For Debate . . .

Controversies in WHO tumour classification

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Clinicians who submit tumour tissue to pathologists are really asking "How will this tumour behave?" or "Will it grow slowly or quickly? Will it infiltrate locally? Will it metastasise? How will it respond to treatment?" In reply the pathologist tends to give it a name or type on the basis of more or less clearly defined criteria; to grade it according to how malignant he thinks it is; and to stage it according to how far it has spread. To those in different specialties the name alone gives a fairly clear indication of how the tumour will behave and how they should deal with it. Pathologists, however, can never afford to forget that tumour classification—what types there are to choose from—grading, and staging are merely means to the end of predicting biological behaviour. Most pathologists endeavour to work closely with their clinical colleagues to be sure that each understands what the other means by the terms they use.

In epidemiological studies, however, close contact is lost and words may be used in different ways. Then criteria begin to matter if different series, perhaps from different countries, are to be comparable. To define such criteria the World Health Organisation set up a series of tumour typing centres in 1957. These centres have produced 18 "blue books" on the classification of tumours in different sites and systems in the body. Not unnaturally the classifications produced by these international committees have provoked healthy disagreement.

Each tumour centre had to build its classification on the prevailing traditions to have its views generally accepted. But as traditions and conventions differ from hemisphere to hemisphere, from country to country, and even within each country, inevitably the blue books show differences among themselves.

Classifying squamous cell (epidermoid) carcinoma

The handling of the tumour type squamous cell (epidermoid) carcinoma illustrates this problem.

In the book on skin tumours[1] the term squamous cell carcinoma is used, although epidermoid would be more appropriate. The definition —that such tumours are those "that show evidence of squamous differentiation"—is imprecise, incomplete, and tautological. In *Oral and Oropharyngeal Tumours*[2] the term squamous cell carcinoma is also used but defined as a tumour in which the "cells may resemble any or all of the layers of stratified squamous epithelium." Here the definition is more precise and extensive, with reference to the corresponding normal epithelium and to stratification.

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In discussing tumours of the cervix, the book on tumours of the female genital tract[3] uses the term squamous cell carcinoma (epidermoid carcinoma). This is defined as a tumour "composed of cells resembling those of squamous epithelium"—a definition less precise than that in the book on oropharyngeal tumours but also referring to the normal tissue, which implicitly contains the characteristics of stratification. But subtypes are mentioned: (*a*) keratinising, (*b*) large-cell non-keratinising, and (*c*) small-cell non-keratinising. The criteria for calling the last two subtypes, especially the small-cell subtype, squamous cell carcinomas are not at all obvious.

In several other books the same tumour type is mentioned as arising in organs where squamous cells are not normally present (see table). Unfortunately not only the designations but also the criteria for basically the same tumour type vary from centre to centre and from organ system to organ system. The explanation is not to be found in philological confusion but in conceptual views.

Descriptions and definitions of squamous cell carcinoma in several WHO tumour classification books

Book on:	Description	Definition
Breast tumours[4]	Squamous cell carcinoma	"squamous characteristics i.e. spine cells and/or keratin formation"
Salivary gland tumours[5]	Epidermoid carcinoma	"forming keratin or having intercellular bridges"
Thyroid tumours[6]	Squamous cell carcinoma	"showing so-called intercellular bridges and/or forming keratin"
Bladder tumours[7]	Squamous cell carcinoma	"forming keratin or having intercellular bridges"
Intestinal tumours (tumours of the anus)[8]	Squamous cell carcinoma	"most are of non-keratinising type, resembling squamous carcinoma of the cervix"
Lung tumours[9]	Epidermoid carcinoma	"keratinisation or intercellular bridges"

In all sites a squamous cell carcinoma should be defined as a tumour showing one or more of the characteristics of the mother tissue, the stratified squamous cell epithelium, with or without keratinisation. This is well expressed in *Oral and Oropharyngeal Tumours*[2] as "cells [which] may resemble any or all of the layers of stratified squamous epithelium." This definition will embrace among the criteria stratification, whorl formation, and spindle cells.

Typing, grading, and staging

The foundation of tumour typing should be differentiation, which means the changes that take place during development from the fertilised egg cell to the adult cells and tissues. In spite of an established tissue specificity, many cells, especially the stem cells in the different organs and tissues, still preserve considerable developmental potentialities, which under certain conditions can be revealed. If rationally based, typing is a valuable characterisation of a tumour, because it is useful for morphological and especially causal, epidemiological, and clinical research.

On the other hand, the sizes of cells, pleomorphism, number of mitoses, etc, are criteria for grading malignancy, not criteria of

differentiation and diagnosis. This does not mean that certain cytological and histological features which are not part of differentiation may not be sufficiently characteristic to allow the establishment of "types"—for example, oat cell carcinomas. Large-cell carcinoma, on the other hand, is not a type but a vague term describing tumours without adequate diagnostic features. Biologically they may be squamous carcinomas or adenocarcinomas without their morphological criteria being recognisable by light microscopy.

