The term "irritable bowel syndrome" describes a group of clinical features—a syndrome rather than a disease. Almost certainly there are a number of causes, one being lactase deficiency. Knowledge of the underlying disturbance of neural, neurohumoral, and perhaps hormonal (including locally active hormonal) mechanisms is rudimentary and at the moment it is appropriate to think of the disorder as idiopathic, and to maintain completely open minds regarding lines of research inquiry. An important clinical observation is the frequent finding of I.B.S. in subjects who overwork and overreact. There is overt or suppressed fear of cancer in some patients, and doctors who diagnose the syndrome may wish to confirm the absence of Crohn's disease or colonic carcinoma. For these reasons, general practitioners tend to send such patients to a G.I. referral centre rather more readily than the condition itself may appear to merit.

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ANTI-e AND RHEUMATOID FACTOR

SIR,—Dr Furuta (Aug. 13, p. 353) and his colleagues claim that we[1] reported that the e/anti-e system is "identical with the IgG/anti-IgG system." We did not. We wrote: "Both e and anti-e appear to be antibodies formed in response to hepatitis B virus infection . . . The fact that e and anti-e react with each other and neither reacts with normal IgG suggests that their respective antibody-binding sites correspond to idiotypic and anti-idiotypic determinants . . . located in the variable region of immunoglobulins . . . Since anti-e reacts neither with insolubilized normal human IgG nor with soluble IgG . . . antibodies other than anti-e were probably involved in the . . . reaction with normal immunoglobulins . . . . Our results would have also been obtained if e were a small molecule tenaciously attached to IgG . . ."

Reports by Furuta et al. and others[2,3] indicating the presence of rheumatoid factor in some sera positive for anti-e accord with our findings.[1] Human sera positive for anti-e may contain other antibodies and autoantibodies, including rheumatoid factor, which react with the Fc portion of normal IgG and are distinct from anti-e.

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ENDOSCOPY FOR ACUTE UPPER GASTROINTESTINAL BLEEDING

SIR,—Dronfield et al.[4] state that although endoscopy has a somewhat higher yield than radiology for the diagnosis of upper gastrointestinal hæmorrhage, the patient does not seem to benefit. Cotton[5] thought there might be a subgroup of patients with upper gastrointestinal hæmorrhage with ominous prognosis under orthodox management, and suggested that identification of subgroups might pinpoint the weaknesses of the traditional management.

We have found that active bleeding present at emergency endoscopy has prognostic implications.[6] Of 105 patients investigated by endoscopy within 6 h of admission because of clinical signs suggesting massive bleeding requiring emergency management, 60 (57%) were actively bleeding. These patients had a 46% (28/60) mortality, while non-bleeding patients had a 7% (3/45) mortality ($P<0.01$).

Improved diagnostic methods cannot influence outcome unless they are followed by effective management. Endoscopic identification of the actively bleeding patient provides a therapeutic opportunity, but we must wait for definition of a suitable treatment before we can find out if the diagnostic efficacy of endoscopy in upper gastrointestinal hæmorrhage provides a therapeutic advantage.

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D.D.A.V.P. IN HÆMOPHILIA

SIR,—Mannucci et al.[1] used intravenous infusion of D.D.A.V.P. (1-desamino-8-D-arginine vasopressin) to raise the level of factor-VIII-coagulant activity (VIII C.A.) in patients with mild and moderate hæmophilia and von Willebrand's disease, allowing surgery to be undertaken without factor-VIII-concentrate cover. Although D.D.A.V.P. has a powerful antidiuretic action, no consistent effect on plasma or urine osmolality was noted in the twelve patients studied. We gave D.D.A.V.P. to a moderately affected hæmophiliac undergoing dental extraction and noted progressive water retention with mild clinical symptoms, a sixfold rise in factor VIII C.A. on infusion of D.D.A.V.P. at a slower rate than previously used, a marked decline of the VIII C.A. response with repeated doses, and no stimulation of the patient's factor VIII inhibitor, which had previously been present in high titre.

