examination. In the present series the core from each case of obstructive jaundice has shown easily visible green spots scattered throughout, while in each case of parenchymatous jaundice the core has been uniformly coloured. Fragmentation of the specimen is suggestive of cirrhosis and has been observed where the histological report was normal, gross cirrhosis being found at operation for porto-caval anastomosis. Metastases show as pale homogeneous areas, and are found more often than might be expected; foci of lymphadenoma have the same appearance. The greasy appearance stated to characterize fatty livers has not yet been observed. Apart from these conditions, considerable variation in the appearance of the core is compatible with normal histology.

Sequelae

There is often slight aching in the right hypochondrium, and occasionally pain in the right shoulder. This pain seldom lasts more than 24-36 hours and causes no distress. Of the present 72 biopsies 47 have had this reaction. 21 cases denied any pain. In four there was more severe pain, starting suddenly 1-8 hours after biopsy; but no anxiety was caused, and one patient readily agreed to a further biopsy. No other complications have arisen. Chest radiographs of ten patients have shown neither pleural effusion nor pneumothorax.

Complications reported in the literature are infection, perforation of a hollow viscus, and haemorrhage. Infection has been rare. Perforations of the colon, duodenum, and gall-bladder have been reported, usually without any reaction, though non-fatal biliary peritonitis and one death from colonic puncture are recorded. Haemorrhage has followed a tear of the capsule or of a superficial hepatic vessel. Haemothorax requiring blood transfusion has been twice noted.

Summary

Some indications for liver biopsy are given.

A mortality of 0.28% is presented, occurring in 2,479 biopsies reported since 1939, and the published deaths are examined in detail.

A description is given of a method of liver biopsy which has been employed in 72 biopsies with neither death nor significant complication.

I am indebted to Dr. R. Bodley Scott for his encouragement and ready assistance; to Dr. Geoffrey Bourne and the physicians and surgeons of St. Bartholomew's Hospital who have allowed me to carry out needle biopsy on their cases; to Mr. W. J. Ward, curator to St. Bartholomew's Hospital, and Mr. W. T. Harris, of W. H. Bailey and Sons, for their help in producing the biopsy instrument; to the photographic department of St. Bartholomew's Hospital for the illustration; and to the nursing staff of St. Bartholomew's Hospital for their careful reports.

REFERENCES

- Baron, E. (1939). *Arch. intern. Med.*, **63**, 276.
 Beek, C. van, and Haex, A. J. C. (1943). *Acta med. scand.*, **113**, 125.
 Beierwaltes, W. H., and Mallory, O. T. (1946). *Univ. Hosp. Bull., Ann Arbor*, **12**, 13.
 Bingel, A. (1923). *Ver. dtsch. Ges. inn. Med.*, **35**, 210.
 Davis, W. D., Scott, R. W., and Lund, H. Z. (1946). *Amer. J. med. Sci.*, **212**, 449.
 Dible, J. H., McMichael, J., and Sherlock, S. P. V. (1943). *Lancet*, **2**, 402.
 Franseen, C. C. (1941). *New Engl. J. Med.*, **224**, 1054.
 Frerichs, F. T. (1884). *Ueber den Diabetes*, Berlin, p. 272.
 Gillman, T. (1948). *J. Amer. med. Ass.*, **137**, 243.
 — and Gillman, J. (1945). *S. Afr. J. med. Sci.*, **10**, 53.
 Greene, C. H. (1944). *Arch. intern. Med.*, **73**, 349.
 Herrera, G., and Pardo, V. (1947). *Arch. Path.*, **44**, 393.
 Himsworth, H. P. (1947). *Lectures on the Liver and its Diseases*, Oxford.
 Hoffbauer, F. W. (1945). *Lancet*, **65**, 246.
 — (1947). *J. Amer. med. Ass.*, **134**, 666.
 Iversen, P., and Roholm, K. (1939). *Acta med. scand.*, **102**, 1.
 Learmonth, J. R. (1947). *Ann. roy. Coll. Surg.*, **1**, 299.
 Lucatello, L. (1895). *Lav. Congr. med. interna*, p. 327.
 McMichael, J. (1948). *J. Amer. med. Ass.*, **137**, 234.
 Olivet, J. (1926). *Med. Klinik*, **22**, 1440.
 Raby, K. (1944). *Nord. Med.*, **24**, 2161.
 Roholm, K., Krarup, N., and Iversen, P. (1942). *Ergebn. inn. Med. Kinderheilk.*, **61**, 635.
 Roth, A. A., and Turkel, H. (1944). *J. Urol.*, **51**, 66.
 Sherlock, S. (1945). *Lancet*, **2**, 397.
 Silverman, I. (1938). *Amer. J. Surg.*, **40**, 671.
 Stanley (1833). *Lancet*, **1**, 189.
 Tripoli, C. J., and Fader, D. E. (1941). *Amer. J. clin. Path.*, **11**, 516.
 Volwiler, W., and Jones, C. M. (1947). *New Engl. J. Med.*, **237**, 651.
 Watson, C. J. (1948). *J. Amer. med. Ass.*, **137**, 242.

