

## Letter to the Editor

### Growth of Respiratory Syncytial Virus in RK<sub>13</sub> Cells

When preparing viral antisera in rabbits for immunofluorescent work (Herd and MacWilliam, 1971) attempts were made to grow several viruses in RK<sub>13</sub> cells to reduce anti-species antibody production. Although a satisfactory antiserum to respiratory syncytial virus (RSV) was eventually prepared by a different method, the behaviour of RSV in RK<sub>13</sub> cells was followed over a prolonged time and the results are sufficiently interesting to be worth a brief record.

Cells were grown in Parkers medium 199, supplemented with 5-10% rabbit serum for RK<sub>13</sub> cells and 5-10% calf serum for HEp2 cells. In maintenance media the serum concentration was reduced to 2%. It was noticed that inoculation of RK<sub>13</sub> cells with a high concentration ( $10^6$  tcid<sub>50</sub> in HEp2 cells) of RSV produced cellular degeneration after one to four days. Serial passage of material from these degenerated RK<sub>13</sub> cells did not result in any cytopathic effect, but after three blind passes in RK<sub>13</sub> cells, re-inoculation in HEp2 cells gave a cytopathic effect typical of RSV.

An attempt was then made to adapt the Long strain of RSV to RK<sub>13</sub> cells. Respiratory syncytial virus stock was passed alternately in RK<sub>13</sub> and HEp2. The eleventh RK<sub>13</sub> pass was inoculated directly into RK<sub>13</sub> cells and thereafter serial passages were made in RK<sub>13</sub> cells. During the 12th passage the virus titre (in HEp2 cells) was  $10^3$  tcid<sub>50</sub>/ml on the fifth day and then rose to  $10^4$  by day 20 and reached  $10^5$  tcid<sub>50</sub>/ml by day 48 at which time the cells in the tubes inoculated with virus degenerated. Control tubes remained normal throughout the whole period. Passage to HEp2 cells at this stage produced a cytopathic effect in which rounding of the cells was more obvious than the formation of syncytia.

By passage 32 cytopathic effect appeared seven days after inoculation. This was characterized by rounding of cells and syncytia were not seen. Specific immunofluorescence was demonstrated in the inoculated RK<sub>13</sub> cells and the cytopathic effect neutralized by specific RSV antisera. These results showed that the virus being passaged was RSV. By the 36th pass the titre of virus in fully degenerated RK<sub>13</sub> tubes was  $10^6$  tcid<sub>50</sub>/ml when titrated in RK<sub>13</sub> cells but only  $10^2$  tcid<sub>50</sub> for HEp2

cells. A significant degree of adaptation of the virus was thus shown to have occurred, though its antigenic specificity as shown by neutralization and immunofluorescence was unaltered.

The adaptation of RSV to RK<sub>13</sub> cells was repeated with a freshly-isolated strain of respiratory syncytial virus. This was passed serially in RK<sub>13</sub> cells. A cytopathic effect was seen at 11 weeks in the second passage and at decreasing intervals on further passage.

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#### Reference

- Herd, S., and MacWilliam, K. (1971). Preparation of antiviral sera for immunofluorescence in infected tissue culture. *J. clin. Path.*, 23, 304-307.

## Book reviews

**Renal Histopathology** By Robert Meadows. (Pp. xii + 363; illustrated. £14.00.) London, New York, Melbourne: Oxford University Press. 1973.

Dr Meadows has produced a truly substantial body of work on the light microscope appearances of the kidney in both health and disease. The book is divided into two parts. Part 1 deals with techniques and the appearances that may be encountered in the various parts of the nephron, the vessels, and the interstitial tissues. Part 2 is concerned with the histology in specific disease states. This approach, while useful for reference purposes, inevitably leads to some overlap in subject matter. The author has drawn upon his very wide personal experience of both biopsy and postmortem material. The descriptions given are lucid and succinct. The book is profusely and very beautifully illustrated; the photomicrographs, all of which have been taken and processed by the author, must be of a standard unequalled in excellence in any modern medical textbook. For this reason alone it is worthy of a place on the laboratory bookshelf.

