M. M. BODDINGTON *ET AL.*: CYTOGENETIC ABNORMALITIES IN CARCINOMA-IN-SITU

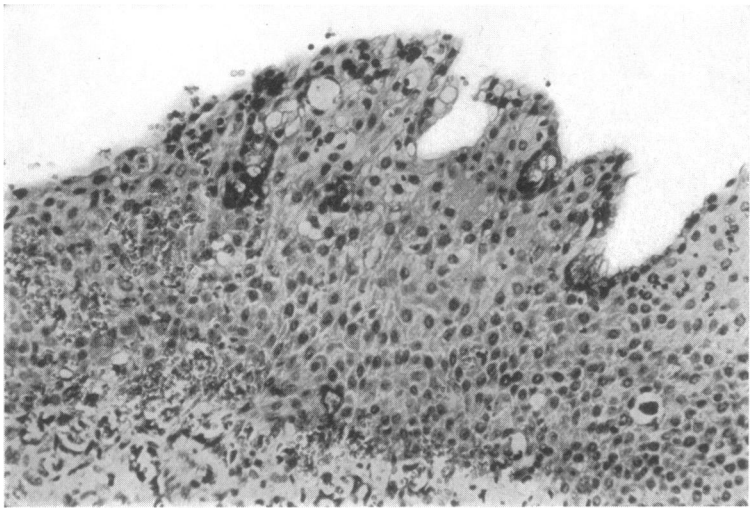

FIG. 4.—Case 9. Section from the posterior lip of the cervix uteri, adjacent to the piece taken for chromosome study. (H. and E. ×175.)