SEVERE RENAL FAILURE AFTER ADMINISTRATION OF APPARENTLY COMPATIBLE BLOOD

BY

A. C. BUCHAN, F.R.C.S.Ed.

Plastic and Jaw Injury Unit, Bangour Hospital, West Lothian

AND

JOHN WALLACE, M.B., Ch.B., B.Sc.

Glasgow and West of Scotland Blood Transfusion Service

The literature on the Rh blood group is vast, but the recent appeal (*British Medical Journal*, 1948, **2**, 344) to publish observations on this subject has prompted us to record the case given below.

The development of irregular haemagglutinins after repeated blood transfusions is now well recognized. Callender and Paykoç (1946) reported that, out of 15 Rh-negative patients transfused with Rh-positive blood, only one developed rhesus antibodies, and Gunz (1946) observed that out of 10 Rh-negative patients who received multiple transfusions two were found to have developed antibodies. These observers point out, however, that had the tests for blocking antibodies (Race, 1944; Wiener, 1944) been performed the percentage of sensitized patients might have been higher. This suggestion is confirmed by Diamond (1946), who in a series of 2,500 Service men transfused under wartime conditions was able to demonstrate rhesus antibodies in the serum of about 50% of the Rh-negative individuals. Hattersley (1947), in a similar but smaller series, demonstrated rhesus antibodies in 11 (55%) out of 20 Rh-negative cases transfused under Service conditions. In all Hattersley's cases the antibodies were in the "blocking" or "incomplete" form, and direct compatibility tests of the patient's serum against saline-suspended Rh-positive cells would not have shown agglutination. However, in spite of this apparent compatibility the transfusion of Rh-positive blood to such a patient would result in a haemolytic reaction. It is for this reason that the following case is presented.

Case Report

A corporal aged 24 received a severe facio-maxillary injury on Jan 1, 1945. At that time he was given 5 pints (2.84 litres) of Group O blood in the course of 36 hours. His Service records make no mention of any reaction to these transfusions.

On July 24, 1946, a bone-graft operation was performed by Mr. A. B. Wallace. During the operation the patient's condition deteriorated, but a satisfactory rise in blood pressure followed the transfusion of 2 pints (1.14 litres) of Group O blood which appeared compatible on direct matching with the patient's serum.

On the morning of July 25 his condition was poor, his pulse rapid and of small volume, and his blood pressure 88/50. His collapse was attributed at the time to post-operative shock. One pint (570 ml.) of plasma and 1 pint of blood were given, and within four hours his general condition had improved, the blood pressure being 106/68. This latter blood was Group O, and appeared compatible with the patient's serum.

On the 27th he complained of nausea and vomiting, and his urine was blood-red in colour. The microscopical report

on the urine was: "Vast numbers of red blood cells and a few pus cells." The urinary output was 560 ml. in 24 hours.

By the morning of the 29th the urine was clear to the naked eye, but the microscopical report stated that a few red cells were present. The nausea and vomiting were more severe. Next day his general condition had deteriorated. Investigation of the blood chemistry gave the following results: urea, 340 mg. per 100 ml.; chlorides, 491 mg. per 100 ml.; uric acid, 4.1 mg. per 100 ml.; plasma albumin, 3.6 g. per 100 ml.; plasma globulin, 1.9 g. per 100 ml. Analysis of the urine showed: chlorides, 0.1 g. per 100 ml.; urea, 1.3 g. per 100 ml.; urinary output, 660 ml. in 24 hours. Because of the increasing vomiting a slow glucose-saline infusion was started on July 30.