A 46-year-old moderately affected hæmophiliac (previously described[2]) had a high titre of factor-VIII inhibitor after surgery, causing major wound bleeding which responded to prothrombin complex concentrate; the inhibitor subsequently became undetectable. No further factor-VIII-containing preparations have been administered. The patient required extraction of two adjacent molar teeth, and, because his VIII C.A. was 0·05 units/ml,[3] it was thought possible to achieve a level of 0·3 units/ml using maximum dosage of D.D.A.V.P. (0·5 μg/kg bodyweight): we consider this level sufficient to cover extraction, in combination with tranexamic acid. To avoid cardiovascular reactions, D.D.A.V.P. was infused over 15–20 min instead of the 5 min infusion used by Mannucci et al. Factor VIII C.A. was measured immediately before and 15 min after the end of infusion. 48 h before surgery a test dose of D.D.A.V.P. (0·4 μg/kg) raised VIII C.A. from 0·05 to 0·25 units/ml; no adverse effects or change in plasma osmolality or sodium were seen. 90 min before extraction of the two teeth, D.D.A.V.P. (0·5 μg/kg) raised VIII C.A. from 0·05 to 0·33 units, falling to 0·26 units/ml 3 h later. Oral tranexamic acid (0·5 g 6-hourly) and penicillin V (250 mg 6-hourly) were given before surgery and continued for 10 days; the patient was asked not to drink too much. A further four infusions of D.D.A.V.P. (0·5 μg/kg) were given every 12 h. On the first postoperative day, VIII C.A. was 0·05 units/ml before and 0·08 units/ml after infusion; plasma osmolality had fallen from 284 to 262 mmol/kg and plasma-sodium from 137 to 132 mmol/l. On the second postoperative day VIII C.A. was 0·04 units/ml before and 0·06 units/ml after infusion; plasma osmolality was 250 mmol/kg and plasma-sodium was 124 mmol/l; the only clinical feature of water retention was headache. D.D.A.V.P. was stopped and fluids restricted to 500 ml in 24 h; 48 h later plasma osmolality and sodium had returned to normal and the headache had gone. Persistent ooz-

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ing at the extraction site started 5 days after surgery, and after 24 h prothrombin complex concentrate ('Proplex'), 25 units factor IX/kg, was infused. The partial thromboplastin-time was shortened from 122 to 79 s; bleeding stopped within 2 h and did not recur. Stitches were removed 8 days after surgery following a further dose of proplex. No features of disseminated intravascular coagulation were observed during proplex therapy. Factor-VIII inhibitor was assayed[4] before surgery and postoperatively at 2 days, 7 days, and 4 weeks; the level remained below 1 unit/ml. A biochemical, asymptomatic, HB_sAg-negative hepatitis was detected 4 weeks after extraction.

It seems that water retention can occur when large doses of D.D.A.V.P. are given 12-hourly, despite the short half-life of the drug: the renal tubular effect may be cumulative. We suggest close monitoring of plasma osmolality and sodium during repeated D.D.A.V.P. infusions and early institution of fluid restriction with withdrawal of D.D.A.V.P. if they fail. We observed a similar rise in VIII C.A. to Mannucci et al.,[1] using a slower infusion which may help to avoid any cardiovascular side-effects of these large doses of D.D.A.V.P. However, the response weakened on repeated infusion, as noted in two of Mannucci's patients. Our patient, who had had a high titre of factor-VIII inhibitor and might have been expected to show an anamnestic response to factor-VIII transfusion, did not show any rise in inhibitor level after increase of endogenous factor VIII. D.D.A.V.P. may, therefore, be of use in achieving hæmostatic levels of VIII C.A., without inhibitor stimulation, in mild and moderate hæmophiliacs who have a history of high-titre inhibitors.