W. A. SOUTER: BOLUS OBSTRUCTION OF GUT AFTER USE OF LAXATIVES

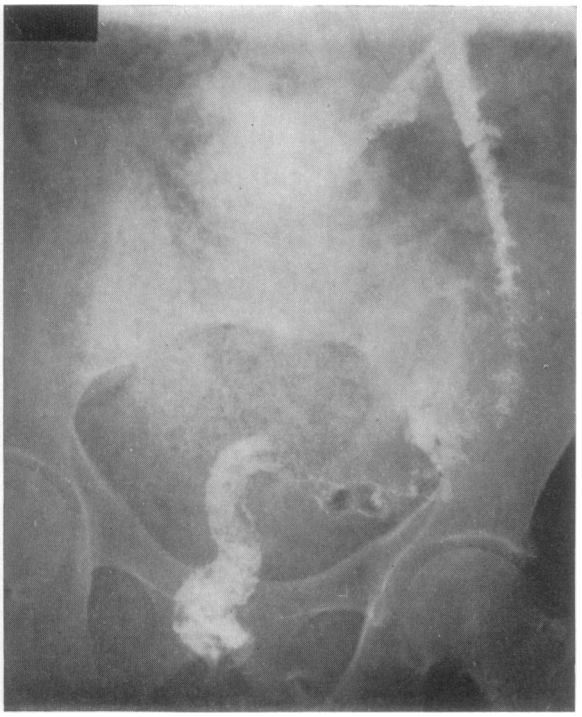

FIG. 1

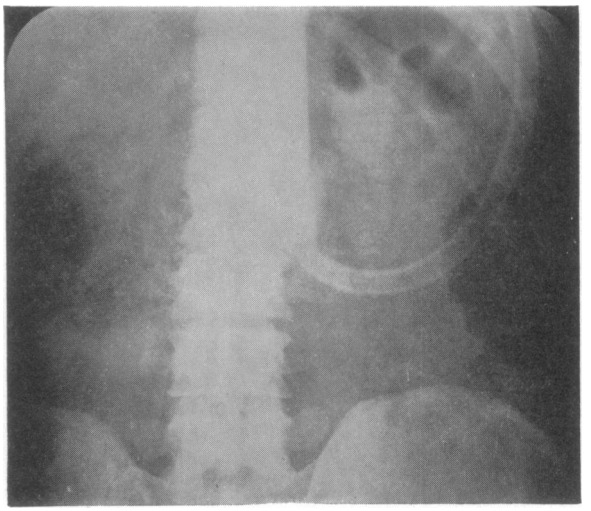

FIG. 2

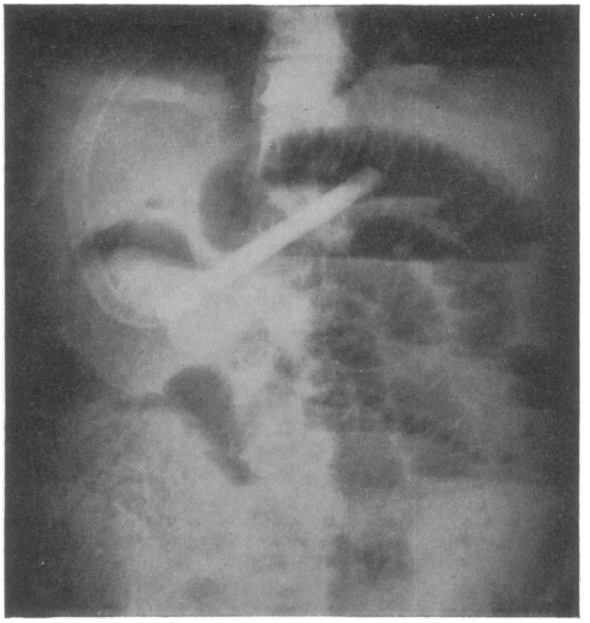

FIG. 3

FIG. 1.—Case 1. Radiograph of abdomen showing immense faecal distension of caecum, ascending colon, and hepatic flexure. The collapsed bowel distal to the colostomy has been outlined by barium for comparison.

FIG. 2.—Case 2. Radiograph showing faecal distension of hepatic flexure.

FIG. 3.—Case 3. Radiograph of abdomen showing multiple fluid levels throughout small bowel together with marked faeculent distension of caecum and ascending colon.

between the haemoglobin levels of 10 patients with renal artery stenosis causing hypertension and 10 control patients.

There can be little doubt that in the above patient the hypertension and the polycythaemia were caused by the effects of severe reduction of renal blood-flow, since after nephrectomy there was a reduction in blood-pressure and return of blood values to normal. Osnes (1958) suggested that the juxtaglomerular apparatus might be the site of production of erythropoietin as well as renin, and recent experimental work (Hirashima and Takaku, 1962) has tended to support this hypothesis. Unfortunately no specific stains for the juxtaglomerular apparatus were carried out, but the present case would support the claim that erythropoietin production can be stimulated by reduction in renal blood-flow rather than by renal parenchymal disease *per se*. There is no indication whether polycythaemia antedated hypertension or vice versa; but certainly the short history does suggest that they probably developed almost simultaneously, and the negative electrocardiogram and chest *x*-ray picture suggest hypertension of short duration.

It is interesting that the features of "primary" polycythaemia were absent—that is, there was no leucocytosis, thrombocytosis, or splenomegaly. Most authors suggest that the absence of these three features should make one consider renal polycythaemia, although the validity of this view is questioned by Brandt *et al.* (1963).

In 1905 Gaisböck described the syndrome which bears his name. He used the term "polycythaemia hypertonica," which was characterized by polycythaemia without splenomegaly but with hypertension, cyanosis, arteriosclerosis, *renal disease*, and often cardiac hypertrophy. It is interesting to postulate that some of these patients may indeed have been cases of renal polycythaemia and hypertension, as in the case of Kurrle (1954) with polycystic kidneys, hypertension, and polycythaemia. Perhaps Gaisböck's syndrome is a true entity, being due to renal hypertension and renal polycythaemia, the latter being "secondary" and not associated with splenomegaly.

Arising from this case we would suggest two practical considerations: (1) where polycythaemia is associated with hypertension renal artery stenosis should be considered as well as other renal causes of polycythaemia, and (2) polycythaemia should be looked for in all cases of renovascular hypertension.

## Summary

A case of renal artery stenosis, hypertension, and polycythaemia in a 54-year-old man is presented. Blood values returned to normal and blood-pressure to near normal after nephrectomy. The mechanism of production of "renal" polycythaemia is discussed in the light of this case report.

We are grateful to Dr. A. Muir, Consultant Physician, Law Hospital, who referred this patient to us.

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# Bolus Obstruction of Gut After Use of Hydrophilic Colloid Laxatives

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[WITH SPECIAL PLATE]

*Brit. med. J.*, 1965, **1**, 166–168

Hydrophilic colloid laxatives are of two types—namely, derivatives of natural gums, such as psyllium, and synthetic products based on methylcellulose. As they have a reputation for being a safe form of medication, it may be salutary to draw attention to a serious, if rare, complication of their use—namely, bolus obstruction of the gut. It is the purpose of this paper to report three such cases of obstruction occurring in patients receiving a laxative based on extracts of certain tropical seeds and marketed under the trade name of I-so-gel. The dose in each case was ½ oz. (15 g.) b.d.

