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 colonicoscopic screening and surveillance. Jenkins and colleagues had found that 35 (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 adenomas2 and colonicoscopy 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 colonicoscopy studies of asymptomatic average risk volunteers (n=720).

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 the normal population, we have carried out a retrospective study of left sided adenomas 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 than 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 colonicoscopy studies of asymptomatic average risk volunteers (n=720, table 1).1,2 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 the normal population.

For colorectal cancer, Jenkins and colleagues3 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 colleagues4 reported 13 colonic cancers in 1041 male veteran acromegatics (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 colleagues5 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 colonscopic screening and subsequent regular surveillance above that of the normal population cannot be supported by the evidence currently available.

A G RENEHAN
S T ODWYER
Department of Surgery, Christie Hospital NHS Trust, Wilmslow Road, Withington, Manchester M20 4BX, UK

S M SHALET
Department of Endocrinology, Christie Hospital NHS Trust


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

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>n</th>
<th>&lt;40</th>
<th>40–49</th>
<th>50–59</th>
<th>60–69</th>
<th>70+</th>
<th>Total</th>
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<tr>
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<td>0</td>
<td>21</td>
<td>34</td>
<td>34</td>
<td>44</td>
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<td>1000</td>
<td>20</td>
<td>19</td>
<td>27</td>
<td>35</td>
<td>27</td>
<td>35</td>
</tr>
<tr>
<td>Steummermann and Yatani3</td>
<td>202</td>
<td>42</td>
<td>35</td>
<td>52</td>
<td>9</td>
<td>63</td>
<td>62</td>
</tr>
<tr>
<td>Rickert and colleagues4</td>
<td>518</td>
<td>–</td>
<td>17</td>
<td>35</td>
<td>56</td>
<td>58</td>
<td>47</td>
</tr>
<tr>
<td>Van and Staib5</td>
<td>449</td>
<td>6</td>
<td>23</td>
<td>33</td>
<td>11</td>
<td>30</td>
<td>26</td>
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<tr>
<td>Jass and colleagues6</td>
<td>303</td>
<td>3</td>
<td>11</td>
<td>30</td>
<td>30</td>
<td>36</td>
<td>24</td>
</tr>
<tr>
<td>Colonicoscopy studies in screened populations</td>
<td>DiSario and colleagues1</td>
<td>119</td>
<td>–</td>
<td>–</td>
<td>21</td>
<td>45</td>
<td>53</td>
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<td>–</td>
<td>–</td>
<td>28</td>
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<td>58</td>
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<td>–</td>
<td>–</td>
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<td>2914</td>
<td>9</td>
<td>15</td>
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<td>20</td>
<td>30</td>
<td>37</td>
<td>31</td>
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</table>

1 Three other autopsy studies (Correa and colleagues; Eide and colleagues; Williams and colleagues) were considered but not included as the age bands in these studies did not correspond with those used by Jenkins et al.

2 Patients aged 60–64; †patients aged 65–75.

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 and colleagues,1 Mouveroux and colleagues2 and Iattaure et al.,3 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.4 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,1 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 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 Renihan 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 colonicoscopic 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 colorectal adenomas. By contrast, our control groups were taken from similar populations to the patients with acromegaly, and in one group, the colono-
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 adenoma 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 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.

P JENKINS
P FAIRCLOUGH
M BESSER
Department of Endocrinology and Gastroenterology, St Bartholomew’s Hospital, West Smithfield, London EC1A 7BE, UK

References

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

N C FISHER
Specialist Registrar in Gastroenterology, Manor Hospital, Walsall, West Midlands WS2 9PS, UK

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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 insertion. Interestingly, the one patient who responded to TIPS still had an increased gradient after the treatment (14 mm Hg); in this patient, the favourable outcome of GAVE was paralleled by a noticeable improvement in liver function.

One study has suggested that arteriography may have a diagnostic value in GAVE. 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 muscular 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.

G POMIER-LAYRARGUES Liver Unit, Hôpital Saint-Luc, 1058, rue Saint-Denis, Montréal, Quebec H2X 3J4, Canada.


BOOK REVIEWS


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 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 definitive clinical paradigms for how to approach GI patients. £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
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A G RENEHAN, S T O'DWYER and S M SHALET

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