Misconceptions of the pathology of intracranial arterial aneurysms

Correction of errors and misleading data is an educational precept, and Weller's misconceptions of cerebral (berry) aneurysm pathology is a case in point. His illustration of their frequency distribution depicts basilar aneurysms arising from the crotch but other aneurysms arising at lateral angles of forks or junctions. Though this was perhaps inadvertent, it is grossly misleading: such localisation is rare. Furthermore he neglects the internal carotid bifurcation and incorrectly infers that posterior cerebral artery aneurysms are more common.

Weller's concept of cerebral aneurysm aetiology ignores a substantial body of research on cerebral aneurysms and the experimental production of similar changes and berry aneurysms by haemodynamic means. His study involved random sections of several resin embedded forks which do not provide the necessary three dimensional structural detail. The localisation of intimal proliferation at branching sites is incorrect. An oval pad at the extremities of flow dividers is depicted when, in neonates, intimal proliferation covers the entire flow divider, with separate pads just inside the daughter branches proximally where flow separation would be expected. Similar intimal proliferation occurs over the flow dividers of extracranial arteries and the aneurysms' appearance of eccentricity and wall thickening is not shown encroachment on the lumen, which actually expands laterally by as much as 50%. Due to poor methodology he underestimates the incidence of raphés (60% of subjects).

Based on serial sections on several hundred human cerebral forks, I assert that medial raphés, rather than defects to indicate their true function, are universal in human cerebral aneurysms and animals studied. Serial sections are essential for successful detection of raphés and no localised luminal indentation or rounding of the carina would have been invoked with perfusion fixation.

The concept that pads cause loss of elasticity is false as elastic tissue changes precede intimal thickening and early aneurysmal changes occur more often to the side of the apex and apical pad. Early aneurysmal changes can be produced haemodynamically at experimental forks and in arteries feeding arteriovenous fistulae. They commence as transverse tears of the internal elastic lamina with progressive tearing or fragmentation of the medial elastic laminae and loss of smooth muscle until eventually only endothelium and an attenuated adventitia remain. Such changes result in ectasia or more localised dilatation, and intimal proliferation may be superimposed.

That cerebral aneurysms consist only of endothelium and fibrous tissue is false: intimal proliferation and atherosclerosis characteristically develop in cerebral aneurysms. Thrombus forms over mural tears occurring predominantly at the fundus. Increased pulse pressure is probably the most significant factor, as in arteriovenous fistulae, aortic valve incompetence, hypertension, and collateral circulation which are often associated with aneurysms. Since aneurysms indicate mural weakness, hypertension when present, or any matrix abnormality associated with diminished tensile strength, potentiates aneurysm development: neither is an essential prerequisite.

No scientific evidence exists that smoking or true hypercholesterolaemia are causal in aneurysm formation. Though pathological statements and statistical correlations do not indicate causality, Weller's literature review is superficial and his statements are inconsistent with considerable pathological and experimental evidence. As a result his submission must be considered as speculative, even mythic.

WILLIAM E STEHBENS
Department of Pathology, Wellington School of Medicine, Wellington, New Zealand


The author replies

I am pleased that Dr Stehbens has responded to my leader in the Journal of Clinical Pathology in 1995 that he has added his very considerable experience during the last 45 years of the examination of cerebral saccular aneurysms. Dr Stehbens criticises, and I am sure quite rightly, a number of detailed points in my leader, but I am disappointed that he does not bring his experience to bear upon the main questions posed in my article.

In my leader, I opened a discussion regarding the origin and formation of saccular aneurysms and explored the views commonly held. I am pleased that Dr Stehbens has responded to my leader, but I am disappointed that he does not bring his experience to bear upon the main questions posed in my article.

The debate will continue but we must all retain open minds.

R O WELLER
Department of Neuropathology, Southampton General Hospital, Southampton SO16 6YD, UK

Tissue banks in NHS histopathology laboratories and the Consensus Statement

Since the publication of our paper, which outlined the ethical, legal, and logistic aspects of supplying surplus surgically removed samples to commercial biomedical research organisations, a working party of the Royal College of Pathologists and the Institute of Biomedical Science has produced, jointly, a booklet entitled “Consensus Statement of Recommended Policies for the Use of Human Tissue in Research Education and Quality Control”. The Statement, originally compiled by the American College of Pathologists, is now endorsed by 20 American and British pathology societies. The text includes “Notes reflecting UK law and practice” and we recommend it as essential reading for pathologists, biomedical scientists, and pathology managers, whether they are contemplating human tissue banking or not. Commercial organisations using human tissue should also be aware of the contents.

