new islets from the epithelium of exocrine ducts. The condition has been described in adults, in isolation and in association with other disorders: chronic pancreatitis, pancreatic duct obstruction, cystic fibrosis, gastrinoma, multiple endocrine neoplasia (MEN) and sulphonylurea therapy. The association of nesidioblastosis in an adult with an insulinoma has been reported on three occasions.¹⁻³ We describe here a fourth.

A 60 year old Caucasian male was admitted as an emergency with only a 5 day history of episodic drowsiness, slurred speech and confusion. Although he was obese, there was no history of recent weight gain. On examination he was drowsy, but rational and cooperative. History and examination were otherwise unremarkable and he was on no medication. Blood glucose was 1.7 mmol/l, with inappropriate elevation of serum insulin (80 mU/l) and C-peptide (2.7 mmol/l). Recurrent hypoglycaemia in ensuing days was only prevented by infusion of 4 litres of 10% dextrose each 24 hours, reducing to 1 litre of 10% dextrose in combination with oral diazoxide 250 mg twice daily. Abdominal computed tomography (CT) and coeliac axis angiography were unhelpful but a 1 cm tumour was found in the tail of the pancreas at exploratory laparotomy. 50% distal pancreatectomy and splenectomy was followed by an uncomplicated recovery. Apart from pneumococcal prophylaxis, he has received no further treatment and remains free from symptoms or other evidence of hypoglycaemia after two and a half years. Histological examination identified three discrete endocrine tumours, the largest 1 cm in diameter. Each showed a predominantly alveolar pattern, with copious amyloid. There was positive immunohistochemical staining for insulin and glucagon, but not for somatostatin. There was nesidioblastosis throughout the remaining pancreatic tissue and extending to the limit of the resection. The hyperplastic islets showed positive staining for the neuroendocrine marker PGP 9.5, as well as for insulin glucagon and somatostatin. The distribution of D-cells appeared normal.

This is the fourth reported case of nesidioblastosis occurring in association with an insulinoma. We believe the hypoglycaemia leading to presentation was the result of insulin secretion by the insulinomas, rather than by the surrounding tissue; nesidioblastosis must have been present throughout the unresected pancreas, and yet there has been no recurrence of hypoglycaemia. The pathogenesis of nesidioblastosis is unknown. It has been suggested that islet proliferation may result from reduced somatostatin secretion by pancreatic D-cells because somatostatin normally exerts a negative paracrine effect on islet cell function.⁴ Alternatively, it has been suggested that islet cell hyperplasia may occur as a result of islet stimulating immunoglobulins.⁵ In this case, the multiple insulinomas may have developed as a result of field change in pre-existing hyperplastic tissue, but it is equally likely that the insulinomas may have arisen *de novo*, and caused the nesidioblastosis by a paracrine effect. Such an effect could have been caused by insulin itself or, conceivably, by excessive secretion of amylin (IAPP) – as suggested by the presence of copious amyloid. If so, the absence of somatostatin in the insulinomas may have facilitated the development of nesidioblastosis by allowing proliferation of adjacent pancreatic tissue to take place unopposed.

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Masked faecal peritonitis in Cushing's syndrome

Sir,

We wish to report the case of a 71 year old woman who was admitted with a 3 week history of diarrhoea, anorexia, weight loss and abdominal pain. The past medical history revealed diverticular disease diagnosed 7 years previously. On examination, she was hirsute with generalized muscle weakness. She was in atrial fibrillation with mild left ventricular failure and ankle oedema. Investigations revealed a marked hypokalaemia (plasma potassium 1.2 mmol/l). Sigmoidoscopy was normal and a barium enema confirmed uncomplicated diverticular disease. The results of endocrinological investigations led to the presumptive diagnosis of ectopic Cushing's syndrome. A chest radiograph was normal. A limited abdominal computed tomographic (CT) scan showed bilateral adrenal hyperplasia. The patient was treated with metyrapone and over the subsequent 3 weeks plasma cortisol levels fell with an improvement in her clinical condition. A repeat abdominal CT scan was performed to locate a possible source of ectopic ACTH. Alarming extensive intra- and extra-peritoneal gas was demonstrated! The source of the ACTH was not.

