

The Peutz-Jeghers Syndrome

A Report of 3 Cases

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SUMMARY

Three cases of the Peutz-Jeghers syndrome are reported and the literature is reviewed. The difficulties in the management of these patients are described and the importance of radiology and endoscopy is emphasised.

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In 1921 Peutz¹ described the unusual syndrome of familial gastro-intestinal polyposis and mucocutaneous pigmentation, although cases had been documented previously.² In a review in 1949 Jeghers *et al.*³ emphasised the dominant pattern of inheritance of the condition. Over 300 cases have now been reported,⁴ including a family from Johannesburg.⁵ This report describes 3 patients who have been seen at the Gastro-intestinal Clinic at Groote Schuur Hospital since 1970.

CASE REPORTS

Case 1

A 29-year-old White woman, born in England, had been diagnosed as having the Peutz-Jeghers syndrome in early childhood. Her father and 2 of her 4 brothers were known to have the disease. She had had episodes of rectal bleeding at the ages of 10, 18 and 21 years, and had undergone surgery for resections of polyps on those occasions. She was referred to us in 1975, with a 1-year history of intermittent rectal bleeding, and after she had been given four blood transfusions at another hospital. Colicky pain in the left upper quadrant of the abdomen had recently become marked, with attacks occurring every week. During these attacks, the patient noticed a sausage-shaped abdominal mass, which disappeared when the attack resolved after 4-8 hours, with the passage of flatus.

The patient was fair-skinned, with striking dark pigmentation on the lips, buccal mucosa, face and eyelids, as well as on the bases of the thumbs and the dorsa of the feet, where pigmentation has not often been described. The patient's systems were normal. There was occult blood in her stools and she had an iron deficiency anaemia with a haemoglobin concentration of 10 g/100 ml. The erythrocyte sedimentation rate was normal.

Barium studies revealed clusters of polyps in the stomach, duodenum, jejunum, ileum, and colon (Figs 1 and

2). Several very large jejunal polyps caused intermittent intussusception during the radiological examination, with production of colicky pain. Oesophagogastroduodenoscopy showed clusters of small polyps, both sessile and pedunculated, in the cardia, antrum and duodenum. No polyps were found in the oesophagus. Biopsy of the polyps revealed normal gastric and duodenal mucosa. The patient declined to undergo colonoscopy.

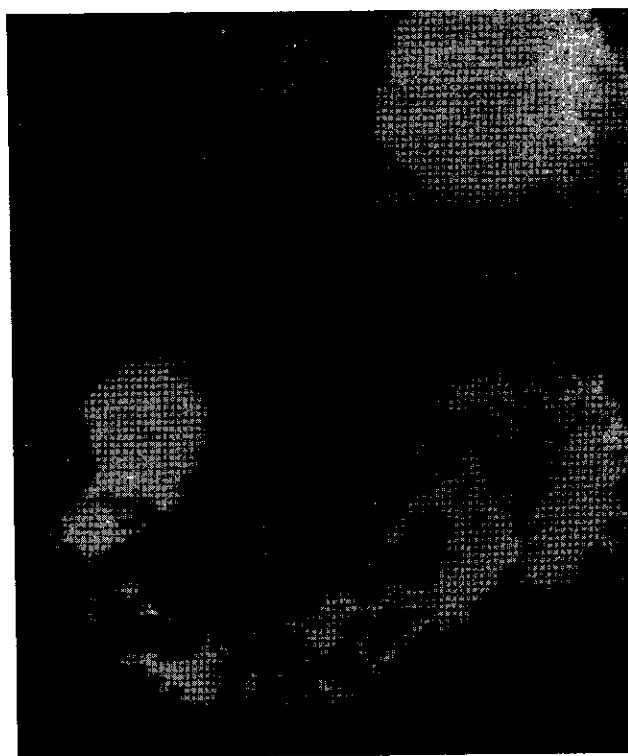


Fig. 1. Clusters of polyps in the duodenum.

The patient was given a transfusion of 2 litres of blood, and antispasmodic drugs for the pain, which settled rapidly. Iron turnover studies using ⁵¹Cr revealed that the gastro-intestinal blood loss was 16 ml/24 hours. A total-dose iron infusion was given.

