

seven days and then reduce the dose to 45 mg. daily.

Eleven days later she was readmitted with an acute psychotic illness characterized by paranoid delusions. She was febrile and her pulse rate varied between 110 and 145. Clinically she was considered to be euthyroid and the serum P.B.I. was 4.3 µg./100 ml. Serum urea, electrolytes, full blood count, electrocardiogram, chest x-ray, and urine culture were normal. Three days later her temperature was normal and she was transferred to a psychiatric hospital (Dr. J. G. Henderson). She was treated with chlorpromazine and benzotropine and continued on carbimazole 20 mg. daily. Two months later she was mentally normal and during her illness she remained clinically and biochemically euthyroid.

Subtotal thyroidectomy was carried out two months after her discharge (Mr. W. Michie), and at her most recent review, 10 months after operation, she was euthyroid and normal in all other respects.

At the time of her first admission this patient was considered to have severe hyperthyroidism, and the treatment rapidly altered her thyroid state towards normal. There was no evidence of hypothyroidism at any time during her illness. It is suggested that her psychiatric disturbance may have been due to either the acute change in her metabolic state, induced by the antithyroid drug, or to the drug itself. Similar findings have been reported previously.¹⁻³—We are, etc.,

ANTHONY J. HEDLEY.

P. D. BEWSHER,

Department of Therapeutics
and Pharmacology,
University of Aberdeen.

REFERENCE

- 1 Williams, R. H., Clute, H. M., Anglem, T. J., and Kennedy, F. R., *Journal of Clinical Endocrinology and Metabolism*, 1946, 6, 23.

Diverticular Disease of the Colon

SIR,—It seems to me unfortunate that in a recent article (24 August 1968, p. 475) and a leading article (9 August, p. 311) on diverticular disease of the colon no mention should have been made of the work of H. C. Edwards. As long ago as 1932 he won the Jacksonian prize for his work on diverticula of the intestine, later published in the *Lancet*,¹ the *British Journal of Surgery*,² and later still as a book.³ In these publications Edwards brought forward much evidence to show that diverticular disease is a result of irregular or abnormal contraction of the muscle. He also referred to the work of A. P. Stout⁴ as pointing to the same conclusion. Stout's paper, written in 1923, dealt with diverticula of the appendix. It was a pioneering effort in that it demolished the theory that distension produces diverticula. But nobody paid any attention, any more than they did to the work of Edwards published a decade later.

I think it is regrettable that the work of these two eminent men should have been forgotten, when now, at length, their judgements have been vindicated.—I am, etc.,

R. R. WILSON.

Department of Pathology,
Stobhill General Hospital,
Glasgow N.1.

REFERENCES

- 1 Edwards, H. C., *Lancet*, 1934, 1, 221.
- 2 Edwards, H. C., *British Journal of Surgery*, 1934, 22, 38.
- 3 Edwards, H. C., *Diverticula and Diverticulitis of the Intestine*, 1939. Bristol, Wright.
- 4 Stout, A. P., *Archives of Surgery*, 1923, 8, 793.

Serum Hepatitis in a Haemophilic

SIR,—Serum hepatitis after the use of cryoprecipitated antihæmophilic globulin (cryo) is unusual. The only reported case is that of Del Duca and Eppes,¹ who described a 39-year-old haemophilic who developed transient jaundice 60 days after receiving 28 units of cryo for dental extraction. He recovered rapidly after one day of nausea and vomiting. We report a second case with a fatal outcome.

A 41-year-old male haemophilic presented in January 1969 with spontaneous bleeding into his right knee joint of two days' duration. He was given 18 units of cryo over 48 hours and allowed to go home. Two weeks later an injury to his left knee caused a large haemarthrosis. Sixty ml. of blood was aspirated with strict aseptic technique under cover of 6 units of cryo. Sixty units of cryo were given over the next two weeks, but the haemarthrosis was slow to resolve, and for the next two months he had twice weekly physiotherapy under cover of 6 units of cryo, receiving a total of 162 units in all.

