Steatorrhoea and jejunal reticulum cell sarcoma occurring in a patient on long-term colchicine therapy for gout

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Summary
A second case is described where steatorrhoea developed following long-term colchicine therapy for gout; the relationship of therapy to the development of a reticulum cell sarcoma of the jejunum is discussed.

Introduction
The onset of gout in steatorrhoea has been described in only a few cases (Talbot, 1959; Lewis, 1962). The development of steatorrhoea following long-term colchicine therapy for gout has been recorded only once to our knowledge (Hawkins, 1961). The present case report describes similar associations of abnormalities.

Case report
Aged 56.
Aged 41. Onset of episode or acute gout in the metatarsophalangeal joints.
Aged 46. Mild anaemia noted by blood transfusion service.
Aged 47. Mild transient ankle swelling.
Aged 53. Recurrence of ankle swelling with breathlessness, malaise, tiredness and increased frequency of gouty episodes. Colchicine 0·5 mg a day given for the next 3 years. He had no change in bowel habit but weight loss began and totalled 41·5 kg.
Aged 56. Persistent, loose, watery diarrhoea developed and pigmentation, pallor and breathlessness were noticed. Admitted to hospital. No family history of gout or steatorrhoea.

On initial examination. He was pale with raised jugular venous pressure, firm enlargement of the liver and gross oedema of the legs. There was generalized pigmentation and clubbing of fingers and toes. BP 120/90 mmHg.

Initial investigations. Hb 5·4/100 ml, 4·6% reticulocytes. The serum iron was low (36 μg/100 ml). Serum folate was depressed (1·7 μg/ml), serum B₁₂ level 397 μg/ml. Faecal fat excretion was 10–13 g/day. ESR 40 mm/hr, plasma albumin 3·5 g/100 ml. X-rays of the feet showed gouty changes. Barium meal and follow through suggested atrophic gastric mucosa but was otherwise normal. Serum vitamin A level normal. Glucose tolerance test normal. A duodenal biopsy (Crosby capsule) showed 'subtotal villous atrophy typical of idiopathic steatorrhoea, with normal mitoses and gross lymphocytic infiltration'.

Progress. As the anaemia corrected on oral iron and folic acid, heart failure cleared. Colchicine was discontinued and the faecal fat fell to 4·9 g/day. He gained 15 kg in weight. On re-assessment 9 months later, gout was occurring more often, faecal fat was 18 g/day and a duodenal biopsy showed unchanged subtotal villous atrophy. The plasma albumin had fallen to 2·7 g/100 ml. A gluten-free diet was started in view of the failure of the steatorrhoea or the duodenal mucosa to improve. After a month on this diet, he first developed upper abdominal pain after eating. This was firstly felt to be due to mild constipation which developed on the diet, even though the steatorrhoea had not improved. This pain was eased dramatically whenever mild diarrhoea developed after colchicine had been used for several episodes of gout. (The use of diuretics for heart failure was felt to have aggravated his gout.) Occult blood was found in the stools after 4 weeks of the abdominal pain, an epigastric mass was palpated and repeat barium studies then showed jejunal narrowing. A laparotomy was performed by Mr A. G. Parks and a reticulum cell sarcoma resected from the jejunum with many local lymph nodes which were free of neoplasm on section. A postoperative course of abdominal deep X-ray therapy was given (2500 rad by Dr H. F. Hope-Stone). Three months later, lethargy, malaise, wasting and ascites developed and he died within 4 weeks.

Necropsy. There was no local recurrence though the liver and bowel contained multiple small secondary deposits. The mucosa of the small bowel showed subtotal villous atrophy.

Discussion
This patient’s illness presented several problems in management in view of the possible interrelations...
of his various diseases and their therapy. The onset of gout after many years of steatorrhoea has been described (Marlock & Rosenberg, 1944) and the possibility that folate deficiency increases circulating uric acid was explored by Zumoff (1953) when investigating a similar case. Folic acid antagonists certainly raise uric acid levels and this supports the suggestion that gout will be aggravated by steatorrhoea. This man's history suggests that he had gout at least 5 years before the anaemia presented. While malabsorption may well have aggravated his gout, it seems unlikely that it initiated the gout in this case. The 3 years' colchicine therapy could be expected to lead to or to aggravate pre-existing mucosal damage in the small bowel, since intestinal function in the rat has been shown to be impaired by this drug (Levin, 1966; Goulston & Skyrig, 1966). The histological lesions seen in these studies were not, however, identical to those of idiopathic steatorrhoea in man.

Changes in ileal mucosal function in man have been reported on long-term colchicine (Webb et al., 1968), despite the absence of overt gut symptoms. There is one case report of steatorrhoea developing after 10 years of colchicine for gout (Hawkins, 1961). Although it cannot be determined whether or not this man would have developed idiopathic steatorrhoea without colchicine administration, this drug could well have made this worse. It has been shown that the development of neoplastic lesions grafted onto mice can be very significantly inhibited by colchicine therapy (Amoroso, 1935) and improvement of the response of gut adenocarcinoma to radiotherapy in patients on colchicine has been reported (Griem & Malkinson, 1966). It is possible, therefore, that this man's neoplasm (of a type known to be associated with idiopathic steatorrhoea), may have been inhibited during his time on regular colchicine and that the withdrawal of this drug in the hope that small bowel function would improve, may, in fact, have allowed this neoplasm to proliferate at an increased rate.

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References
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Monozygous twins with hypothyroidism and diabetes mellitus

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Summary
Monozygous twins with diabetes mellitus and autoimmune hypothyroidism are described. The onset of the hypothyroidism was simultaneous, but one twin had had insulin-dependent diabetes mellitus for 9 years while the other twin developed insulin-independent diabetes concurrently with the hypothyroidism. Two other siblings had diabetes mellitus and one of them had a goitre, possibly lymphadenoid. The aetiology of autoimmune hypothyroidism is discussed, and evidence is presented which supports suggestions that diabetes mellitus may be an autoimmune disease.

Introduction
Hashimoto's disease occurring in identical twins has been reported on a number of occasions (Irvine et al., 1961; Austoni, Callegari & Borimi, 1964;
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