Six months later the patient was feeling tired, her haemoglobin concentration had dropped to 8 g/100 ml, and she was having mild attacks of colic once a fortnight. She was again given a transfusion. Because of the extent of the lesions and the difficulty in establishing the exact site of the bleeding and intussusception, it was decided to defer surgery until it had become absolutely necessary.

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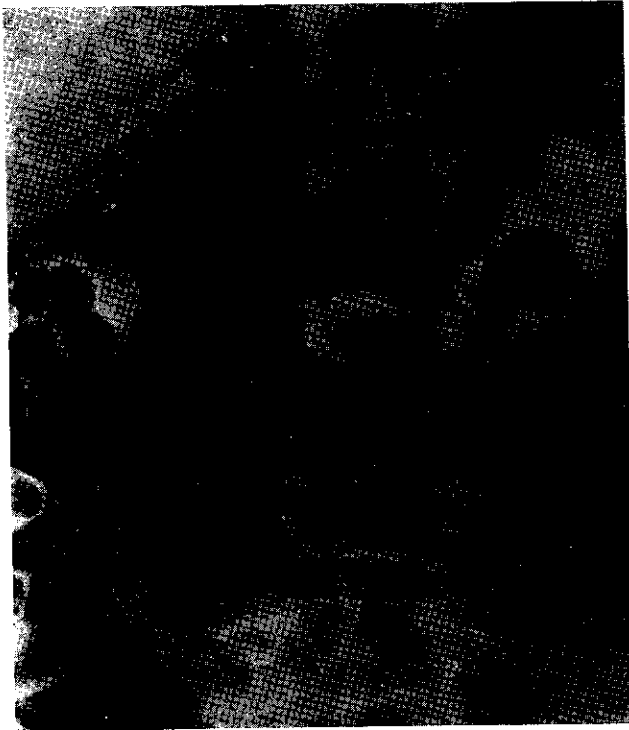


Fig. 2. Colonic polyps.

Case 2

An 18-year-old Coloured woman from Namaqualand was referred to the Gastro-intestinal Clinic in 1972. She had developed intestinal obstruction 3 months previously, and three polyps were removed from the ileum at surgery. Since the patient had been quite asymptomatic before the obstruction developed, and as there was no family history of the condition, she was regarded as a new mutant.

The patient had melanin pigmentation on the lips, buccal mucosa and face (Fig. 3), but there were no other abnormal physical signs. Her haemoglobin concentration was 12 g/100 ml and her erythrocyte sedimentation rate was normal. Her serum iron level was reduced, at 35 µg/100 ml.

A barium enema was normal, but a barium meal examination revealed gastric and ileal polyps.

She developed acute abdominal pain while in the ward, but this subsided within a day on conservative treatment. Oral iron therapy was prescribed. To our knowledge she has remained well since her discharge from hospital.

Case 3

A 34-year-old White woman had melanin spots on the buccal mucosa, lips and pulps of the fingers. Her family history was negative. She had had intussusceptions at the ages of 12 and 16 years. These had been reduced at surgery and several ileal polyps had been removed. She again presented in an acute state in 1971 and at surgery a jejuno-jejunal intussusception was reduced, and several large polyps were removed by enterotomy. Two large polyps



Fig. 3. Pigmentation on the buccal mucosa and lips.

could not be removed from the unprepared colon. Histologically the excised polyps had an adenovillous structure, composed of fronds of small-intestinal epithelium on a core of smooth muscle. Subsequent barium studies confirmed the presence of polyps from the duodenum to the terminal ileum, as well as two colonic polyps. There were no gastric polyps.

Since there was uncertainty about the nature of the colonic polyps, she was referred for colonoscopy during which a large polyp with a broad base was found in the descending colon just below the splenic flexure. In the upper ascending colon a fairly large multilocular polyp on a broad base was seen. Since polypectomy equipment was not available in 1972, only biopsy specimens were taken through the colonoscope. These revealed well-differentiated mucus-secreting colonic gland acini, with no signs of malignancy.

It is of interest that anaemia was not a feature of this patient's illness.