However, today surely no renal biopsy taken in a major medical centre is only subjected to light microscopy. Immunofluorescent techniques and electron microscopy are of great value in elucidating the diagnosis in the nephrotic syndrome. This is particularly true when distinguishing between minimal change lesions and early membranous or mild proliferative glomerulonephritis. Yet this receives but a passing mention. I find the author's defence of his lack of attention to ultrastructural appearances somewhat unconvincing. Renal pathology is in a state of great evolution but the book contains relatively little in the way of comment on modern views of the pathogenesis of renal disease. This is a pity as with the considerable volume of material at his command the author must have formed some interesting and instructive opinions on the wider aspects of his subject; we would like to have read them.

M. S. DUNNILL

**The Spread of Tumours in the Human Body** 3rd ed. By R. A. Willis. (Pp. xi + 417; illustrated. £8.00.) London: Butterworth Group. 1973.

Professor Willis's book is a long, selected and annotated bibliography, particularly, and almost inevitably, rich in the older

**Book reviews**

literature dealing with those manifestations of the spread of human tumours which are to be observed by clinician and pathologist. It is a curious mixture consisting of catalogues of secondary tumours in various sites, little clinical asides, interesting short scientific essays based on his wide experience and reading, anecdotes, and of course a hobbyhorse or two—mesothelioma, Ewing's sarcoma, and details of all-but-forgotten polemics.

With his direct and deceptively effortless style he has produced a work which, though parts of it are recondite, is for the general medical reader and is as readily to be comprehended and enjoyed by medical student and staff nurse as by their seniors. It is interesting, informative, and thought-provoking, but marred by the author's deliberate avoidance of mention and discussion of contemporary interests in tumour behaviour, for example, the modification of tumour spread resulting from treatment, the nature and spread of Hodgkin's disease, Burkitt's lymphoma, the immunological factors in tumour behaviour, and, though the retrogression of several varieties of metastatic tumours is listed, the matter is left there without comment.

Where he does discuss topics that interest him, he is marvellously lucid and a fine protagonist for his beliefs.

Far too much space is taken up with statements of the type 'multiple intestinal deposits but with the liver clear were recorded by Ogle (1856), Godlee (1847), Thompson (1899), Davidson (1909), Goldzicher (1913), di Biassi (1926) . . . ' or 'Sturt (1900) saw secondary growths in stomach, small intestine, colon, kidneys, adrenals, pancreas, gall bladder, bones, lung and brain but only two small sub-capsular nodules in the liver.'

What we could do with is drastic pruning of the cataloguing, and expansion of Willis's mature considerations of the wider aspects of tumour spread, in which field he is a savant. The illustrations are excellent and well related to the author's theme.

R. L. CARTER

**Practical Clinical Hematology. Interpretations and Techniques** By Paul L. Wolf, Patricia Ferguson, Irma Torquati Mills, Elisabeth Von der Muehl, and Mary Thompson. (Pp. xviii + 468; 127 figures. £8.50.) Chichester, New York, Sydney, Tokyo, Mexico City: John Wiley and Sons. 1973.

As its title would suggest this book is mainly concerned with the practical aspect of clinical haematology, but

essentially from the laboratory viewpoint. It in no way attempts to, nor does it, supplant what must be recognized as the standard text in this field, Dacie's 'Practical haematology'. However, it might usefully be considered as an adjunct to the latter, in which more space is given over to theoretical considerations than is the case here.

The authors have described, in alphabetical order, a range of about 120 tests, ranging from the acid serum test to Wright's stain, the great proportion of which are infrequent laboratory use, as practised at the Stanford Clinical Laboratory.

The methods, both haematological and chemical, are described in considerable detail, under headings of 'Principle', 'Specimen requirement', 'Reagents and equipment', and 'Procedure', and are easy to follow. Each one is accompanied by a short section on interpretation and a modest number of references are included where appropriate.