The patient remained in a state of uraemia until Aug. 4, when a diuresis occurred, 5.25 litres being excreted in 24 hours. The specific gravity of the urine, which had remained constant at 1010 since the operation, now began to vary, thereby showing the return of the kidney's concentrating power. From this time the blood chemistry revealed a gradual return to normal. On Aug. 10 analyses showed: urea, 55 mg. per 100 ml.; uric acid, 4 mg. per 100 ml. The blood pressure on July 30 was 154/96 and on Aug. 3 it rose to 206/120.

Convalescence was slow. Renal function was investigated by the water concentration, the urea range, and urea-excretion tests in October, and all showed a normal degree of kidney function. Blood pressure was then 128/70.

Special Investigations.—Not until six weeks after the transfusions had been given were these performed, so a complete investigation was not possible. The results were: patient's blood group, O, Rh-negative (genotype rr); patient's serum contained anti-A agglutinin, titre 1/32, anti-B agglutinin, titre 1/16, and incomplete anti-D agglutinin, titre 1/8.

Compatibility Tests.—The routine test of the patient's serum against twelve random Group O cells suspended in physiological saline showed no agglutination. However, when the red-cell suspensions were prepared with AB serum instead of saline there was agglutination of the Rh-positive but not of the Rh-negative cells. Although no agglutination of the Rh-positive cells occurred in the saline suspension, these cells showed that they had been sensitized by a rhesus antibody when tested by the indirect anti-human globulin reaction (Coombs *et al.*, 1945).

In the accompanying Table the total fluid intake, urinary output, daily urinary excretion of sodium chloride and urea, and the level of the blood urea are shown.

Table Showing Urinalysis

Day after Transfusion	Total Fluid Intake (ml.)	Urinary Output (ml.)	Total Daily Urinary Excretion		Blood Urea (mg. per 100 ml.)
			Chloride (g.)	Urea (g.)	
1st ..	—	—	—	—	—
2nd ..	—	150	—	—	—
3rd ..	—	560	—	—	—
4th ..	2,490	600	—	—	—
5th ..	1,590	630	0.6	8.1	—
6th ..	2,190	660	0.7	8.6	340
7th ..	2,580	1,080	1.1	14.4	320
8th ..	2,730	1,380	3.5	18.4	340
9th ..	3,090	1,920	4.9	25.5	340
10th ..	4,050	2,970	9.9	39.6	340
11th ..	5,100	3,000	9.0	42.0	325
12th ..	4,740	5,250	6.8	73.5	270
13th ..	4,860	5,190	—	78.0	230
14th ..	5,010	4,800	6.2	92.0	210
15th ..	4,470	4,740	5.2	74.2	150
16th ..	3,840	3,870	—	—	—
17th ..	3,870	3,480	—	—	—
18th ..	4,080	3,390	4.1	66.0	55
19th ..	2,850	2,790	—	—	—

Before the onset of a copious diuresis on the twelfth day there had been a gradual daily increment in the 24-hour urinary output. For a few days after the onset of the diuresis the urinary output was greater than the total fluid intake. Muirhead *et al.* (1948) found that with the onset of diuresis not only was the water excretion markedly raised but the daily urinary excretion of sodium chloride was greatly increased. These workers suggested that the renal tubules had recovered sufficiently to allow for urine volume production, but that the recovery was not yet advanced enough to allow for the

conservation of water and salts. In the present case there was a marked increase in the daily excretion of urea, but the excretion of sodium chloride, while increased, remained within normal limits. It would seem that the kidney had recovered sufficiently to conserve sodium chloride. It has been emphasized (Muirhead *et al.*, 1948) that with the onset of the diuresis the kidneys may discard water and salts to the extent of causing pronounced dehydration or even death. It is therefore essential in the treatment of this phase to replace the water and salt lost from the body.

Discussion

The differential diagnoses considered at the time of the reaction were: (1) *Haemolytic transfusion reaction*:—This was considered unlikely on account of the careful compatibility tests made in the hospital laboratory and in the absence of the classical features, such as rigor, pain in the back, fever, or jaundice. There was no question of the blood having been overheated or being haemolysed by faulty or prolonged storage. (2) *Sulphonamide haematuria* can be excluded, as the patient was receiving penicillin but no sulphonamide drugs. (3) *Acute nephritis*:—This appeared the most likely diagnosis in view of the picture of uraemia associated with oliguria, red cells in the urine, and hypertension. Against such a diagnosis, however, was the absence of any recent infection, the absence of casts, and the low specific gravity of the urine.