Extension of growth is a criterion for staging malignancy.

Typing, grading, and staging thus represent three different co-ordinate systems for assessing the biology of a tumour. The systems must be kept strictly separate to be valuable. If they are not kept separate they add only to the existing confusion.

Discussion

The purpose of tumour classification is ultimately to indicate biological behaviour. The WHO books on tumour classification have greatly enhanced international comparisons of tumour incidence, but there are discrepancies between them—for example, with regard to squamous cell carcinoma. The interrelationships between the books need examination, and an extra book in which the criteria for recognising tumours common to various sites could be defined should perhaps be considered. Such criteria should themselves, however, have a common pattern based on: (*a*) consideration of the relevant normal stem cell and tissue; (*b*) the possible pathways of differentiation for the stem cells; and (*c*) the recognition by light microscopy of such differentiated cells. (Techniques other than light microscopy are unlikely to be universally available for international practical work.)

Now that the series of classifications is due for revision, we hope that these points will be considered and that the historically determined "provincial" points of view will yield to a more general approach to typing. Pathologists should co-operate more closely with comparative anatomists and embryologists to produce a uniform biological approach to tumour classification.

References

1 *International Histological Classification of Tumours No. 12: Histological Typing of Skin Tumours.* Geneva, WHO, 1974.
2 *International Histological Classification of Tumours No. 4: Histological Typing of Oral and Oropharyngeal Tumours.* Geneva, WHO, 1971.
3 *International Histological Classification of Tumours No. 13: Histological Typing of Female Genital Tract Tumours.* Geneva, WHO, 1975.
4 *International Histological Classification of Tumours No. 2: Histological Typing of Breast Tumours.* Geneva, WHO, 1968.
5 *International Histological Classification of Tumours No. 7: Histological Typing of Salivary Gland Tumours.* Geneva, WHO, 1972.
6 *International Histological Classification of Tumours No. 11: Histological Typing of Thyroid Tumours.* Geneva, WHO, 1974.
7 *International Histological Classification of Tumours No. 10: Histological Typing of Urinary Bladder Tumours.* Geneva, WHO, 1973.
8 *International Histological Classification of Tumours No. 15: Histological Typing of Intestinal Tumours.* Geneva, WHO, 1976.
9 *International Histological Classification of Tumours No. 1: Histological Typing of Lung Tumours.* Geneva, WHO, 1967.

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Conference Report

BMA at Ipswich

BY A SPECIAL CORRESPONDENT

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Anyone who argues that with the growth of postgraduate centres the BMA's scientific meetings have become outdated should have been brought to Ipswich on 12-14 October. At the lectures and social events about two-thirds of the crowd were local doctors (and their husbands and wives); most of the remaining third were primarily medical politicians or BMA officials and the two groups had a lot to learn from each other. Such an interchange between the stars of the *Supplement* and clinicians who might otherwise never have a medicopolitical thought must be good for all concerned.

The meeting was, indeed, opened by a politician: Dr Eric Holst, the president of the Standing Committee of Doctors of the EEC. Society had, he said, been watching the rapid expansion of the share taken by health of each nation's productivity, and economists were becoming increasingly doubtful of the value of this growth. Whether or not the results justified the costs would depend on the needs being met. There would be pressures by economists for rationalisation, said Dr Holst, and doctors should not resist these: in particular, he thought there would have to be closer co-operation between primary and hospital care and between the medical and other professions.

Child care

After lunch the meeting moved on to paediatrics, with Mr J Stark's account from the Hospital for Sick Children, London, of the advances that had been made in the management of infants with congenital heart disease. Deaths still occurred, especially in the neonatal period in infants with inoperable or complex lesions, but there had been a striking fall in the mortality rate in open-heart operations, from 65% in the mid 1960s to 25% in the mid 1970s. Furthermore, most of the survivors had a normal exercise tolerance and would probably have a normal life expectation.

There had been nearly 1300 accidental deaths in children last year, said Dr R H Jackson (Newcastle upon Tyne). Road accidents accounted for 541 deaths and for 11 000 serious injuries—not, perhaps, surprising when one-fifth of mothers asked at what age their children could safely cross a main road answered "3." Much more could, he said, be done to prevent accidents: the environment needed to be safe for children as well as adults—a message that had to be brought home to architects, designers, and manufacturers.

Dr N D Barnes (Cambridge) opened his talk with a slide of one of the famous royal dwarfs painted by Velasquez and reminded dwarf-owners who were commoners never to show them to an acquisitive queen. He reviewed the treatable and