Almost everything is covered, except serology which is planned for a further volume.

The final section is a collection of black and white photographs of cytology and cytochemistry, which is well produced, but which would have benefited from being in colour, particularly for teaching purposes. This would, no doubt, have made the cost prohibitive, but I have my doubts as to the value of special stains, in particular, photographed in black and white.

The book should prove a valuable reference and will be particularly useful in laboratories perhaps for the less frequently performed investigation. This is not to imply that there is a mass of esoteric tests; far from it, these have been kept to an absolute minimum.

A useful addition.

H. M. CLINK

**Medical Microbiology. A Guide to the Laboratory Diagnosis and Control of Infection 12th ed. Volume 1. Microbial Infections** Edited by Robert Cruickshank, J. P. Duguid, B. P. Marmion, and R. H. A. Swain. (Pp. xii + 667; illustrated. £4.75, paperback; £6.50, cased.) Edinburgh and London: Churchill Livingstone. 1973.

'Medical microbiology', now edited by a distinguished quartet of Scottish microbiologists, has undergone binary fission. The first volume deals with microbial infections and is aimed at those who work at the bedside rather than in the laboratory; technique is to be dealt with in the second volume to be published shortly.

This change will undoubtedly be welcomed by medical students and clinicians interested in microbiology because they can now acquire a comprehensive volume containing sufficient information to satisfy them about bacteria, viruses, fungi, and protozoa without a large amount of technical detail. There is also a clear account of the principles of infection and immunity. A section on diagnosis and control of infection is provided and also appendices dealing with specimens required for diagnosis. There is no extensive bibliography but references for further reading are recommended at the end of each chapter. This volume is well illustrated with diagrams, electron micrographs, and some colour photographs and is very good value at £4.75 (paperback).

The strategy of antimicrobial therapy is dealt with in only 13 pages and the student will need to follow the recommendation for further reading especially as the information given in this section is confusing. For example, lincomycin and clindamycin are dealt with as though they are two quite different antibiotics. Moreover, the antibiograms in appendix 3 do not tally with the information in this section. It is unfortunate that the recommendation to read 'Antibiotic and chemotherapy' quotes an out-of-date edition published, incidentally, by the same firm.

The contributors to this volume (now increased by six to 17), the editors, and the publisher are to be congratulated on producing a very useful book which will undoubtedly be as successful as its predecessors. I hope in future editions, if the discovery of penicillin is to be mentioned, recognition may also be given to Florey and Chain as well as to 'Fleming, a Scot'.

E. JOAN STOKES

**Glomerulonephritis. Morphology, Natural History, and Treatment Parts I and II** Edited by Priscilla Kincaid-Smith T. H. Mathew, and E. Lovell Becker. (Pp. 1238; illustrated. £22.50.) London, New York, Sydney, Toronto: John Wiley and Sons, 1973.

This is the proceedings of a conference in Melbourne in 1972. After an attempt at classification of glomerulonephritis, several papers from different centres of the world are presented on each of some of the diagnoses, usually defined morbid anatomically; there is also brief discussion. Morbid anatomy, including immunofluorescence, dominates the argument; even in a 'long-term follow up of post-



# The Spread of Tumours in the Human Body

R. L. Carter

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## Letter to the Editor

**Malignant Haemangioendothelioma Involving the Liver**

I read with interest the article by Pollard and Millward-Sadler (*J. clin. Path.*, 1974, 27, 214-221).

Concerning possible aetiological relationships, it is to be noted that seven cases of angiosarcoma (malignant haemangioendothelioma) of the liver have been diagnosed among individuals employed at a local vinyl chloride polymerization plant.

The first case was diagnosed in April 1964, and two recent cases in February 1974. Four additional cases of liver fibrosis with sinusoidal cell activity have been documented histologically. All individuals had close and prolonged contact with the vinyl chloride polymerization process.