At urgent laparotomy faecal peritonitis was found originating from a perforated diverticular abscess of the sigmoid colon. A sigmoid colectomy and ileostomy was performed. Post-operatively her condition deteriorated despite intense supportive therapy and she died of cardiorespiratory failure 6 days later. The autopsy showed that death had occurred as a direct result of perforated diverticular disease and peritonitis. Microscopic examination of the pancreas revealed a benign ACTH-secreting tumour which was not macroscopically evident.

The striking feature of this case was the lack of symptoms or signs of faecal peritonitis. In particular the patient was never pyrexial and the white cell count was

normal on serial testing. A review of the recent medical literature yielded only one case in which hypercortisolism disguised symptoms and signs of an abdominal surgical crisis in a patient who died of an unrecognized gallbladder perforation.¹ Presumably in both these cases the well-documented anti-inflammatory and immunosuppressive effects of hypercortisolism^{2,3} masked the development of infection and reduced the host's response once it has become established. Cushing's syndrome is known to predispose to opportunist infection, in the past up to 46% of patients with Cushing's syndrome died of sepsis, many following major surgery.⁴ In the modern era opportunist infection is less commonly seen. This case illustrates the need for continuing vigilance in patients with Cushing's syndrome. It reaffirms the commonly held belief that hypercortisolism, whether due to Cushing's syndrome or exogenous steroids, can mask severe abdominal pathology.

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Trimethoprim-induced vasculitis

Sir,

Adverse drug reactions associated with co-trimoxazole may be caused by either trimethoprim or sulphamethoxazole. However, the skin rashes are so similar to those caused by sulphonamides alone that most are attributed to these.¹ We report a case of vasculitis which was induced by trimethoprim.

An 83 year old woman was admitted with severe anaemia (Hb 3.8 g/dl) secondary to vitamin B₁₂ deficiency, attributed to a previous vagotomy and pyloroplasty and a coliform septicaemia secondary to a urinary tract infection. She was treated with intravenous cefuroxime for 11 days. She then suffered a right cerebro-vascular accident.

Following this she made a good recovery. During her rehabilitation, 2 months later, she developed a further urinary tract infection. A mid-stream urine grew coliforms, which were sensitive to trimethoprim, but resistant to ampicillin and nalidixic acid. She was given a week's course of trimethoprim 200 mg twice daily. Nine

days later she developed a florid leucocytoclastic vasculitis on her hands, tongue, shins and feet. This was associated with acute arthritis of her interphalangeal joints and haematuria. Previous urinalysis for blood had been negative.

Her daughter then remembered that her mother had had a similar rash 2 years previously when she had been treated with co-trimoxazole for a urinary tract infection. A case summary was obtained and this confirmed that our patient had had a vasculitis, secondary to co-trimoxazole.

Other causes of a vasculitic rash were looked for: a full blood count showed a white cell count of $3.3 \times 10^9/l$, haemoglobin of 14.9 g/dl and platelets of $120 \times 10^9/l$. Blood cultures, rheumatoid factor and auto-antibodies were negative. Routine viral titres showed no recent infection. Serum electrophoresis showed a double M band in the gamma region but there was no Bence-Jones protein. Serum complement and cryoglobulins were in the normal ranges. An ultrasound of her abdomen was normal.

She was treated with hydrocortisone (200 mg 4 times daily) and intravenous antibiotics (to cover for a possible diagnosis of endocarditis). She responded dramatically to treatment over a week but developed a chest infection and died 4 weeks later.

We are convinced that the vasculitis was caused by trimethoprim because of the recurrence of the rash on subsequent exposure and because of the lack of another explanation. The Committee on the Safety of Medicines has a number of reports of various types of rashes being associated with the use of trimethoprim. These include maculo-papular, morbilliform, erythematous, angioedema and purpuric. There was only one previous reported case of a vasculitis from Holland (unpublished, Wellcome Foundation Ltd files) which was described as purpuric and is distributed over the trunk and lower limbs.

Patients who have adversely reacted to co-trimoxazole should receive neither trimethoprim nor sulphamethoxazole in future.

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Listeria rhombencephalitis in a previously healthy adult

Sir,

We report a case of listeria rhombencephalitis (brain stem encephalitis) in a healthy adult.

An 85 years old previously well woman was admitted with a 10 day history of right seventh cranial nerve paresis. She was pyrexial and slightly confused. The neurological examination revealed nystagmus towards