As a haemolytic transfusion reaction was considered unlikely at the time, no special investigations were undertaken in the hospital, apart from checking on the ABO grouping of the patient and the donors and repeating the compatibility tests. These routine tests were satisfactory.

At the time of the special investigations six weeks later it was confirmed that the findings in the hospital laboratory were substantially correct, but the additional investigations revealed that the patient was Rh-negative and had "incomplete" rhesus antibodies in his serum. The development of these antibodies probably followed the original transfusion at the time of wounding in 1945. The transfusion of Rh-positive blood to an Rh-negative patient with "blocking" antibodies would then result in a haemolytic reaction, and it is believed that this is the explanation of the severe renal failure which developed.

There are several points about this particular case which seem worthy of mention.

1. Absence of the Classical Features of a Haemolytic Reaction

The absence of such reactions as tingling sensations of the skin, tightness in the chest, severe backache, dyspnoea, and cyanosis may be explained by the fact that the patient was anaesthetized during the transfusion of the first two bottles of blood. On the other hand, Mollison (1943) mentioned that reactions to incompatible transfusion seemed to be less severe than formerly, and Drummond (1944) describes a case of symptomless incompatible transfusion.

The presence of vast numbers of red blood cells and a few pus cells in the urine seemed to be in favour of a diagnosis of nephritis rather than of a haemolytic reaction. However, the presence of intact red blood cells in the urine is common, and white blood cells, often in clumps, are present during the oliguric period following an incompatible transfusion (Muirhead *et al.*, 1948). Pigment granules, often about the size and shape of a red blood corpuscle (for which they are not infrequently mistaken), are seen in haemoglobinuria (Bywaters and Dible, 1943).

2. The Severity of Renal Failure

In general, sensitization to the Rh antigen which occurs as a result of repeated transfusions develops slowly and early reactions are mild or inapparent (Mollison, 1948). In this case the reaction was severe after virtually the

second transfusion. The original transfusion of 5 pints of blood within 36 hours at the time of wounding can be regarded as a single antigenic stimulus. It is of comparative interest that Cappell (1948) has found that the first recorded manifestation of haemolytic disease of the newborn due to Rh incompatibility is usually one of the severer forms, contrary to the widely held belief that the first one or two affected children in a family show only mild symptoms.

Unfortunately, the volume of incompatible blood transfused in the case is not known with certainty, but the late Dr. Douglas Macrae, of the Edinburgh Blood Transfusion Service, informed us that at the time of the transfusion it was the practice to screen all Group O donors with a diagnostic anti-D serum, and, as it is certain that blood specifically marked Rh-negative was not given to this patient, the probability is that 1,600 ml. of incompatible Rh-positive blood was given. Bordley (1931) stated that cases receiving larger volumes of incompatible blood tend to be more serious—a conclusion with which Muirhead *et al.* (1948) are in general agreement. On the other hand, one of us (J. W.) has recently seen a Group O patient who had only a transient haemoglobinuria following a transfusion of 4 pints (2.27 litres) of Group A blood and did not develop renal failure. The anti-A titre of this Group O patient's serum four weeks after transfusion was 512,000. The probability is that several factors play a part in producing renal failure in such cases, the most important being renal anoxia (Maegraith *et al.*, 1945).

3. Compatibility Tests

The direct compatibility test in which the patient's serum is set up against saline suspensions of red cells will fail to detect the presence of blocking antibodies. To detect such antibodies the red cells must be suspended in AB plasma or preferably in 20% bovine albumin solution (Mourant, 1948). There is of course no proof that in this case blocking antibodies would have been detected in the patient's serum *before* transfusion. These antibodies may disappear after the original sensitization, but can be produced again very rapidly following the appropriate antigenic stimulus.

The two most important lessons to be learned from this case are : (i) always to determine the Rh blood group of any patient previously transfused, and (ii) the so-called compatibility test is not an absolute safeguard against incompatibility.

4. Survival of the Patient

Many forms of therapy have been advocated in the treatment of haemolytic transfusion reactions—e.g., alkaline therapy, forced fluids, transfusion of compatible blood, splanchnic block, and decapsulation of the kidney (Kilduffe and De Bakey, 1942)—but opinions differ on the value of these methods. Few observers are in a position to study a large controlled series of such cases, and this renders assessment of a particular form of therapy difficult. According to De Gowin (1938) some patients recover spontaneously, while others die in spite of the therapeutic measures advocated. The present case illustrates that even severely damaged kidneys may recover completely without any heroic therapy.

