This page contains a scientific discussion on various topics related to cell proliferation, including an analysis of PCNA (proliferating cell nuclear antigen) and its correlation with malignancy, as well as the use of silver staining techniques to evaluate nucleoli and nuclear proteins.

The text is divided into sections discussing different aspects of cell proliferation and its implications in various contexts such as neoplasms, lung carcinomas, and transcriptions. The authors reference various studies and works by different authors, including Cocher J, Bolda DY, Egan MJ, Levinson DA, J Clin Pathol 1991;44:655-9; and others.

The discussion is supported by references to multiple sources, indicating a comprehensive analysis of the topic. The authors conclude with a section on the implications of these findings for diagnostic and therapeutic approaches in clinical settings.

This text is part of a larger document discussing the role of diagnostic markers in the assessment of cancerous tissue, highlighting the importance of PCNA and other markers in distinguishing between benign and malignant conditions.

The reference list includes numerous citations from reputable journals, suggesting a well-researched and validated approach to the topic.

Overall, this page provides a detailed and scholarly perspective on the subject, suitable for readers interested in the field of diagnostic pathology and oncology.
appropriate treatment. This method for histological grade has been adopted by the Royal College of Pathologists Working Group for use in the NHS Breast Screening Programme.

Parham and colleagues have concluded from a small series of cases (105) that mitotic counts and semiquantitative assessment of tumour necrosis are the most significant factors. Unfortunately, despite their criticism of the Bloom and Richardson method, the authors have fallen foul of exactly the same imprecision which they eschew. Although they have followed us in defining the field area for mitotic counting, they do not state in their paper how many mitoses per field they counted for each point scored. Their evaluation of tumour necrosis also lacks clarity. It is admissible to define the dimensions of an area of necrosis but there is surely a flaw in the assessment of multiple foci if only the largest focus is counted. This basis a tumour could have several foci of necrosis each of which might score 1 or 2 points, but this only qualifies it for an overall score of 2; less than a tumour with a single focus. This relative lack of numerical data in this paper is also surprising and we are not told the number of cases in each necrosis group. For these reasons we must conclude that not only are there doubts about the validity of this new method, but fear that for lack of an adequate description no one else will actually be able to use it.

A number of other points are pertinent. The study is concerned with tumours of no special type. The method we describe is one which was developed in the Royal College of Pathologists Working Group, and the authors have shown a close correlation between tumour necrosis and nodal status. Finally, any method which divides patients into four rather than three groups will appear to be more discriminating. We would refer the authors to our paper confirming the utility of the Nottingham Prognostic Index.2 Using the scoring system of five groups of patients are identified with an annual mortality ranging from 1·5 to 32%. In practice, however, prognosis must be related to the available treatment. We have experience that the use of more than three groups serves no useful purpose.

Dr Parham comments:

Des Elston and Ellis express surprise that in our paper proposing a simplified method of grading breast cancer4 we do not cite their recent publication on histological grading.1 I must confess that while myself and my co-authors have some different attributes, we are not clairvoyants. Our paper was accepted for publication, in its submitted form, on the 1 November 1991 (indicated in the bottom left hand corner of the first page). Their paper was published only later the same month (8/11/91).

The aim of our study was to produce a simple method of grading breast tumours. The measurement of multiple areas of necrosis, while commendable, has some drawbacks. It is complex and probably less reproducible. For this reason, the largest dimension of necrosis was utilised. For clarity, the scoring of mitotic counts in our paper is the same for both, the new grading method, and the conventional Bloom and Richardson grading method.

Des Elston and Ellis comment that breast tumours of no special histological type account for only 50% of breast cancers and that this limits the utility of our new grading method. My experience and the findings of others suggest that the figure is nearer 70-75%.7 8 The remaining tumours, apart from infiltrating ductal carcinomas (accounting for approximately 10% of cases), have special histological features which tend to place them into favourable prognostic groups.

No mention of lymph node stage is made in our preliminary paper, as we concentrated on presenting the prognostic information that can be obtained from the primary tumour. We do, however, stress that the combination of the new grading method, with tumour stage and hence lymph node status, may provide further prognostic information. These aspects are currently being investigated.


Immunophenotype of multinucleated cells in giant cell lesions

I read the interesting paper by Dr Doussis and colleagues1 and discuss it here in the light of our own results. In our investigation enzyme histochemistry was applied to cryostat sections of unfixed and undecalciﬁed specimens of 101 different tumours or tumour-like lesions of bone.2 In all cases the osteoclast-like giant cells showed the same pattern of reactions, which was identical with that of osteoclasts but different from that of the multinucleated nonosteoclast cells: a lack of demonstrable alkaline phosphatase, but clearly detectable activity of tartrate-resistant acid phosphatase (TRACPase) activity, non-specific acid esterase, leucinaminopeptidase, and NADH-tetrazolium oxidoreductase activity. Microdensitometry of the enzyme reaction products4 5 in giant cells of varying sizes in six different bone tumours exhibited the same trend in all cases: a continuous decline of the relative activities of non-specific esterase and NADH-tetrazolium oxidoreductase, but an increase in the TRACPase activity with increasing cell size. Among the very large giant cells, however, there were cells with both high and very low TRACPase activities. Additionally electron microscopic examination of these showed swollen mitochondria with cristolysis, fragmentation, and swelling of cisternae of endoplasmic reticulum and the nuclear envelope, more and larger digestive vacuoles with myelin-like material in some vacuoles of variable size scattered throughout an electron dense cytoplasm.2 3 This pattern differed from that seen in the smaller giant cells and we hypothesised that with an increase in cell size osteoclast-like giant cells changed their physiological activities and that at least some of the very large cells demonstrated these activities.

It is interesting to note that in the study by Doussis et al the pattern of reactivity for anti-CD 68 was quite similar to that of non-specific esterase and NADH-tetrazolium oxidoreductase, because the giant cells with larger diameter clearly oxidoreductase-negative and a density of the immunoperoxidase reaction product that the smaller ones (figs 2A and 3A of the paper by Doussis et al). We think that these photographs confirm our theory. A micrometric examination of the slides of these sections would certainly demonstrate a size dependent pattern of the anti-CD68 reaction product comparable with that obtained in the study of the above mentioned two enzymes.

Doussis et al show that giant cells of giant cell tumours can be distinguished from other giant cell containing bone tumours by the absence or paucity of the HLA-DR reaction.3 The authors mention a number of possible explanations, that this phenomenon might be due to differences in the nature of the giant cells. But our study of enzyme physiology and ultrastructure of osteoclast-like giant cells in various bone lesions does not support this hypothesis. Furthermore, despite some differences, osteoclast-like giant cells of both giant cell tumours and other giant cell containing tumours or bone lesions share many antigens in common.4 5 Bearing in mind the observation that lymphokines modulate the expression of HLA-DR in human monocytes and macrophages,6 we suggest that this also is the case for the osteoclast-like giant cells. Therefore, we favour the alternative explanation given by Doussis et al, that the differing HLA-DR expression may reflect variations in the tissue matrix or in the immunological responses to it among the various bone tumours or tumour-like lesions.