Cellularity and oestrogen receptor content in breast cancer microsamples

In a recent issue of the Journal Parham et al evaluated the relation between breast cancer cellularity and oestrogen receptor (ER) content.1 The authors concluded that, “there is no single direct correlation between tumour cellularity and oestrogen receptor content”. We feel that such a definitive conclusion cannot be drawn from this study, primarily because of its sampling technique. It is well established that the ER content of a tumour exhibits regional variability,3 thus to assess the effect of cellularity on receptor content, it is important that these variables are assayed using immediately adjacent samples. In Parham’s study the cellularity was assessed retrospectively using tissue sections which are assumed to represent the tumour as a whole, and the portion submitted for ER analysis in particular. We suggest that this sampling procedure does not address the issue of regional variability and therefore agree with the authors’ statement that, “it may be possible to obtain a better correlation if contiguous samples are taken”. We have addressed the issue of cellularity, and its effect on ER content using a “micromethod” technique. This procedure attempts to correct for regional variability by assaying contiguous samples. Briefly, a 40 mg “micromsample” is divided in half lengthwise so that one half can be analysed for cellularity and the other for ER. Using this method, the two analyses are performed on tissue samples that are no more than 1 mm apart. This technique was used to investigate the possibility that fluctuations in ER content are not random, but are associated with specific regions of a tumour (peripheral, intermediate, central). The ER content reported in that study was a composite of biochemical and histological data, but the issue of cellularity and ER content was not addressed directly. Using these data, we calculated the correlation between cellularity and ER content in 25 breast tumours. The results are summarised in the table. It should be noted that a total of five samples were taken from each tumour, size permitting. We acknowledge that the assessment of cellularity is a potential source of error and have attempted to minimise this problem by using the estimates of four independent observers. In a recent study these estimates fell within 10% of the mean (n = 107).3

Our data show that the correlation between cellularity and ER is highly variable, both between and within tumours. This observation indicates that the authors’ assumption that ER content and cellularity can be evaluated at different regions may not necessarily be correct. Experimental evidence thus corroborates our argument that cellularity and ER measurement should be made on contiguous samples. In our study the overall correlation between cellularity and ER, for ER positive tumours was r = 0.68 (n = 20); for ER positive as well as negative tumours the correlation was lower, r = 0.33 (correlation estimates fell within 10% of the mean = 25) but still positive. We believe, however, that ER negative tumours should be excluded from the analysis as, clearly, ER content and cellularity are not related. In conclusion, we believe that it is premature for the authors to conclude that there is “no significant correlation between tumour cellularity and ER content” in breast cancer.

Dr DM Parham et al comment

The design of our study did not allow contiguous tissue samples to be examined. We believe, however, that this does not invalidate our findings or conclusions.

A previous study by van Netten et al in 1988 using the “micromethod technique” would suggest that regional variation in oestrogen receptor content may not be important. They showed that the average oestrogen receptor content, when corrected for cellularity, was 20% higher in the intermediate zone than in the tumour core or periphery. The mean oestrogen receptor contents in the different regions of 25 tumours corrected for cellularity were: central zone

Comparison between cellularity (%) and oestrogen receptor content in breast cancers

<table>
<thead>
<tr>
<th>Region within a tumour</th>
<th>Peripheral</th>
<th>Intermediate</th>
<th>Central</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellularity ER</td>
<td>Cellularity ER</td>
<td>Cellularity ER</td>
<td>Cellularity ER</td>
</tr>
<tr>
<td><strong>Patient’s age</strong></td>
<td><strong>Peri</strong></td>
<td><strong>Inter</strong></td>
<td><strong>Cent</strong></td>
</tr>
<tr>
<td>49</td>
<td>18</td>
<td>4</td>
<td>25</td>
</tr>
<tr>
<td>53</td>
<td>6</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>61</td>
<td>80</td>
<td>166</td>
<td>15</td>
</tr>
<tr>
<td>63</td>
<td>20</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>65</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>66</td>
<td>0</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>67</td>
<td>7</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>69</td>
<td>19</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>73</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>75</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>79</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>81</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>85</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>87</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>89</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>94</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Sample not analysed.*
Matters arising


It is 11 years since the publication of the last edition of this book. This decade has seen rapid advances in many aspects of gastrointestinal pathology. Many of the advances have been made by the team of St Mark's Old Boys who now join the senior authors in the production of this edition.

The format is familiar with descriptive sections corresponding to the topographical segments of the gut from oesophagus to anus. An additional section covers diseases of the peritoneum and there is an invaluable discussion which deals with histological methods and general principles of examining and reporting gastrointestinal specimens. Without good preparations much pathology is doomed to be mediocre and it is appropriate that this section is placed firmly at the front of the book.

Within each section the same systematic approach is followed — normal anatomy, embryology and developmental anomalies, inflammatory, immunological, neoplastic and parasitic disorders, and neoplasms. The style is clear and succinct. It is remarkably uniform given that there are so many authors. The references are up to date and sufficient and include classic papers.

The standard of presentation of photographs and micrographs is up to the usual standard of the publishers, but the index in this edition is not so good as previously — try Paneth cells as a marker of its value.

