, 33% (5.15 g.); red cells, 1,200,000; colour index, 1.3; M.C.D., 8 μ ; P.C.V., 18%; M.C.V., 150 μ^2 ; M.C.H.C., 29%; M.C.A.T., 3.3 μ ; reticulocytes, 24%; late normoblasts 3 per 100 white cells: the red cells showed anisocytosis and slight anisochromia with numerous polychromatic cells and macrocytes; white cells, 9,800 (polymorphs 70%, eosinophils 1%, basophils 1%, lymphocytes 21%, monocytes 1%, myelocytes 4%, metamyelocytes 2%); the polymorphs showed a left shift. The red-cell fragility was slightly increased: haemolysis started at 0.55% saline, and was complete in 0.30% saline. The direct Coombs test was positive. Chemical: serum bilirubin, 2.25 mg. per 100 ml.; van den Bergh direct test, delayed response; empirical liver tests (thymol turbidity and flocculation and colloidal gold) were negative; test meal, histamine-fast achlorhydria.

A diagnosis of acute haemolytic anaemia of unknown cause was made. The patient was transfused on three occasions without incident. A course of penicillin was given to combat any possible infective cause of the haemolysis. She continued pyrexial and jaundiced for some time, but was sufficiently improved by August 2 to be discharged, her haemoglobin then being 13.26 g. per 100 ml.

When seen at the out-patient department on September 28 and October 8 and 26 her haemoglobin was falling. In

addition palpable left axillary lymph nodes were noted, and an ill-defined mass was felt in the abdomen. She was now found to be rhesus-negative, and to have produced low-titre antibodies, presumably from her earlier transfusions. The direct Coombs test was still positive, and this could not be attributed to the effects of transfusion more than three months previously.

She was readmitted on November 7. The blood, no longer macrocytic, showed: haemoglobin, 8.58 g.; red cells, 3,000,000; reticulocytes, 5%. The urine contained an excess of urobilin. Further investigations showed no occult blood in the stools, normal radiographic appearances following barium meal and enema, and a normal intravenous pyelogram. A probable diagnosis of a malignant mass in the mesentery was made, and laparotomy was performed on December 19. The mass lay in the mesentery; it consisted of matted glands, and other retroperitoneal lymph nodes were also enlarged. A biopsy was taken and the abdomen closed. In spite of transfusions, now with rhesus-negative genotyped blood, the haemolytic process increased rapidly and her general condition deteriorated. She died on January 3, 1950.

Section of the biopsy material showed lymph-node tissue with severe reticular hyperplasia suggestive of reticulum-cell sarcoma.

Post-mortem Findings.—The main finding was enlargement of all the abdominal lymph nodes, a number of which were matted to form a definite mass in the mesentery. The nodes were white and homogeneous on section. Similar white areas were scattered over the lower part of the ileum. The liver was pale and enlarged. The spleen was enlarged but rotated and fixed by adhesions above the costal margin. Histologically the lymph nodes showed complete loss of normal pattern, with much lymphoid and reticulum-cell hyperplasia and occasional giant cells. Numerous mitotic figures were seen. There was no fibroblastic activity or erythrophagocytosis. The spleen was grossly congested and the widely spaced cellular elements appeared normal. The liver was infiltrated with lymphoid and reticulum cells around the portal tracts and in two diffuse areas. The picture was that of reticulum-cell sarcoma.

Comment.—This case shows a typical acute haemolytic anaemia preceding clinically the development of signs of a reticulum-cell sarcoma.

Case 2

A widow aged 68 had suffered from anaemia since 1930. Treatment with both liver and iron had had little effect, but later myxoedema was diagnosed, and she had received thyroid extract, 1 gr. (65 mg.) daily, for several years.

She was admitted on February 23, 1949, for anaemia and recent precordial pain, following a report of abnormal white cells seen during a routine count. She was considered still to be myxoedematous, and the dose of thyroid was increased. A blood picture showed: haemoglobin, 68% (10.61 g.); red cells, 3,300,000; M.C.D., 7.5 μ ; and, later, haemoglobin 68% with 1% reticulocytes. The film appearances showed definite spherocytosis and the red-cell fragility was greatly increased, haemolysis starting in 0.65% saline and being complete in 0.35%. The Coombs test was negative, and the sternal marrow normal. She improved with transfusion and increased thyroid dosage, and was discharged on March 30. The B.M.R. had risen from -20 to -4.