## Case 1

A man aged 64, in whom sigmoid diverticulitis had been demonstrated by barium enema in 1957, was admitted to Derbyshire Royal Infirmary in June 1962 with symptoms and signs of perforated pelvic diverticulitis.

Treatment was effected by pelvic drainage and a defunctioning loop transverse colostomy. Within 48 hours he was passing flatus and some loose faeces from the colostomy. As the stools continued to be profuse and watery in consistence, he was started on I-so-gel medication on the sixth post-operative day. The consistency of the stools thereafter improved and he appeared to make steady progress.

Two days later he complained of some general malaise and nausea. As the colostomy was moving perfectly satisfactorily, no real concern was felt about his general condition. By the following afternoon, however, it was clear that he was far from well. Though the colostomy had again moved satisfactorily, he had developed faecal vomiting and was markedly distended, with a palpable tender mass in the right iliac fossa. A radiograph of the abdomen revealed the surprising finding of gross feculent distension of caecum and ascending colon (Special Plate, Fig. 1). At laparotomy the caecum and colon as far distal as the colostomy were found to contain a vast gelatinous mass of faeces, though no kinking or narrowing of

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the colostomy could be demonstrated. The caecum, which was on the point of rupturing spontaneously, was opened, and with difficulty the semi-solid faecal matter was aspirated. A caecostomy was fashioned and the abdomen closed with drainage. Unfortunately, the patient post-operatively developed a very severe staphylococcal pneumonia which proved fatal.

### Case 2

The patient, a man aged 55, had suffered from attacks of diverticulitis of the sigmoid colon for seven years. In October 1962 he developed a vesico-colic fistula. At laparotomy on 23 October, because of the extent of the inflammatory changes, surgery was restricted to the fashioning of a defunctioning loop transverse colostomy. As the stools remained persistently loose, he was started on I-so-gel on 29 October. Thereafter his progress was perfectly satisfactory until 1 November, when he developed acute colicky pain and vomited twice. An *x*-ray examination of the abdomen taken some seven hours after the onset of symptoms showed faecal distension of the hepatic flexure and proximal transverse colon, together with a few fluid levels in the small bowel (Special Plate, Fig. 2). I-so-gel therapy was withdrawn and intravenous infusion and gastric suction were instituted. A suppository was given on the following day, and a large bowel motion, thoroughly impregnated with I-so-gel, was passed. By 3 November intravenous fluid therapy and gastric aspiration were stopped. Steady progress was thereafter maintained.

That the impaction of the I-so-gel material was the cause of this patient's obstructive episode seems very likely, as he made steady and uninterrupted progress after the passage of the large gelatinous stool.

### Case 3

The patient, a man aged 62, underwent in November 1963 a parasacral excision of a segment of rectum containing a very extensive villous papilloma. His immediate post-operative course was satisfactory, but on the sixth post-operative day a profuse faecal fistula developed through the wound. This was treated by a defunctioning loop transverse colostomy. Though flatus was passed freely in the post-operative period, no solid motion was passed until five days after the second operation. Thereafter profuse diarrhoea set in, and to alleviate this he was started on I-so-gel. Satisfactory colostomy function was obtained thereafter.

On the 10th post-operative day, though the colostomy continued to move well, he developed recurrent vomiting, his abdomen became distended, and the bowel sounds were definitely obstructive in timbre. A radiograph of the abdomen showed numerous fluid levels in the small bowel, while the ascending colon was distended with faeces (Special Plate, Fig. 3). An intravenous infusion was begun and gastro-intestinal suction instituted, using a Miller-Abbott tube. In the light of the successful outcome of conservative treatment in Case 2 it was decided to postpone laparotomy. By the next morning he seemed much improved. Quite suddenly, however, at 5 p.m., he complained of severe upper abdominal pain and rapidly became extremely shocked. There was marked abdominal tenderness and complete absence of bowel sounds. After vigorous resuscitative measures laparotomy was performed. The abdominal cavity was found to be full of gelatinous feculent material, leaking from a large longitudinal tear in an immensely distended caecum. Part of the wall of the latter showed gross ecchymosis with incipient gangrene and had to be excised. The patient's general condition was desperate. As much of the faecal mass as possible was removed by suction, an ileostomy was fashioned, and a very large tube drain was passed down to the ruptured and now defunctioned caecum. His post-operative course was critical for many days, the gross intra-abdominal infection being accompanied by bilateral basal pneumonia.

A very gradual improvement did, however, take place, and about five weeks later a definitive right hemicolectomy was attempted. This further intervention unfortunately proved fatal, the patient dying within 48 hours.