So far so good. Clearly, those with old editions will want to replace them, but in this new Britain, what of market forces? There is a new competitor — Whitehead's multiauthor "Oesophageal and Gastrointestinal Pathology" and its format allows more chapters on functional aspects and pathophysiology of gastrointestinal disease. I find it hard to choose either in preference to the other. When gastrointestinal pathology makes up about one third of diagnostic biopsy specimens it would be remiss not to have both volumes as standards in the reporting room library.

Finally, the two senior authors have now retired. Their book is in good hands and they can look forward to the next edition.

G SLAVIN


This new edition of the atlas is very welcome. I am sure it will find its way into the collection of many general haematologists. The improvement in quality of reproduction of megaloblastic change, for example, is striking. The pictures of trypanosomes and borrelia are almost as good as the view down a microscope. The section on storage diseases is a valuable reference source. Well done for including a film of abetalipoproteinaemia (not included in another recently published atlas of haematology). All reviewers criticise some aspects of a book. The habit of calling chronic granulocytic leukaemia "adult type", presumably gastrointestinal, leaves distinguished it from the confusingly named juvenile chronic myeloid leukaemia, fails to highlight the relative frequency of the former. Finally some photographs give the red cells a greenish hue—all taken by the same camera, since the foreign body in the optics leaves its "fingerprint" on them all. Minor carpings from a happy (re)viewer.

MM REID


This slim volume comprises six reviews, written in 1987/8, on different parasites from various disciplinary viewpoints. From the skilled histopathologist's standpoint the well-illustrated account of the clinical pathology of onchocerciasis is the best, though much will be familiar to owners of the AFIP fascicles of 1976. The ultrastructure of Cryptosporidium in the human duodenum is managed with respect, while telling us, unfortunately, little of its pathogenesis. The chapter on schistosomiasis in China is mainly epidemiological, and the aetiological association with rectal (but not colorectal) carcinoma is discussed in an unconvincing way. A succinct clinicopathological presentation on intestinal capillaritis (not to be confused histologically with strongyloidiasis) which may be more widespread than we initially thought. Perhaps surprising is the summary of the latent hypnozoite phase of relapsing human malariais; and (with an eye on future chemotherapy) a detailed account of the role of calcium/calmodulin functions in malarial parasites.

S LUCAS


This book consists of a series of abstracts of recent scientific papers judged by the editors to be of interest to a general audience. Each abstract is followed by a paragraph or two prepared by one of the expert panel of editors commenting on the paper with regard to its importance and usually prompts (but not always) key references to support their comments. In general, the editors who are all based at the University of North Carolina have done a good job. There is a clear policy of grouping papers of similar interest together and they have succeeded in providing useful comment and criticism.

It is interesting to observe how many of the papers received are dependent on one or other of the technological advances which have been made in recent years with molecular biology particularly in evidence, and yet there is still a place for high quality formal descriptive papers.

I was intrigued by the fact that within a day or so of encountering my first case of Alagille's syndrome (syndromic paucity of interlobular bile ducts) I was reading the abstract of a relevant article in the "Year Book of Pathology". Perhaps surprisingly, there are only nine abstracts from papers dealing with AIDS. The papers reviewed were from late 1987 and early 1988 and for those topics which relate to one's own particular interests, the abstracts, and even the comments, tended to be out of date already. For those fields in which one is less knowledgeable the formula is useful. This style of book is perhaps of most value to those who wish to be aware of papers across a broad field of knowledge. I found the book difficult to read because it is so concentrated. I assume it is meant to be dipped into

BOOK REVIEWS


This book is an unillustrated compendium of mycoses in man and non-human infections given roughly equal prominence. It has a brief introduction about host defences against fungal infections. The varying immunodeficiency states are discussed in moderate detail with respect to individual infections.

The main sections are on candidiasis, cryptococcosis, aspergillosis, the phlycomycoses, and "others" including the chromycomycoses. A chapter on antifungal agents, and a pre-publication addendum (written in May 1989) complete the monograph. We should be grateful to Dr Smith for his accumulation of data. Thirty seven per cent of the pages in his book are references (which total over 1800). Clinical, diagnostic, therapeutic, and taxonomic aspects of the mycoses are well tabulated.

If I have any criticisms—and perhaps the second edition can take note—the naming of references in the text blocks its flow (try numbers instead); and there is a lack of subheadings to guide the reader through the paragraphs, though the index is good. I shall find it very useful for information on clinical mycology.

SB LUCAS

141 units, intermediate zone 173 units, and peripheral zone 142 units. The difference among regions is therefore small. In our study substantially larger portions of tumour, up to 10 mm2, were used. These often incorporated different tumour zones and are therefore probably more representative of the tumour as a whole.

The findings presented by van Netten et al support our conclusions. At any given cellularity there was a considerable variation in the oestrogen receptor values. A similar picture is obtained by examination of the results in different regions. This would indeed suggest as we stated that there is "no single direct correlation between tumour cellularity and oestrogen receptor content".
Cellularity and oestrogen receptor content in breast cancer microsamples.

J P van Netten, P Coy and C Fletcher

doi: 10.1136/jcp.43.8.698

Updated information and services can be found at:
http://jcp.bmj.com/content/43/8/698.citation

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/