Subsequently she sought attention elsewhere, and was found to have an abdominal tumour (Hb, 7.7 g.; red cells, 2,700,000). A laparotomy was performed and a mass involving the ileo-caecal junction and the glands at this site was resected. This mass consisted of the terminal 4 in. (10 cm.) of the ileum and a portion of caecum. The mucosa on either side of the ileo-caecal valve showed nodular thickening up to 1 cm. in depth in the ileum and 2 cm. in the caecum. The cut surface was white and neoplastic. Two enlarged lymph nodes were found, the larger being 1 cm. in diameter.

On section the nodules in the caecum and ileum consisted of lymphoid tissue lying in the submucosa and infiltrating the muscular layers. The lymph nodes showed loss of normal pattern. There was a diffuse and uniform lymphoid hyperplasia. Most of the cells were small with darkly staining nuclei. There was no fibrosis or any evidence of erythrophagocytosis. The picture was that of lymphosarcoma.

Post-operative progress was satisfactory. The patient was well six months later. The anaemia had improved, but a mild degree was still present: Hb, 10.8 g. per 100 ml.; red cells, 3,800,000. Red-cell fragility: haemolysis of the patient's cells started in 0.52% saline and was complete in 0.44%; haemolysis of normal control cells started in 0.44% saline and was complete in 0.36%. The Coombs test was again negative. Re-suspension of the patient's washed cells with bovine albumin produced no agglutination.

Comment.—The anaemia in this case, although mild and chronic, was of classical spherocytic haemolytic type. The associated lesion was a mass showing the characteristic features of lymphosarcoma. The question arises, particularly in view of the negative serological findings, whether this is a chance association, and the patient suffers from congenital (familial) haemolytic anaemia. This cannot be definitely excluded. Such a diagnosis would, however, introduce a third condition in this case. In addition there is no family history, although no relatives were available for investigation. The patient had been observed haematologically for many years without spherocytosis or other evidence of haemolysis being noted until a few months before the malignant process became apparent. Her age was 68, and she gave no history of jaundice or of marked periodicity in her anaemia. It therefore seems reasonable to suppose that the haemolytic process was of recent onset and related to the development of the lymphosarcoma.

Case 3

A man aged 28 had been fit until 1948. He was married and had served in the Navy during the recent war. In 1948 he complained of an enlarged gland in the left posterior triangle. A biopsy was taken and a diagnosis of Hodgkin's disease was made. He received a course of deep x-ray therapy to the neck (four exposures). The gland subsided and he returned to work. In June, 1950, he started to complain of lassitude and breathlessness, and he noticed an enlarged gland in the left axilla. He was admitted to hospital on August 23. Pallor, dyspnoea, and slight jaundice were noted. There were enlarged, firm, and discrete glands in the left axilla.

Investigations.—The van den Bergh direct test gave a biphasic response. Serum bilirubin was 2.2 mg. per 100 ml. Blood: haemoglobin, 4.4 g. per 100 ml.; red cells, 1,120,000; white cells, 15,700 (polymorphs 72%, stab 5%, lymphocytes 13%, monocytes 5%, metamyelocytes 5%); there was marked polychromasia and macrocytosis with moderate numbers of late normoblasts; reticulocytes, 24.8%; red-cell fragility normal; Group O, Rh-positive; Coombs test negative. Urine showed an excess of urobilin. Wassermann reaction and Kahn test negative. X-ray film of chest and long bones normal. Blood culture sterile. Sternal marrow cellular and normoblastic.