DISCUSSION

The Peutz-Jeghers syndrome is defined as the triad of mucocutaneous pigmentation, gastro-intestinal polyposis and, in most cases, an autosomal dominant pattern of inheritance.³

This syndrome may sometimes, though rarely, include urinary, bronchial and nasal polyps, clubbing, skeletal anomalies, and ovarian cysts and tumours.⁶ Recently a patient with pigmented oral papillomas has been reported.⁷

The mean age at presentation is the third decade, with one third of patients being diagnosed under the age of 15 years. The incidence in the two sexes is equal, and a positive family history is elicited in 70% of cases, the remainder being new mutations.⁸ Cases have been reported from many racial groups.⁴

The pigmentation appears as early as the first year of life and the distribution is typical, as in our patients.

After puberty the cutaneous pigmentation tends to fade in many patients, while the buccal pigmentation persists and is the more useful diagnostic feature.⁹ The pigmented areas are discrete macules, 2-5 mm in size, and brown or black in colour. The pigment is melanin.

The distribution of the polyps is as follows: in the jejunum in 64% of patients, ileum 52%, rectum 30%, colon 29%, stomach 24%, duodenum 16%, and appendix 3%. The polyps tend to occur in clusters, but a few patients have had only a solitary polyp.⁸ The polyps may be as large as 7 cm, as in our first patient, and they are most commonly pedunculated. Morson and Dawson¹⁰ believe that the polyps result from the overgrowth of the muscularis mucosae, producing a tree-like branching which is covered with normal mucosa. The polyps develop later than the pigmentation, and appear in crops in different parts of the bowel rather than simultaneously. The polyps are strictly hamartomata.

The symptomatology is related to the polyps and not to the pigmentation. Our patients demonstrated the typical symptoms of anaemia and intussusception. The former is the more common, although both often coexist. The blood loss is occult in 25% of patients, while another 25% may have rectal bleeding or melaena. Haematemesis from gastroduodenal polyps is less common.⁸ The episodes of intestinal obstruction tend to be intermittent. This is related to the characteristic growth spurts of the polyps, interspersed with quiescent periods.

Present-day methods of contrast radiology, angiography and endoscopic viewing of the gastro-intestinal tract allow accurate diagnosis and localisation of the polyps. It should be noted that sigmoidoscopy will detect polyps in 20% of affected patients.

The management of these patients is difficult because of the extreme variability and unpredictability of the clinical course.⁶ The best policy is a conservative one. The acute problem of intussusception usually settles spontaneously within a few hours. If surgery is required, it should be limited, if possible, to reduction of the intussusception, rather than resection. Otherwise, the history of the syndrome becomes one of repeated operations, with increasing hazards for the patient. Surgery should therefore be delayed as long as possible. As in 2 of our patients, there may be phases of abdominal trouble, followed by short or long periods of quiescence. It has been shown, however, that new crops of polyps are constantly appearing throughout life.⁹

The management of blood loss consists of adequate iron replacement, with blood transfusion when necessary. It may be very difficult to locate the polyps which are causing the blood loss, especially slow blood loss, and more than one polyp may be involved. Since the problem may

be impossible to resolve at surgery, upper gastro-intestinal endoscopy should always be performed first, and if any one polyp is seen to be bleeding or to have bled recently, then it may be removed by endoscopic polypectomy.¹¹ If the patient has rectal bleeding, then colonoscopy and polypectomy of any suspicious-looking polyps should be undertaken. During an acute bleed angiography may help to locate the site of bleeding, and an infusion of pitressin may be given to try to avoid surgery. Blood loss may be intermittent or continuous and can remit completely.

There is no simple answer to the question of malignant change in this syndrome. Jeghers *et al.*³ stressed the apparent malignant potential of colonic and small-intestinal polyps, while Dormandy⁶ held a conflicting view. Difficulties with the interpretation of the histology of polyps has led to erroneous diagnoses of malignancy in many patients.¹⁰ Reid¹² recently extracted 14 case reports of Peutz-Jeghers syndrome with metastases from the literature, and found primary lesions in the stomach and duodenum (9 patients), jejunum (1), ileum (2), colon (1) and rectum (1). The high incidence of gastroduodenal carcinoma is in contrast to the reduced incidence of polyposis in the area.⁴ The increased risk of carcinoma in Peutz-Jeghers patients is 2-3%. While prophylactic surgery is neither feasible or indicated, careful follow-up, including endoscopic and radiological examination, is mandatory.¹²

It is important to examine the families of affected persons, and to explain the prognosis and genetics of the conditions to them. Patients with the mutant form of the disease have the same course and subsequent pattern of inheritance as patients with the familial syndrome. There is at present no method for antenatal diagnosis of the Peutz-Jeghers syndrome.

