LETTERS TO THE EDITOR

Colorectal neoplasia in acromegaly: the reported increased prevalence is overestimated

EDITOR,—We read with interest a recent paper by Jenkins *et al* (*Gut* 1999;**44**:585–587). However, we are concerned with their assertion that acromegaly is a high risk condition for colorectal neoplasia, and their recommended advice on colonoscopic screening and surveillance. Jenkins and colleagues had found that 33 (26%) of 129 patients (updated to 155), treated for acromegaly at St Bartholomew's Hospital, had at least one adenoma and six (5%) had adenocarcinomas.[1]

We feel that the choice of controls in this study was inappropriate because although there is no ideal control population, the authors used comparative data on the incidence of adenomatous polyps from only two cohorts: a published study of left sided adenomas,[1a] and colonoscopic records of all patients without acromegaly that had been examined by one of the authors. Matched for age (and side), the relative risk of adenomas was higher in patients with acromegaly when compared with data from the first study, but not when compared with data from the second.

In an attempt to estimate more appropriately the prevalence of adenomas in the normal population, we have carried out a comprehensive review of the literature on adenoma prevalence per decade of life from which two groups of studies emerged. The first group comprised six necropsy studies (n=2914), and the second comprised three screening colonoscopy studies of asymptomatic average risk volunteers (n=720, table 1).[2–13] With the exception of those patients between 50–59 years old, the prevalence rates of adenomas in patients with acromegaly are remarkably similar to those for individuals in screening colonoscopy studies, and less than those from necropsy studies. We find no evidence that patients with acromegaly are at increased risk of developing adenomas.

For colorectal cancer, Jenkins and colleagues[1] used comparative data from a regional cancer registry and estimated increased relative risks of 13–90. These figures are exaggerated in comparison with studies using standardised age and sex adjusted population data. Ron and colleagues[14] reported 13 colonic cancers in 1041 male veteran acromegalics (standardised incidence ratio (SIR) 3.1; 95% CI 1.7 to 5.1) and, using uniform methods of ascertainment of cases and comparison groups, Orme and colleagues[15] found 12 cases of colonic cancer in a larger study of 1362 patients with acromegaly (SIR 1.68; p=0.06).

There are approximately 1500 patients with acromegaly in the United Kingdom, and it would seem sensible for strategies for large bowel screening to be evidence based. The data given above suggest that the reported increased prevalence of colorectal neoplasia in patients with acromegaly is overestimated and thus, the recommendations given by these authors for early colonoscopic screening and subsequent regular surveillance above that of the normal population cannot be supported by the evidence currently available.

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1 Jenkins PJ, Fairclough PD, Richards T, *et al*. Acromegaly, colonic polyps and carcinoma. *Clin Endocrinol (Oxf)* 1997;**47**:17–22.
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Reply

EDITOR,—Our conclusion that acromegaly may be a high risk condition for the development of colorectal cancer is based not only on our own data (we have now discovered 10 patients with cancer from approximately 210 patients who have had a colonoscopy), but also on those of several other studies. In the prospective studies by Archambeaud-Mouveroux and colleagues[1] and Ituarte *et al*,[2] cancers were discovered in 12.5% and 20% respectively of patients with acromegaly. Retrospective epidemiological surveys may have failed to show an increased risk of cancer because of differences in methodology—for example, in one study case ascertainment depended upon death certificate entries and cancer registrations which may have been incomplete.[3] Furthermore, these studies did not discuss the relevance of the age of the patients. The mean and range of age during follow up were not stated,[3] and in another study the mean age of the patients at diagnosis of acromegaly was 52 years old and that at follow up was only 61 years old.[4] Our results clearly show that colorectal cancer is a late complication of acromegaly, as the mean age of our affected patients was 67 years old.

The situation for adenomas is less clear and we agree that there is a lack of proper control groups. However, many of the prevalence figures given by Renehan and colleagues were obtained from necropsy studies and therefore cannot provide a valid comparison because the resected bowel was thoroughly washed on up to three occasions, repeatedly examined under magnification in optimal lighting, and lesions as small as 1 mm were classified as adenomas. This gives an increased prevalence of the disease compared with incidences of neoplasia revealed by colonoscopic screening. Furthermore, these studies were of populations with very different demographic, socioeconomic and dietary influences, which are factors known to influence the incidence and prevalence of colonic adenomas. By contrast, our control groups were taken from similar populations to the patients with acromegaly, and in one group, the colono-