The patient was treated with transfusions, and a biopsy of an axillary lymph node was taken. On September 26 he was transferred to Guy's Hospital. On examination there was pallor but no jaundice. The tip of the spleen was just palpable. Enlarged glands were present in the left posterior triangle and there was a recent biopsy scar in the left axilla. Haemoglobin at this time was 8.7 g. per 100 ml. The film showed much anisocytosis and polychromasia but little poikilocytosis. The presence of small dark-staining cells was also noticed. The appearances were suggestive of spherocytosis. Red-cell fragility, however, was normal. P.C.V., 28%; M.C.V., 112 μ^3 ; M.C.T., 2.4 μ ; thickness-diameter ratio 3.1:1. The direct Coombs test was now

strongly positive. The biopsy showed Hodgkin's disease of typical morphology.

Further transfusions were given, the blood being cross-matched in saline and albumin. There was considerable general improvement, and the patient was discharged on October 21 free from jaundice but still anaemic.

Comment.—This case illustrates the rather more common association of a haemolytic anaemia with Hodgkin's disease. The development of anaemia occurred during the first relapse two years after the initial attack and deep x-ray therapy. It is of interest that the haemolytic picture was fully developed before the Coombs test became positive. There is no reason to suppose that this finding was in any way related to the earlier transfusions, and it can be accepted as evidence of the activity of an immune haemolysin.

Case 4

An unmarried woman aged 66 had been in good health until one year previous to admission. She then noticed a tendency to bruise easily, and transient purpuric eruptions appeared. In April, 1949, she had acute pain in the left hypochondrium lasting two to three days. This recurred six weeks later. Some pain had persisted during the intervening seven months, and there was complaint of increasing lassitude.

She was admitted to hospital on February 3, 1950. The only abnormalities on physical examination were pallor and enlargement of the spleen, which was tender, the lower border being palpable below the umbilicus.

Investigation showed anaemia; haemoglobin, 32% (4.99 g.); red cells, 2,400,000. The film appearances did not suggest spherocytosis, but there was pronounced polychromasia with many stippled cells, reticulocytes 15%, and many late normoblasts. The red-cell fragility was slightly increased: haemolysis started at 0.55% saline and was complete at 0.30%. The direct Coombs test was positive.

The picture was typical of an acute haemolytic anaemia. As the course appeared to be progressive, and the cause was uncertain, the only hopeful line of treatment seemed to be splenectomy. This was performed on March 21. The operation was without unusual incident. After twenty-four hours, however, the anaemia increased rapidly and death occurred on March 24.

Post-mortem Findings.—Significant changes were confined to the reticulo-endothelial system. The liver was large, soft, pale, and without evidence of fibrosis. All the lymph nodes showed a slight fleshy enlargement. Microscopically the spleen (removed at operation) was congested but very cellular. Lymph follicles were present, showing central hyperplasia. The pulp was filled by histiocytic proliferation, many of these cells showing erythrophagocytic activity. In addition there were fairly numerous giant cells with bizarre and contorted nuclei (Figs. 1 and 2, Special Plate). Stained for iron, the sections showed a marked excess, both intracellular and extracellular, but none was present in the giant cells. The lymph nodes were very similar on section; and the same unusual type of giant cell was found in relation to the sinusoids in the liver. The marrow contained many histiocytes and giant cells, and was apparently devoid of erythropoietic tissue.

Comment.—This was a characteristic acute haemolytic anaemia associated with a widespread lymphadenopathy revealed only at necropsy. The histology was not characteristic of any of the commoner reticuloses. It was therefore considered whether the histological picture represented reactive changes in the reticulo-endothelial system such as may occur with prolonged haemolysis (Gittins, 1933; Davidson and Fullerton, 1938; Israëls and Wilkinson, 1938; Dyke and Young, 1938). Dameshek and Schwartz (1940), reviewing this subject, stated that of 29 cases of idiopathic acute haemolytic anaemia 12 showed histiocytic proliferation, often with giant-cell formation and erythrophagocytosis and ectopic marrow activity. The histological picture in Case 4 is in keeping with these

descriptions, although no foci of myeloid metaplasia were seen. Nevertheless the bizarre nature of the giant cells, and the fact that they themselves showed no phagocytic activity or intracellular iron deposition, suggested disordered growth of neoplastic type. Considered, therefore, as a primary reticulosis, the picture closely resembles that of histiocytic medullary reticulosis (Scott and Robb-Smith, 1939). There are some points of difference. First, in life there was no clinical enlargement of the lymphatic nodes in this case, and even at necropsy the enlargement was not remarkable. Secondly, the clinical course of one year is longer than that recorded in histiocytic medullary reticulosis, the longest in the series quoted above being 32 weeks. Nevertheless, it is considered that the lymphadenopathy here is a primary reticulosis and falls into the group of histiocytic medullary reticulosis.