## Survey of the Literature

A survey of the English and French literature has yielded only two case reports comparable to the above. Friedman and Alessi (1954) reported a case where spontaneous retroperitoneal rupture of the sigmoid colon had occurred in a patient who had been on methylcellulose for two weeks. At laparotomy the entire sigmoid was distended to a diameter of 7.5 cm. by an enormous gelatinous mass of stool. There was no organic obstruction in the bowel below this level. It must also be stressed that the patient had been having apparently normal bowel function right up to the time when perforation occurred. Exteriorization of the affected sigmoid loop resulted in the patient's eventual recovery after a stormy post-operative course.

The second case (Lyall and Akey, 1957) presented as a closed loop obstruction between the ileocaecal valve and a carcinoma of the ascending colon in a patient who had been on psyllium (Serutan) off and on for six months and who, just before the onset of his acute symptoms, had been subjected to a rather enthusiastic enema. At operation the closed loop was found to be immensely distended by gelatinous faeces. Treatment was by exteriorization of a loop of ileum, with subsequent recovery.

## Discussion

The obstruction occurring in the above five cases would seem to be directly comparable to the unusual type of acute bolus obstruction described by Shepherd (1960). The cases he described exhibited a form of ileal stasis in which marked distension of the last few inches of the small gut by semi-solid material occurred without there being any demonstrable organic obstruction. I have seen one such case in which an ileal segment 6–8 in. (15–20 cm.) long and lying 6 in. (15 cm.) proximal to the ileocaecal valve was markedly distended by a sludge of partially digested peas. The bolus was not impacted, at least in the normal meaning of that word, but was certainly the cause of the acute obstructive episode.

Obstruction by colloid laxatives would seem to operate in the same manner. Here, however, the mechanical stasis is aggravated by the progressive swelling of the colloid bolus due to its hydrophilic power. When the distension of the gut reaches a certain critical level the bowel becomes incapable of passing the bolus onwards in the normal manner. Perforation will inevitably result if surgical intervention is not undertaken.

It is of great importance, in these patients, not to be beguiled by the maintenance of apparently normal bowel function. In four of the five above cases the absence of complete constipation tended to give a false sense of security in assessing the other clinical indications of developing obstruction. Such bowel evacuation as occurs, especially from a colostomy, is to be likened more to an overflow extrusion of excess gelatinous faeces, rather like toothpaste from a tube, than to normal active defaecation.

## Conclusions

Intestinal obstruction by colloid laxatives must be a very rare occurrence, but the fatal outcome in two of the three cases reported here leaves no doubt regarding the dire nature of the condition when it does develop. Lyall and Akey (1957) point out that colloid laxatives are absolutely contraindicated in the presence of organic disease, and it may be that they are also a very risky form of medication in the post-operative period of abdominal surgery, when peristaltic activity may not have fully returned to normal.

The occurrence of even mild obstructive symptoms in patients who are taking hydrophilic colloid laxatives demands the immediate withdrawal of the drug. Evacuation of the bowel may be stimulated by suppositories, but the giving of enemata may be highly dangerous, as it may precipitate the intra-abdominal catastrophe of spontaneous rupture of the large bowel. If radiological examination of the abdomen shows marked faecal distension of any segment of the large bowel, urgent laparotomy is indicated.

**Summary**

Three cases of intestinal obstruction directly attributable to the use of a hydrophilic colloid laxative have been reported. A survey of the literature has revealed only two similar cases.

The pathological process in this type of obstruction is discussed, and some suggestions are made with regard to its management.

I wish to thank Mr. A. J. Wilson for permission to report the findings in Cases 1 and 3, and Mr. F. G. Hollands for similar permission regarding Case 2. I also wish to acknowledge the help of Mr. Fayers, of the photographic department, in the preparation of the slides.

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# *Medical Memoranda*

## Hepatic Coma due to Liver Metastases

*Brit. med. J.*, 1965, **1**, 168

Hepatic coma occurs as a complication of almost any serious diffuse liver disease, such as cirrhosis and acute hepatocellular necrosis. Sherlock (1958) in 108 cases of hepatic coma saw no hepatic malignancy, while Willis (1960) in 120 cases of hepatic coma from Singapore saw eight cases of hepatoma and one case of metastasizing carcinoma of the stomach.