Table 1 Prevalence (%) of adenomatous polyps by decade of life

		Age group (years)					
	n	*<40*	*40–49*	*50–59*	*60–69*	*70+*	*Total*
*Autopsy studies[2–4]**							
Blatt[5]	446	0	21	34	34	44	39
Arminski and McLean[6]	1000	20	19	27	35	46	33
Stemmermann and Yatani[7]	202	43	–	72	59	63	62
Rickert and colleagues[8]	518	–	17	35	56	58	47
Vatn and Stalsberg[9]	445	–	6	23	31	46	33
Jass and colleagues[10]	303	3	11	33	30	36	24
Colonoscopy studies in screened populations							
DiSario and colleagues[11]	119	–	–	21	45	53	41
Lieberman and Smith[12]	105	–	–	28	41	58	41
Rex and colleagues[13]	496	–	–	20	33†	31‡	26
Weighted averages							
Necropsy studies	2914	9	15	31	40	48	37
Screening studies *v*	720	–	–	20	38	37	31
Acromegalics (Jenkins and colleagues[1])	129	8	12	29	36	39	26

*Three other autopsy studies (Correa and colleagues[2]; Eide and colleagues[3]; Williams and colleagues[4]) were considered but not included as the age bands in these studies did not correspond with those used by Jenkins *et al*.[1]
†Patients aged 60–64; ‡patients aged 65–75.

scopies were performed by the same operator. A comparison between these groups showed a significant increase in the relative risk of adenomas in patients with acromegaly, although we accept that this risk is not as high as that for cancer, and this raises intriguing questions about the causes of colorectal cancer in patients with acromegaly. It is possible that the adenoma–carcinoma sequence in patients with acromegaly differs from that in the non-acromegalic population, or that the cancers arise de novo without an adenomatous stage.

We fully concur that strategies for large bowel screening should be evidence based. Our initial screening recommendations are based on current data and will be modified according to our continuing prospective studies. Subsequent strategies might take into account not only the age of the patients but also the activity of their acromegaly, because preliminary data suggest that those patients in whom the disease is more active (elevated serum IGF-I) are more likely to develop adenomas. Until more multicentre studies involving larger numbers of patients undergoing careful and total colonoscopy allow the risks to be better quantified, it seems prudent for patients to undergo colonoscopic screening every five years, or every three years if an adenoma is found.

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Diversion colitis: a trigger for ulcerative colitis in the instream colon

EDITOR,—We published in 1999, to our knowledge, the first description of diversion colitis appearing to trigger instream ulcerative colitis (*Gut* 1999;**44**:279–282). We have recently encountered a fourth patient with the same rare condition.

A 66 year old non-smoking white man presented in 1997 with large bowel obstruction. His mother had died of colorectal carcinoma at the age of 71 years. There was no family history of inflammatory bowel disease. An instant barium enema revealed obstruction at the level of the mid-sigmoid colon with radiological features suggestive of sigmoid carcinoma. The patient underwent a Hartmann's procedure with colostomy. The resection specimen showed a Dukes's B carcinoma of the sigmoid colon with no evidence of colitis. The patient then received adjuvant chemotherapy consisting of 12 weeks of infusional 5-fluorouracil. Eighteen months later he had a colonoscopy through the rectal stump and the stoma. The colon proximal to the colostomy looked normal but the rectal stump appeared mildly inflamed. Biopsy samples of the rectal stump were consistent with active colitis and a putative diagnosis of diversion colitis was made. Treatment with steroid enemas was effective. Six months later the patient developed bleeding and mucus discharge through the colostomy for the first time. Stool cultures including analysis for *Clostridium difficile* were negative. Colonoscopy through the colostomy to the limit of the examination revealed severe, active colitis. The biopsy samples on this occasion were consistent with ulcerative colitis with chronic inflammation in the lamina propria, cryptitis and crypt abscess formation. The patient responded well to treatment with oral corticosteroids and mesalazine.

We have postulated previously that the development of ulcerative colitis may be initiated by inflammation of another aetiology at an anatomically discontinuous site of the bowel. This description of an additional case would support the hypothesis that diversion colitis might be one such trigger for ulcerative colitis. The mechanisms underlying this remain speculative but may involve the recruitment of activated lymphocytes from the diverted colon to the phenotypically similar vascular endothelium of the instream colon.

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Gastric antral vascular ectasia and its relation with portal hypertension

EDITOR,—Spahr and colleagues recently published a case series which described the poor response of a haemorrhage from gastric antral vascular ectasia (GAVE) to portal decompression by insertion of a transjugular intrahepatic portosystemic shunt (TIPS) (*Gut* 1999;**44**:739–742). However, the authors' claim that this indicates the absence of a relation between GAVE and portal hypertension is seriously flawed. The failure of this condition to respond to portal decompression cannot exclude a primary role for portal hypertension in the pathogenesis of the disorder. Furthermore, this study would have been more informative if aortoportography—that is, superior mesenteric and splenic angiography with venous phase imaging, had been performed in order to determine the pattern of portosystemic shunting before and after TIPS insertion. The authors have not addressed the question of whether portosystemic shunts supply the vascular lesions of GAVE; it would have been helpful if they had performed angiography in at least some patients after the TIPS procedure to confirm that blood flow had been restored to the liver from all portal vein tributaries, as it cannot be assumed that normalisation of portal vein pressure will completely ablate all preformed portosystemic shunts. Finally, it was not stated whether splenic vein thrombosis was excluded in all patients. If present, this could have caused ongoing segmental portal hypertension which could not have been expected to respond to TIPS insertion.