The Statement includes a useful and practical definition of genetic information. The potential use of genetic information was an
area that concerned our local research ethics committee (LREC). Our proposal was not helped when we attended an LREC meeting along with a commercial collaborator, shortly after Dolly the Sheep had first been shown to the world. The LREC allow for extraction of RNA and DNA but not for cellular immortalisation or cloning. In order to monitor this, our legal contract requires the commercial organisation to provide research protocols before we supply tissue to them.

We expressed the fear that one day a genetic research finding might have far reaching clinical and ethical consequences for an individual donor patient. The Statement provides useful guidance on this and recommends treating genetic discoveries in the same way as own research findings, although the "Notes reflecting UK law and practice" point out some of the potential ethical risks of DNA databanks to society as a whole.

A section on confidentiality emphasises the importance of system safeguards in preventing the leak of patient data. According to the working definitions in this section, the samples we provide to commercial companies are, strictly speaking, “linked” rather than anonymised. However, in our tissue bank, “linkage” can only be made by the medical intermediary and it is difficult to conceive a situation where we would agree to do this. In order to do so, we would need the consent of the patient. In practical terms, therefore, the tissue we provide to commercial firms is “anonymised”.

The final section on consent further reinforces our views.1 We would argue that a general agreement to donate tissue as part of a signed consent-to-treatment form does not constitute proper informed consent which, if properly placed, carries an additional burden of explanation on the surgeon, whose role in adhering to the latest GMC guidelines is difficult and time consuming enough. Furthermore, the “Notes reflecting UK law and practice” mention a European Directive, due to be implemented by 2000, which implies that informed consent will be required in every case. However, over a patent application is filed—the dream of a man.

At Peterborough, we now employ two research nurses to obtain consent and collect tissue before operation. The nurses have redesigned the consent forms, produced a patient information pack, and are able to spend time with patients answering questions. This experience was presented to the British Association of Tissue Banks (BATB) in March 1999 and we hope to publish the results in due course.

There have also been important developments in the “whole body donation project”. Working within informal arrangements with the North East Thames National Blood Service Tissue Services (NBSTS) is now covered by a formal written agreement. Donors who have expressed a wish to give more tissues than are currently routinely banked by NBSTS, and others identified as being unsuitable for the transplant programme by the transplant coordinators, are referred to the Peterborough Tissue Bank for postmortem tissue collection. Comparable to surplus surgical material in hospital, the consent procedures undertaken by the transplant coordinators are more complicated. This is largely because of the issues that need to be covered:

- Where possible, and relatives under-
remains a "nuts and bolts" book that provides fundamental information on the practical aspects of in situ hybridisation techniques.

The format of the previous edition is retained in this book. Individual chapters deal with different hybridisation technologies. Each starts with a section on basic principles and proceeds to cover practical points including probe manufacture, the conditions needed for using the technique concerned, and the standards required. The chapters end with specific illustrative examples, a reference list, and an appendix that contains precise laboratory protocols for the in situ method(s) discussed. The latter are highly detailed and include sources for many of the reagents required.

The book begins with a chapter on the general principles of in situ hybridisation and follows this with three chapters on design, preparation, and use of different probe types. These cover DNA and RNA probes, together with strategies for non-radioisotopic hybridisation. Quantitative in situ hybridisation methods are covered in the next two chapters. Following this there is a completely new section on detecting genetic changes in cancer using interphase cytogenetics and comparative genomic hybridisation. The colour plate accompanying this chapter is a spectacular illustration of the power of these techniques. Other areas covered include detecting nucleic acids in clinical material, combining in situ hybridisation and immunocytochemistry and supersensitive methods of in situ detection.

The book is reasonably priced, up to date, and well referenced. The chapter structure leads to some minor overlap of content but this does not detract from the book's value as a practical guide to in situ hybridisation technology. It is not a book for casual reading and is not aimed at pathologists or clinicians who simply want an outline of the latest techniques. However, workers wishing to establish in situ methods in their laboratory will find this an excellent starting point and a useful resource to have on their shelf.

A RAMSAY

CD-ROM review


As the authors admit, this CD-ROM is not really a source of detailed information and in-depth knowledge: "other texts are more encyclopaedic." But what a nice toy to feed before you lose interest, I should hasten to mention: the quality of quite a number of images is very poor. But you will be disappointed.