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## Book reviews

**General Pathology** By J. B. Walter and M. S. Israel. (Pp. x + 681; illustrated. £10.00.) Edinburgh and London: Churchill Livingstone. 1974.

Publication of the fourth edition of Walter and Israel is an occasion to pause and admire the temerity of the two authors who dared not only to span such an immense subject but have striven ever since to keep the contents up to date. One formula would have been to stick to broad principles and well chosen examples, giving references as needed to more detailed sources, but that is not their way. Indeed the outstanding characteristic of the book is the sheer quantity of factual detail that is compressed into 680 pages. This has the merit that the student will usually find some mention of any topic he runs across but the compression may be such as to confuse hopelessly. For example, what is one to make out of the following (p. 170)? 'Curiously enough, although the delayed-type hypersensitivity which develops during an infection with the tubercle bacillus is specific, the increased phagocytic activity of the macrophages which accompanies it is much less specific. The cellular immunity is effective against many micro-organisms, and is not specific for the tubercle bacillus that induced it. Indeed, this is the basis for giving BCG in an attempt to control malignant disease. Anergy, indicating a lack of cell-mediated responses, can lead to an increased susceptibility to infection: measles has a reputation for reactivating a tuberculous infection.'

Here are a number of tenuously related observations and hypotheses not all well founded. In fairness to the authors the next sentence, 'It is evident that the inter-relationship between delayed-type hypersensitivity, cell-bound antibodies and immunity is poorly understood' illustrates the honesty of the book in admitting ignorance—a virtue much appreciated by students.

Another virtue is the wealth of recent references in some sections, but elsewhere there are important gaps. Thus in the chapter on ionizing radiation only three of 28 references are dated after 1965 and so we are told 'It is doubtful whether any of our present treatments of cancer can be regarded as producing a "cure", if by this is meant the complete eradication of all malignant cells'. Persistence of this view

might still prevent the proper eradicated treatment of many tumours such as nephroblastoma, seminoma, and childhood leukaemia.

Let us hope the fifth edition will correct such lapses, since it seems fairly certain that the book will retain its popularity for some years to come.

H. E. M. KAY

**Handbook of Forensic Pathology** By Abdullah Fattah (Pp. xxi + 349; illustrated. £11.00.) Philadelphia, Toronto: J. B. Lippincott Company. Oxford: Blackwell Scientific Publications. 1973.

There has recently been a small spate of new books on forensic pathology, written by experienced and practical pathologists. They are very much concerned with the morbid anatomy of medico-legal work, and quite different from the traditional British volumes on forensic medicine or medical jurisprudence. Professor Fattah's is one of the smaller books, but covers similar topics to the larger recent works.

Much of what is said should be well known to anyone engaged in forensic pathology, some of it describes the personal techniques of the author, and much is self-evident. 'If the pedestrian is hit while standing, the impact on the left side of the body results in tearing of the left side of the trousers . . . If the pedestrian is hit on the right side while crossing a road a converse picture results.' Well, perhaps someone somewhere might find that sort of statement useful.

On the credit side there are some useful tables, eg, on osteology, an interesting chapter on the negative necropsy, some valuable details of necropsy and toxicological findings in poisoning by a number of modern drugs, and a few simple (if potentially misleading) toxicological tests 'for pathologists'.

A. C. HUNT

**Advanced Haematology** Edited by Richard G. Huntsman and George C. Jenkins. (Pp. ix + 162; illustrated. £2.50.) London: Butterworths Ltd. 1974.

In the preface the editors state that 'each contributor was asked to imagine that he was explaining a particular topic to a postgraduate trainee haematologist or to an experienced technologist'. As is known by any lecturer who has had the dubious pleasure of addressing 'mixed' audiences,

**Correction**

The signature given to the review of 'The Spread of Tumours in Human Body' by R. A. Willis (*J. clin. Path.*, 1974, 27, 432-433) is incorrect. It should be A. Levene.