It is evident from previous case series, which suggested that GAVE might occur without portal hypertension, that some did not exclude portal hypertension in their patients.[1] A rigorous exclusion of portal hypertension would require liver biopsy and/or measurement of the portocaval pressure gradient, together with imaging of the portal venous system in order to exclude portal or splenic vein thrombosis. The importance of this is illustrated by the series of patients with GAVE after bone marrow transplantation, cited by Spahr *et al*.[2] In this series, all patients with available liver histology were found to have hepatic veno-occlusive disease, a well recognised cause of portal hypertension. A further link between GAVE and autoimmune disorders may be explained by extrahepatic or non-cirrhotic portal hypertension in some of those patients.[1 3] The possible association of GAVE with chronic renal failure cited by Spahr *et al* presumably refers to an early series of patients with diffuse haemorrhagic gastric lesions in the absence of any overt liver disease; however, these lesions would probably not be classified as GAVE by current criteria, therefore this association is questionable.[1 4]

Thus, the pathogenesis of this interesting disorder remains uncertain but the strong association of portal hypertension (whether overt or covert) with the majority of cases of GAVE means that this is likely to be a key contributory factor.

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Reply

EDITOR,—We appreciate Dr Fisher's comments on our recent paper, in which we provided evidence against the role of portal hypertension in the pathogenesis of GAVE. Firstly, lowering or normalisation of portal pressure was not followed by improvement in either the endoscopic findings or the rate of transfusions needed for recurrent bleeding. In this case series, one patient had to be transfused repeatedly for five years despite a patent surgical end to side portocaval shunt (portocaval gradient 2 mm Hg). Furthermore, the degree of residual portal hypertension was not correlated with clinical and endoscopic evolution in patients treated by TIPS. Interestingly, the only patient that responded to TIPS still had an increased gradient after the treatment (14 mm Hg); in this patient, the favourable outcome of GAVE was parallelled by a noticeable improvement in liver function.

One study has suggested that arterioportography may have a diagnostic value in GAVE.[1] However, typical findings were shown on the arterial phase (hypervascularisation of the antrum and early arteriovenous shunting), and none of our patients had a coeliac axis arteriogram. On direct portography, it was impossible to show dilated mucosal blood vessels in the antrum. In all non-responders, bleeding recurred despite a

reversed portal blood flow observed after TIPS or surgical shunt. In addition, splenic vein thrombosis was not observed in any of our patients, obviously because such a finding would contraindicate TIPS, which is not a treatment of segmental portal hypertension. Therefore, we are still convinced that portosystemic shunting and liver function could both influence liver metabolism of the vasodilating substances that contribute to the pathogenesis of GAVE, whereas portal hypertension alone has no influence.

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BOOK REVIEWS

ABC of Colorectal Diseases. 2nd edn. Edited by Jones DJ. (Pp 109; illustrated; £18.95.) London: BMJ Books, 1999. ISBN 0-7279-1105-8.

The series of ABC articles in the *BMJ* is always enjoyable. This book brings together articles that were published several years ago and were well received in the first edition of 1993. These articles have been updated and eight additional chapters have been added on constipation, diarrhoea, irritable bowel syndrome, inflammatory bowel disease, anal cancer, colorectal trauma, tropical colonic diseases, and paediatric problems.

The editor (DJ Jones) has turned vision into reality to produce a basic and useful coloproctology text. He has also worked hard as he has written half of the chapters (nine solo and three shared). The authors of the first chapter on Anatomy and Physiology of the Colon, Rectum and Anus are Mr Hill and Professor Irving: the former runs the immensely successful M62 Coloproctology Course and the latter needs little introduction and is President of the Association of Coloproctology of Great Britain and Ireland. Not surprisingly they combine forces to produce three pages with all the basic facts and 10 superb illustrations.

Chapter 2 takes the reader through examination (I appreciated time spent on how to perform a rectal examination) and tests from proctoscopy to colonic transit studies. Chapters 3–23 then cover all aspects of colorectal disease before the final chapter on drugs. Each chapter is concise (3–6 pages) and packed with really good photographs and illustrations. All credit to the various departments of medical illustration involved in this venture!

For me the prize chapter is on inflammatory bowel disease: the authors (Mr Scott and Professor Thompson) bridge the gap between a presentation of the vital facts and the thorny management issues so eloquently.