Discussion

The Type of Anaemia

Loutit and Mollison (1946), writing of the distinction between the congenital and acquired forms of haemolytic anaemia, list the known general causes of haemolytic anaemia as: (i) congenital defects of the erythron, (ii) blood-stream infections, (iii) exogenous toxins, and (iv) endogenous antibodies leading to red-cell destruction. Dameshek and his colleagues speak of idiopathic and symptomatic acute haemolytic anaemias which clearly belong to the fourth group above. In many such symptomatic cases the basic pathology is malignant disease.

Essential features of this type of anaemia are spherocytosis and increased fragility of the red cells. These two features are directly related, and have been shown to result from the exposure of normal cells to immune haemolytic serum (Dameshek and Miller, 1943). An inactive or aplastic state of the marrow heralds haemolytic crises (Owren, 1948; Dameshek and Bloom, 1948). In Case 4, in which the terminal stage of the disease was rapid and progressive, the marrow was aplastic at necropsy. Usually a normoblastic or macronormoblastic response follows (Cases 1 and 2). Thus when the patient is first seen the peripheral blood picture is often regenerative (Cases 1, 3, and 4). At such times, owing to the large number of young red cells in circulation, the fragility is often either slightly increased or within normal limits, and the spherocytic appearances may be masked. Evidence of the action of an immune-body haemolysin is usually found in these cases. A positive direct Coombs test is so interpreted. Recent figures of the incidence of such positive tests, and of haemolysin tests on the patient's serum using trypsinized red cells, showed 83% of acquired haemolytic anaemias, 32% of hereditary types (familial acholuric jaundice), and 27% of thrombocytopenic purpuras (Wright *et al.*, 1951). These tests are therefore of limited diagnostic value, although their development has led to important new views of pathogenesis.

Haemolytic Mechanisms in Malignant Disease

Three mechanisms capable of producing haemolytic anaemia seem possible in malignant disease of the types recorded here. First, infiltration of the bone marrow may cause some maturation abnormality, resulting in increased fragility. Secondly, the changes may be due to a circulating haemolysin. Thirdly, red-cell destruction can result from abnormal erythrophagocytosis.

The early appearance of haemolytic signs in two of the present cases (Cases 1 and 2) suggest that extensive marrow involvement is an unlikely cause; and this is supported by the case of Singer and Dameshek (1941) in which haemolytic anaemia was associated with a localized ovarian tumour and complete recovery followed removal of the tumour. Furthermore, the process by which marrow disturbance could result in spherocytosis is difficult to understand.

The frequency of positive haemolysin tests has already been referred to. The interpretation of these tests is somewhat speculative, but, taking them to indicate the sensitiza-

tion of red cells as a result of adsorption of antibody, it may be argued that the antibody in these cases is some product of the malignant tissue, or of reaction to this tissue.

Alternatively, the abnormal tissues may destroy excessive numbers of red cells, and thus provoke haemolytic antibody production. Whether this is the first step may depend on the type of reticulosis. Erythrophagocytosis is a usual and pronounced feature of histiocytic medullary reticulosis and an occasional finding in Hodgkin's disease; it occurs rarely if ever in significant degree in lymphosarcoma, while in carcinomatosis the abnormal cells have no phagocytic ability. In the last-named types, therefore, some factor other than phagocytosis must initiate the haemolytic process. The early appearance of haemolytic signs is also more readily understood on the basis of an antibody mechanism.

Summary

Four cases of haemolytic anaemia are described. They were associated with different types of reticulosis.

The type of anaemia and possible mechanisms of haemolysis are discussed.