We again noted shortening of the partial thromboplastin time and cessation of directly observable bleeding in this patient after the administration of prothrombin complex concentrate, in keeping with our previous experience.[2]

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RENAL CARCINOMA 30 YEARS AFTER ABDOMINAL IRRADIATION FOR TESTICULAR SEMINOMA

SIR,—Most patients with pure testicular seminoma can be cured by orchiectomy followed by irradiation to lymphatic drainage areas. Radiation is carcinogenic and potentially can stimulate[6,7] all malignancies. Here we describe a patient who had a carcinoma on the side irradiated for seminoma 30 years earlier.

A 75-year-old man had had right-sided seminoma in 1945. After orchiectomy he received orthovoltage radiation (roughly 3000 rad) to the right half of the abdomen. In 1975 he presented with nausea, vomiting, and progressive obtundation. Brain scan showed multiple lesions in the frontal and parietal lobes. Chest X-rays revealed bilateral, multiple lesions which on biopsy showed adenocarcinoma consistent with renal origin. Ultrasound examination confirmed a right superior pole renal lesion. The urine cytology was also positive for adenocarcinoma. He was started on dexamethasone 4 mg four times a day and his neurological signs improved. He was given multiple agents such as progesterone,[8] cyclophosphamide, and I.C.R.F. 159, but his disease progressed and he died 6 months after the diagnosis of renal carcinoma. Permission for necropsy was refused.

The development of renal carcinoma in this patient could be fortuitous and may not be related to radiation. However, the fact that it developed after a latent period of 30 years and on the side previously irradiated, suggests radiation carcinogenesis. Biopsy of the right kidney could have been helpful if it had shown radiation nephritis.

Acute leukæmia has been described after radiation for seminoma,[1] but we know of no case of renal carcinoma developing in this way. Long-term follow-up of a large series of patients with seminomas is required to determine the frequency of secondary neoplasms in the irradiated field in this group.

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SEVERE MYOPATHY AFTER STATUS ASTHMATICUS

SIR,—We have seen an unusual severe myopathy in a patient treated for status asthmaticus.

A 24-year-old woman was admitted with a 1-day history of breathlessness. She had had asthma since the age of 2 and had had two hospital admissions, 2 years and 1 year previously, in status asthmaticus. These attacks had responded to short courses of oral prednisolone and hydrocortisone injections. No weakness had been reported after this therapy and she normally used a salbutamol inhaler.

She was treated with intravenous hydrocortisone and aminophylline, but deteriorated and was ventilated. She remained on the ventilator for 8 days and received large doses of hydrocortisone sodium succinate (up to 3 g in 24 hours by constant infusion), salbutamol infusion (5 μg/min), and ampicillin. She was also given intermittent doses of pancuronium bromide, phenoperidine, metoclopramide, and promethazine. Her serum-potassium was consistently normal during her illness.

After 8 days, airway obstruction had ceased, but she had great difficulty in breathing off the ventilator. Her peak expiratory flow was only 50 l/min and this seemed to be due to weakness of her respiratory muscles. She was also unable to lift her limbs against gravity. Cranial nerves, tendon reflexes, and sensation were normal. Nerve conduction velocity was normal at 70 m/s (common peroneal nerve). Electromyography of the anterior tibial muscle revealed no increased insertional activity and silence at rest. Maximal contraction produced low-amplitude motor potentials of short duration compatible with a myopathy. Serum calcium, magnesium, thyroxine, creatinine, and phosphokinase and liver-function tests were all normal.

She gradually improved and was able to walk unaided after 3 weeks. At 2 months she still had weak legs, more distally, and repeat electromyography revealed a persistent myopathy. She had been off steroids for 7 weeks.

Her severe myopathy was unusual in that during recovery it affected mainly distal muscle groups.[1] It was unlikely to be due to a metabolic cause and may have been caused by the large doses of hydrocortisone. The 9α-fluorinated steroids are usually implicated as the cause of steroid myopathy[2] and hydrocortisone has not previously been associated with severe muscle weakness. Much smaller doses of hydrocortisone (3 mg/kg infused 6-hourly) have been shown to be maximally effective in severe asthma.[3] Patients with severe asthma should, therefore, not receive such large doses of hydrocortisone in view of the possible severe side-effects.

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