Who should read this book? Let us first consider the exciting and challenging times that we are living in. At long last colorectal cancer is receiving due recognition from the Government, primary care physicians, managers, and the general public. Attention is upon us and our daily work load is ever increasing. How encouraging that at a time like this the arms of colorectal surgeons from Penzance to John O'Groats have been or are soon to be strengthened by the colorectal nurse specialist. This book will be very useful to them.

Who else will find this book useful? Well certainly medical students, trainees in gastroenterology and surgery, and our general practitioner colleagues. And dare I also suggest gastroenterologists and colorectal surgeons. Not because we'd learn anything of course. Actually, that's rubbish because I was full of the new facts I learnt over this last weekend and I was educating everyone in theatre this Monday afternoon! I definitely will be using this book in preparing for both undergraduate and postgraduate teaching.

A LEATHER

Key Topics in Gastroenterology. Edited by Anderson SHC, Davies G, Dalton HR. (Pp 286; £21.95.) Oxford: Bios Scientific Publishers, 1999. ISBN 1859962815.

Simon Anderson has put a lot of work into this book. He writes clearly, concisely and well. But, does the world need another handbook on gastroenterology?

What is the role of professional books, large or small, nowadays? Down at your local bookshop, Delia Smith will tell you how to make an omelette, Charlie Dimmock how to build that water feature; there's no real alternative. So, in the hospital who will tell you about haemachromatosis? The professional book has always held pride of place as the font of all knowledge. Owning such book gave peace of mind, but this was at a hefty price and that has always been the problem. How often will people keep paying the ransom for the latest edition, or the newest series? It is not surprising that cutting edge books on cimetidine still adorn many bookshelves. Time to mention the "I" word.

If anything, the problem currently for professional books is that knowledge is cheap, plentiful and easily obtained. Case reviews, subject overviews and clinical slides are painfully easy to obtain through the Internet. They are free and bang up to date. A 1999 review on haemachromatosis can be found and printed off within 15 minutes. Game set and match to the Internet, Woolworth vouchers to the poor runner up, books. Not quite. Whereas books are concise, tidy, handy, and look good, the Internet is disparate and its out-pourings are a mess. Books have editors, the Internet doesn't. Today, to be worth buying, a book must address either a very specialised audience or a very broad one. A book must gather together information that is difficult to obtain elsewhere in a coherent form (e.g. clinical classifications and research scoring systems, etc.), or that is timeless (clinical manifestations). The *Key Topics* series does reflect some of these qualities, though weakly.

The stated church for *Key Topics in Gastroenterology* is senior house officers (SHO) and registrars preparing for the MRCP and all doctors wishing to keep up to date—the usual publishers' non-specific audience of anyone that can walk upright, do joined up writing and has a medical degree. The format is lists of key points, many of which are expanded to short paragraphs. Topics are presented alphabetically which leads to a strange contents page with Nausea and vomiting coming before Neuroendocrine tumours and after Menetrier's disease, but that is a quirk of the *Key Topics* series and of little importance. All the major areas of gastroenterology are covered and although I wouldn't agree with several of the statements made, these areas are covered well. The section on small bowel transplantation lacks any great substance, however, though it does at least serve to highlight the fact that such work is being carried out. So, who should buy it?

Dr Anderson has used up to date references throughout, but as he and his collaborators point out, this book is not intended to be a complete textbook on gastroenterology. If you need a reference book, gastroenterologist or general physician alike, this is not for you. Go and look it up on the Internet. If you are a gastroenterology house-officer, SHO or registrar consider it, although you should look around first, particularly at the Little Brown series. If you are a non-GI SHO you're probably better off buying a cardiology or neurology book. The case for buying this book would be stronger if it provided more definite clinical paradigms for how to approach the GI patient. £21 is still a lot of money for something that doesn't provide immediate gratification; however, in these days when even the *Sun* is buying books for schools, if pharmaceutical companies changed their mission from "chicken korma for all by 2000" to something of more tangible benefit, perhaps this book would reach a wider audience as it should.

J MEENAN

NOTES

Second Annual Gastrointestinal Cancer Update: A Multidisciplinary Approach

The Second Annual Gastrointestinal Cancer Update conference will be held at the Yarrow Hotel and Conference Centre, Park City, Utah, USA, on 15–19 March 2000. Further information from: Rosalie Lammle. Tel: +1 801 581 8664; fax: +1 801 581 3647; email: rosalie.lammle@hsc.utah.edu

European Courses on Laparoscopic Surgery

The European Courses on Laparoscopic Surgery will be held at the University Hospital Saint Pierre, Brussels, Belgium, on 4–7 April 2000 and 21–24 November 2000. Further information from: Conference Services S.A., Drève des Tumuli, 18, B-1170 Brussels, Belgium. Tel: +32 2 375 1648; fax: +32 2 375 3299; email: conference.services@skynet.be