I wish to thank the physicians of Guy's Hospital, under whom these patients were admitted, for the use of the case histories. Mr. E. S. Bolton, of Yeovil, and Dr. A. M. Thomas, of Taunton, gave generous help in the follow-up of Case 2. Dr. K. S. Rodan, of Shoreham-by-Sea, kindly supplied a section of the biopsy from Case 3. I am greatly indebted to Dr. C. W. Shuttleworth for the photomicrographs.

REFERENCES

- Dameshek, W., and Bloom, M. L. (1948). *Blood*, 3, 1381.
 — and Miller, E. B. (1943). *Arch. intern. Med.*, 72, 1.
 — and Schwartz, S. O. (1940). *Medicine*, 19, 231.
 Davidson, L. S. P. (1932). *Quart. J. Med.*, n.s. 1, 543.
 — and Fullerton, H. W. (1938). *Ibid.*, n.s. 7, 43 (Case 9).
 Dyke, S. C., and Young, F. (1938). *Lancet*, 2, 817.
 Gittins, R. (1933). *Arch. Dis. Childh.*, 8, 367.
 Israël, M. C. G., and Wilkinson, J. F. (1938). *Quart. J. Med.*, n.s. 7, 137.
 Loutit, J. F., and Mollison, P. L. (1946). *J. Path. Bact.*, 58, 711.
 Lucey, H. C. (1939). *Lancet*, 2, 76.
 Owren, P. A. (1948). *Blood*, 3, 231.
 Pollard, H. M. (1948). *Gastroenterology*, 10, 138.
 Scott, R. B., and Robb-Smith, A. H. T. (1939). *Lancet*, 2, 194.
 Singer, K. (1940). *Amer. J. med. Sci.*, 199, 466.
 — and Dameshek, W. (1941). *Ann. Intern. Med.*, 15, 544.
 Stats, D., Rosenthal, N., and Wasserman, L. R. (1947). *Amer. J. clin. Path.*, 17, 585.
 Waugh, T. R. (1936). *Amer. J. med. Sci.*, 191, 160.
 Wright, C. S., Dodd, M. C., Bouroncle, B. A., Doan, C. A., and Zollinger, R. M. (1951). *J. Lab. clin. Med.*, 37, 165.

On June 19 Tiverton and District Hospital celebrated its centenary. It was first opened as a dispensary for out-patients and intended for the relief of the sick poor. In 1865 additional wards were built and the whole converted into an infirmary for accident cases. The infirmary received its first in-patient in 1868. A children's ward of four cots, an isolation-room, and additional rooms for out-patients and nursing staff were added in May, 1892. In commemoration of Queen Victoria's diamond jubilee £1,700 was collected and spent on pay-wards for private patients and a new operating-theatre. Further gifts of land and money made it possible for more extensions and improvements. In 1932 Sir John Amory presented the hospital with a portion of the site, until then occupied by brewery premises. These were demolished and an extension built at a cost of £6,500, comprising a new kitchen, staff quarters, and other improvements. This was completed and brought into use in 1933. Finally, in 1947 the remainder of the old brewery premises was purchased and the accommodation for nursing staff enlarged. When the National Health Service started the hospital was placed under the authority of the Exeter and Mid-Devon Hospital Management Committee. It has 50 beds, of which four are for private or semi-private patients, and also a nursery with 11 cots. Since its foundation the work of the hospital has increased enormously. During the first 16 years of its existence 7,090 out-patients were treated, while during the year 1951 alone 5,595 out-patients were treated, involving a total of 14,847 attendances. There were also 1,703 in-patients admitted during the year, while the maternity department dealt with 241 births.

UNUSUAL FEATURES IN A FATAL CASE OF INFECTIOUS MONONUCLEOSIS

BY

STANLEY MARSHALL, M.D.

Consultant Pathologist, Rush Green Hospital, Romford

AND

KEITH S. MILLINGEN, M.B., B.S., M.R.C.P.
M.R.C.P.Ed.