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The Curative Limb of the Paradox

We have cleared the air slightly if we agree that the traditional dogma of the infinite value of the individual has acquired some definable exceptions. The application of scientific technology has already reduced some of the traditional implications of the dogma to absurdity, e.g. the maintenance of artificial respiration for an individual with irreversible brain-damage when there is no meaningful life. Other advances in scientific and medical technology will certainly force us into the recognition that other traditional implications are wrong, e.g. that the recently fertilised ovum or even the early fetus is an 'individual'.

Nevertheless, to me, the dogma of the infinite value of the individual is one of the highest expressions of our civilisation and of our medical idealism. It has served us well since before the days of Hippocrates. It is a source of compassion without which there is no satisfactory medical practice. That scientific advances should show up some of its tacitly accepted implications as out of date, does not destroy the dogma. But it does demand its revision in certain respects, as for example, in the acceptance of definable exceptions to its applicability.

In discussing the nature of a paradox I quoted as a 'received opinion' or dogma the proposition that 'individual human life is infinitely valuable'. I am now proposing the addition of a few words so that the dogma becomes 'individual human life, with certain definable exceptions, is infinitely valuable'. The contrary tenet of 'the greatest good for the greatest number' is now less clearly contrary, and we may be on the way towards a solution of our paradox 'for our time'.

The Preventive Limb of the Paradox

Can the apparently insatiable demands of this other limb of the paradox be scaled down? I believe that they can be. Such necessary action as the provision of nutritious food, housing, hygiene, etc. is in no sense a medical responsibility. The shortages are determined by our socio-economic system, which in turn depends on our politics. The programme of preventive medicine should rightly begin only after all the physical, educational and other needs of the whole population have been provided. It should then be the task of preventive medical services to ensure through health education their proper use, i.e. consumption of the right kinds of food, control of population pressure, the application of the principles of cleanliness and hygiene. This is largely a task for non-medical personnel acting under the direction of preventive medical practitioners. The latter should not have to spend time trying to persuade the government that the population or any part of it needs more or better food. The requirements of millions of people of any class or colour are laid down in tables of nutrients which are easily translated into those foods which the country can most easily grow or rear. This should be the work of agronomists, not of medical practitioners. Unfortunately our preventive medicine practitioners will for a long time have to keep up the hue and cry against bad government.

Similar arguments apply to housing, hygiene and general education.

CONCLUSION

Although I cannot pretend to have resolved the paradox, I have suggested some ways in which the apparent competition between preventive and curative medicine for national funds and medical personnel can be relieved. These measures depend upon a medical consensus between all branches of the medical profession and continued mutual understanding and respect between its curative and its preventive wings. I believe that a recapitulation of principles and priorities upon which a consensus can be based will also serve as a summary of my answer to this particular medical paradox.

Principles and Priorities

1. The historic 'dogma' of the infinite value of the individual must be reaffirmed again and again by the medical profession and supported by the community. Its emerging threat to engulf our resources can be neutralised by defining exceptions.

2. The comparatively new specialised group of public health practitioners or practitioners in preventive medicine must support their curative or clinical colleagues in this first principle and must help to develop machinery for medical consensus on principles, priorities and exceptions.

3. They must, as the mouthpieces of the medical profession to government and parliament, analyse the problem of curative versus preventive medicine, and so formulate a public consensus.

4. This consensus must recognise that the provision of most of the requirements for health such as food, housing, hygiene and general education, is a matter of good government upon which preventive medical services can build through medical education. Doctors should not have to spend their specialised time urging government to provide these physical necessities.

5. Both the curative and the preventive medical services can be diluted with specially trained medical and health auxiliaries so that the long and expensive training of the medical practitioner can be used where it will always be most needed, namely in the direct or indirect care of the infinitely valuable individual in the context of his home and community.

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