Summary

A severe degree of renal failure from which the patient subsequently made a complete recovery occurred after a blood transfusion.

The transfused blood appeared to be compatible when tested against the patient's serum.

On investigation the patient, who had been transfused previously as a war casualty, was found to be Rh-negative and to

have rhesus antibodies of the incomplete, blocking, or albumin-agglutinating variety in his serum.

The importance of determining the Rh group in any patient previously transfused, and the danger of relying on the direct compatibility test only, are stressed.

The clinical features and treatment of haemolytic transfusion reactions are discussed.

We wish to thank Dr. W. M. McAlister, medical superintendent of Bangour Hospital, for permission to publish this case. We also acknowledge with thanks the help received from Dr. I. A. Purdie in the biochemical investigations and the helpful co-operation of Mr. A. B. Wallace, who was in charge of the case.

REFERENCES

- Bordley, J. (1931). *Arch. intern. Med.*, **47**, 288.
 Bywaters, E. G. L., and Dible, J. H. (1943). *J. Path. Bact.*, **55**, 7.
 Callender, S. T., and Paykoç, Z. V. (1946). *British Medical Journal*, **1**, 119.
 Cappell, D. F. (1948). *Ibid.*, **2**, 323.
 Coombs, R. R. A., Mourant, A. E., and Race, R. R. (1945). *Lancet*, **2**, 15.
 De Gowin, E. L. (1938). *Ann. intern. Med.*, **2**, 1777.
 Diamond, L. K. (1946). *Proceedings of International Haematol. and Rh Conference*, Dallas, Texas.
 Drummond, R. (1944). *British Medical Journal*, **1**, 483.
 Gunz, F. W. (1946). *Ibid.*, **1**, 601.
 Hattersley, P. G. (1947). *J. Lab. clin. Med.*, **32**, 423.
 Kilduffe, R. A., and De Bakey, M. (1942). *The Blood Bank and the Technique and Therapeutics of Transfusions*. St. Louis.
 Maegraith, B. G., Havard, R. E., and Parsons, D. S. (1945). *Lancet*, **2**, 293.
 Mollison, P. L. (1943). *British Medical Journal*, **1**, 529.
 — (1948). *Med. Res. Council, Mem. No. 19*, p. 27.
 Mourant, A. E. (1948). *Ibid.*, No. 19, p. 60.
 Muirhead, E. E., Haley, A. E., Haberman, S., and Hill, J. M. (1948). *Blood*, Special Issue, No. 2, p. 101.
 Race, R. R. (1944). *Nature*, **153**, 771.
 Wiener, A. S. (1944). *Proc. Soc. exp. Biol., N.Y.*, **56**, 173.

DYSENTERY IN SOUTH PERSIA

BY

IAN S. STEWART, M.B., Ch.B.

Pathologist, Anglo-Iranian Oil Company

The control of this group of diseases, apart from the relief of the patients' discomfort, is of importance because they are productive of much time-wastage and inefficiency, matters of outstanding interest to a commercial concern. Moreover, the opportunity of identifying and segregating the patients who continue to be infective after apparent recovery will bring about a steady reduction in the incidence of the dysenteries in the province of Khuzistan, South Persia.

Accordingly arrangements were made in March, 1947, for all cases regarded as dysenteric, either on clinical grounds or from the initial examination of the stools in the laboratory, and arising among the company's 30,000 male artisan employees on Abadan Island, to be admitted to the Isolation Hospital, a segregated wing of which was allocated for this purpose. The project had been under consideration for two years but had been delayed by the restricted supplies of sulphaguanidine. The arrival of a hundredweight (50 kg.) of this drug in March was followed by the opening of a forty-bed ward on April 1, and the figures subsequently quoted relate to the admissions between April 1, 1947, and April 1, 1948.

The survey relates to a permanent and static civilian population and therefore has a value greater than that of a survey of the same diseases during the conditions of war, when large masses of population are moved into abnormal sites and situations. Apart from its local value it has a bearing on the steadily increasing flow of short-term visitors of all nationalities drawn to the Persian Gulf by its