The feature I liked best is the self search for a rare entity, chances are that it will reveal. Many entities can be recognised even from the thumbnail sized pictures; the not-so-gratifying mistakes one is bound to make when shooting from the hip at very high speed provide a lession in modesty, and of course data tend to stick in your mind much better when you started out by making a mistake!

The program covers all of surgical pathology, but the level of detail is limited. If you search for a rare entity, chances are that it won’t be included. In that respect, the contents do not really necessitate the rather elaborate searching and bookmarking options which are included. In a way, the CD-ROM is like a modest but nice little bookshop: if you walk around without any specific wish, you will come across many interesting things. If you go in with one specific request that is out of the ordinary, there is a real chance that you will be disappointed.

There is a disturbing flaw, which I need to mention: the quality of quite a number of micrographs is less than optimal. Even entities which are not very rare are sometimes presented with downright poor pictures. But before you lose interest, I should hasten to add that practically always, the key features are clearly visible.

W J MOOI

Notices

The 1999 Annual Acute Healthcare Conference and the 1999 Annual Private Healthcare Insurance Conference
28 and 29 September 1999
Two one-day conferences at the Radisson SAS Portman Hotel, London W1
Speakers at the Acute Healthcare Conference will highlight issues surrounding improving quality, customer choice, investment opportunities, government policy and regulation, and insurer/provider relationships. Topics for discussion in the Private Healthcare Insurance Conference include the OTR report, network products, employer sponsored medical schemes, health care cash plans, and the role of intermediaries.
Further information from: Catherine Horsfield, Conference Coordinator, Laing & Buisson, 29 Angel Gate, City Road, London EC1V 2PT; tel +44 (0)171 833 9123; fax +44 (0)171 833 9129; email: info@laingbuisson.co.uk

Current Concepts in Surgical Pathology
8–12 November 1999
The Four Seasons Hotel, Boston, Massachusetts, USA
A course designed to improve the skills of surgical pathologists by focusing on new information and techniques relevant to their practice. Disease areas to be discussed include bladder, bone, breast, brain, ear, nose and throat, gastrointestinal tract, heart, joints, lung, lymph nodes, placenta, pleura, prostate, sex organs, skin, soft tissue, and thymus.
Fee for the course $895 (residents and fellows $695).
Further information from: Department of Continuing Education, Harvard Medical School, PO Box 825, Boston, MA 02155, USA; tel +1 617 432 1525; fax +1 617 432 1562; email: hms-cre@warren.med.harvard.edu

7th Southeast European Symposium of Paediatric Surgery "Intestinal Motility Disorders", 2–3 June 2000, University of Graz, Austria
Further details from: Professor Günther Schimpl, Department of Paediatric Surgery, Auenbruggerplatz 34, 8-8036 Graz, Austria; tel +43 316 385 3762; fax +43 316 385 3775; email: kinderchirurgie@kfunigraz.ac.at
Instructions for Authors

Papers for publication should be sent to the Editor, Journal of Clinical Pathology, BMA House, Tavistock Square, London WC1H 9JR (tel: 0171 383 6209/6154; fax: 0171 383 6668; email: jclinpathol@compuserve.com). Receipt of manuscripts will be acknowledged by the editorial office. Submission of a paper will be held to imply that it contains original work not being offered elsewhere or published previously. Manuscripts should be prepared in accordance with the Vancouver style. The Editor retains the right to shorten the article or make changes to conform with style and to improve clarity. All authors must sign the copyright form after acceptance.

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- All measurements must be in SI units apart from blood pressure measurements, which should be in mm Hg, and drugs in metric units.
- Abbreviations should be used rarely and should be preceded by the words in full before the first appearance.
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- Any article may be submitted to outside peer review and for statistical assessment.
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- Papers should be no more than 2000 words long and should report original research of relevance and standing and practice of clinical pathology. They should be written in the standard form: abstract; introduction; methods; results; and discussion.
- The journal uses a structured form of abstract in the interests of clarity. This should be short (no more than 250 words) and include four headings: Aims—the main purpose of the study; Methods—what was done, and with what material; Results—the most important results illustrated by numerical data not p values; and Conclusions—the implications and relevance of the results.

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Manuscript checklist:

- Is there an abstract?
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Revised January 1999
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