Senior Medical Registrar, Rush Green Hospital, Romford

[WITH SPECIAL PLATE]

Infectious mononucleosis is generally recognized to be an acute infectious disease characterized by enlargement of the lymphatic glands, changes in the blood cells, especially mononucleosis, and a uniformly favourable course (Tidy, 1945). Fatalities from the disease have been rare. Bernstein (1940), in a comprehensive paper, stated that no one has ever died of uncomplicated infectious mononucleosis, and maintained that most of the fatal cases that have been reported were probably not examples of infectious mononucleosis at all, but rather of generalized sepsis with general gland enlargement. Of the fatalities dealt with in his survey some occurred from associated pulmonary disease (bronchopneumonia and empyema) and one from asphyxia following a ruptured retropharyngeal abscess. In another case a "delicate child" died while convalescing from scarlet fever (no further details are given).

Lassen and Thomsen (1940) recorded a mortality of about 1% in 500 cases admitted to the Blegdam Hospital. They reported two fatal cases due to degenerative processes in the central nervous system, localized apparently selectively to the respiratory centre and thus producing a central respiratory failure. Ziegler (1944) and Smith and Custer (1946) recorded fatal cases due to rupture of the spleen; the latter authors also reported deaths due to nasopharyngeal haemorrhage and laryngeal oedema (Custer and Smith, 1948). Two fatal cases presented as the Guillain-Barré syndrome (Ricker, Blumberg, Peters, and Wideman, 1947). Jersild (1942) performed a necropsy on a patient who died of myocarditis attributed to infectious mononucleosis. So far as we know there have been no reported fatalities from infectious mononucleosis which have been associated with severe jaundice and renal failure.

That liver-cell damage may be a cause of clinical jaundice in infectious mononucleosis was first demonstrated in 1942, when a liver punch biopsy showed focal acute hepatitis, and it was further observed that there was a rough correlation between the severity of the disease and the degree of hepatic impairment (Kilham and Steigman, 1942). However, as early as 1928 it was realized that liver changes, apart from those consequent upon obstruction from enlarged glands at the porta hepatis, occurred in glandular fever. It is now thought that some hepatocellular damage occurs in all cases of infectious mononucleosis, including those which exhibit no overt jaundice. Cohn and Lidman (1946) have described 15 cases without jaundice but all showing impairment of liver function as demonstrated by more than one chemical test. Hall (personal communication), in Liverpool, followed 12 cases with liver biopsies, but actual

A. M. BARRETT, D. GAIRDNER, AND A. M. McFARLAN: ENCEPHALITIS POSSIBLY DUE TO POLIOMYELITIS VIRUS

FIG. 1

FIG. 2

FIG. 3

FIG. 1.—Case 1. Most affected part of spinal cord (cervical). Part of an anterior horn shown at top right. Neurones relatively well preserved; very little cellular reaction. Blood vessels at bottom left surrounded by wide but empty Virchow-Robin spaces. (Ehrlich's H. and E. $\times 65$.) FIG. 2.—Case 1. High-power view Fig. 1. Slight cellular infiltration in anterior horn, with well-preserved neurones. (Ehrlich's H. and E. $\times 640$.) FIG. 3.—Case 1. High-power view Fig. 1. Many neurones shrunk and deep-staining; little cellular infiltration. Circular pale focus possibly petechial haemorrhage in which erythrocytes mostly disintegrated. (Ehrlich's H. and E. $\times 640$.)

FIG. 4.—Case 8. The most affected part of spinal cord. Greater part of an anterior horn included at top right. Note degree of cellular infiltration and disappearance of most of the neurones. (Ehrlich's H. and E. $\times 65$.)

FIG. 5.—Case 8. High-power view of part of the anterior horn seen in Fig. 4. Most cells are microglial. Irregular darkly stained object at top middle is a degenerating neurone showing neuronophagia. (Ehrlich's H. and E. $\times 640$.)

D. R. C. WILLCOX: HAEMOLYTIC ANAEMIA AND RETICULOSES

FIG. 1.—Case 4. Section of spleen. Edge of lymph follicle below. Pulp vascular, contains many histiocytic and some giant cells. (H. and E. $\times 200$.)

FIG. 2.—Case 4. Section of spleen showing details of the unusual type of giant cell. (H. and E. $\times 800$.)