In May 1969 he presented with rigors and generalized abdominal pain associated with a skin rash over his arms and legs. Next day he developed nausea and continuous vomiting and passed dark urine and stools. On admission to hospital four days later he looked ill with cold, moist, jaundiced skin, diffuse upper abdominal tenderness, and a purpuric rash on his arms and legs. He was severely dehydrated. Investigations confirmed the dehydration and showed evidence of gross liver cell damage. He was rehydrated, but continued to vomit. Twenty-four hours later the vomit contained brown watery fluid which contained haemoglobin. One litre of fresh frozen plasma was transfused, and vitamin K₁ (10 mg. every six hours) was added to the intravenous fluids. He continued to vomit blood-stained fluid and his condition gradually deteriorated. Apart from confusion and jaundice there were no signs of liver failure. Serum bilirubin was then 20.5 mg./100 ml., Hb 16.4 g., packed cell volume 45%, and blood urea 133 mg./100 ml.

At this point he vomited fresh blood for the first time. He continued to vomit blood for the next 12 hours: 8 pints (4.5 l.) of blood and six units of cryoprecipitate were given without improvement. Because of his rapid deterioration exchange transfusion of three units of blood was performed. He died 72 hours after admission.

Post-mortem examination (Dr. A. H. Cruickshank) revealed a small liver (1,370 g.). The capsule was wrinkled and the subcapsular surface was extensively mottled by haemorrhage. The cut surface showed mottling with alternate areas of pallor and congestion. The common bile duct was patent, the portal and hepatic veins normal. The gall bladder did not contain any stones. The spleen was moderately enlarged (540 g.) with scattered subcapsular haemorrhages. The stomach, duodenum, and jejunum contained altered blood. There was a submucosal haemorrhage in the lower third of the oesophagus. No obvious bleeding point was found in the gastrointestinal tract. The heart (428 g.) showed subepicardial petechiae and a large (4×1.5 cm.) subendocardial haemorrhage on the left side of the intraventricular septum. Blood was present in the trachea and main bronchi, and haemorrhage in the submucosa of the hypopharynx. There was no laryngeal obstruction. The lungs were moist and deeply congested. Both kidneys showed a pale jaundiced cortex. Histology of the liver showed extensive hepatocellular damage. Complement fixation

tests for viruses (Dr. Bruce White) were performed on serum taken during the actual illness and on stored serum taken in January 1969. Apart from a rather high titre for cytomegalovirus (1/64) both specimens were normal. Serum used successfully as a source of SH antigen gave a weak positive agglutination.

The clinical and necropsy findings here are fully compatible with the diagnosis of serum hepatitis.

Cryo represents a considerable advance in the management of the severe haemophilic. This and other centres have used many thousands of units without mishap and we do not know of a similar case in Britain. It is important to re-emphasize the potential danger of cryo to ensure its use only when strictly needed. A check should be kept of the source of cryo to trace any serum hepatitis which may occur in future.

We are grateful to Dr. T. Black for permission to report this case.

—We are, etc.,

J. A. WHITTAKER.
M. J. BROWN.

Royal Infirmary,
Liverpool.

REFERENCE

- 1 Del Duca, V., and Eppes, R. B., *New England Journal of Medicine*, 1966, 275, 965.

Origin of the Third Heart Sound

SIR,—While wanting to agree with Drs. M. I. M. Noble and K. B. Saunders (16 August, p. 413) that the major part of ventricular filling probably represents a passive process as the heart muscle dilates, these authors have not demonstrated that diastolic suction due to elastic recoil does not occur briefly at the moment of mitral valve opening in very early diastole, as seems to be the case. What they have shown with certainty¹ is that suction from elastic recoil does not measurably persist throughout diastole, although, as Linden² states, "suction" is only one way of looking at a pressure difference and it is likely that the pressures involved are small. The sensitivity of the methods used therefore for measuring these differences is all important. It is only to be expected that elastic recoil pressure effects are small, for ventricular filling, since it is hard to conceive how Starling's law of the heart could otherwise remain valid and an adaptive exercise response occur. Although it is likely that elastic recoil pressure effects are small, this does not diminish their importance as a means of controlling the critical boundary layer as the mitral valve opens.³

It is legitimate to consider the geometry of the adjacent atrial and ventricular chambers as a diffuser whose main function is pressure recovery during diastole. By controlling the boundary layer of fluid entering the ventricle at this critical moment of time, full expansion of the jet is achieved and pressure recovery throughout almost doubled, though the amount of lateral suction that needs to be applied is slight.⁴ Lateral suction as the result of outward movement of the ventricle wall certainly does occur to a major extent throughout diastole with respect to fluid entering the ventricle, and is responsible for continued control of the boundary layer.