### CASE HISTORY

A man aged 59 was admitted on 19 August 1963 after seven weeks' upper abdominal pain. Previous investigations revealed no abnormal signs. The results of a barium-meal examination and radiographs of the spine and chest were normal. A diagnosis of peptic ulcer had been made, but despite a gastric diet and antacids pain increased. On admission he complained of anorexia and a loss of 2½ st. (15.9 kg.) in two months. There was no nausea, vomiting, haematemesis, melaena, or any alteration of bowel habits. Examination revealed a slightly distended abdomen with some free fluid. The liver was hard, irregular, slightly tender, and was palpable 5 cm. below the ribs and 11 cm. from the xiphisternum. The sclerae were icteric. A small polypoid mass was found in the rectum. Biopsy and histology revealed a benign polyp. The results of further physical examination were normal.

The results of investigations on admission were as follows: haemoglobin 91% (13.2 g./100 ml.), W.B.C. 11,400/c.mm., E.S.R. 45 mm. in one hour (Westergren), blood urea 20 mg./100 ml., serum sodium 117 mEq/l., potassium 3.7 mEq/l., chlorides 93 mEq/l., serum bilirubin direct positive (3.6 mg./100 ml.), alkaline phosphatase 40 units, flocculation tests were normal, S.G.O.T. 80 units/ml., total serum protein 5 g./100 ml. (albumin 3.9 g., globulin 1.1 g.), stool benzidine was negative, prothrombin concentration 12%. Results of a barium enema were negative.

His condition deteriorated in the first week (26 August) and he developed mild peripheral circulatory failure, but no drop of blood-pressure (140/90–120/80 mm. Hg). The left foot became cold and blue, arterial pulsations were absent below both popliteals, and he became more jaundiced and apathetic. Biochemical investigations showed serum bilirubin 10 mg./100 ml., serum alkaline phosphatase 72 units, normal flocculation tests, S.G.O.T. 29 units/ml., serum cholesterol 130 mg./100 ml., serum proteins were unaltered. Next day serum bilirubin was 23 mg./100 ml., alkaline phosphatase 48 units, S.G.O.T. 420 units/ml., blood urea 115 mg./100 ml.

On 27 August he became disorientated and drowsy, fetor hepaticus was first noticed, and flapping tremors of outstretched hands were demonstrated. Severe hepatic coma developed with intense jaundice, and test results were serum bilirubin 23 mg./100 ml., alkaline phosphatase 48 units, flocculation tests normal, S.G.O.T. 420 units/ml., blood urea 115 mg./100 ml., while serum electrolytes and bicarbonate remained unaltered. Despite treatment with oral neomycin, withdrawal of protein, and maintenance of fluid and electrolyte balance, he became comatose and died 11 days after admission.

At necropsy Dr. Manners (consultant pathologist) demonstrated metastases in the liver. There were massive, multiple carcinomatous nodules with central necrosis, and macroscopically there was little remaining liver tissue. Lungs showed scattered small metastases beneath the pleurae. The body of the pancreas was completely replaced by carcinomatous tissue extending into the tail, but the head was normal. The brain was carefully dissected but showed no metastases. The kidneys were normal.

### COMMENT

The patient died of hepatic coma due to massive liver metastases from a primary carcinoma of the pancreas. This pathological sequence is an unusual occurrence in the United Kingdom. Watkinson (personal communication, 1963) has never seen this, since the majority of patients with metastases in the liver die from other causes before complete failure of liver function. Approximately 85% of the liver tissue was destroyed by neoplasm in this patient with little constitutional upset until the last two months. In chronic hepatic disease such an accelerated course of hepatic coma is unusual without severe precipitating factors—such as massive gastro-intestinal bleeding (occult-blood tests on the patient were negative), hypotension (his blood-pressure was maintained above 120/70 mm./Hg), infections (none were found at necropsy), electrolytic disturbance (serum sodium was consistently low—117 mEq/l., and serum potassium was from 3.7 to 5.8 mEq/l.), or shock (a mild degree observed three days before death). Rapid increase in serum alkaline phosphatase and bilirubin suggested acute massive hepatocellular necrosis with obstructive jaundice. Rapid elevation of S.G.O.T. to 420 units/ml. in hepatic coma suggested Budd-Chiari syndrome, but the necropsy disproved this. Pryse-Davies and Wilkinson (1958) stated that about 50% of patients with liver metastases show slightly raised S.G.O.T. (ranging from 35 to 100 units). Levels exceeding 100 units are found only in patients in whom liver necrosis accompanies massive liver metastases. The present findings could indicate that massive liver metastases alone could cause marked elevation of S.G.O.T.

We would like to thank Dr. T. Manners and Dr. C. Jobling, consultant pathologists, and their staff for all the biochemical investigations.

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