

Problems of Sickling

Molecular Aspects of Sick-cell Haemoglobin. Clinical Applications. Ed. Robert M. Nalbandian, M.D. (Pp. 199; \$15.75.) Charles C. Thomas. 1971.

This book is based on the fact that sickle-cell anaemia is a molecular disease and that sickle-cell crisis should therefore be treated on a molecular level. The sickle-cell molecules are forming rigid stacks on deoxygenation, but can be separated again from each other by urea. The authors therefore recommend treatment of patients with urea. A foreword by Linus Pauling quotes his 1949 interpretation of the sickling process, which is remarkable for its foresight at a time when the particular molecular feature of this haemoglobin was not yet even known. "Let us propose that there is a surface region of the sickle-cell hemoglobin molecule which is absent in the normal molecule and which has a configuration complementary to a different region of the surface of the hemoglobin molecule . . . under the appropriate conditions, then, the sickle-cell anemia hemoglobin molecules might be capable of interacting with one another at these sites sufficiently to cause at least a partial alignment of the molecules within the cell, resulting in the erythrocytes becoming birefringent, and the cell membranes being distorted to accommodate the new relatively rigid structure within its confines."

Add to this the discovery that in sickle-cell

haemoglobin the sixth residue of the β -chain is the hydrophobic valine instead of the hydrophilic glutamic acid (Ingram) and that the molecule changes its shape when it is deoxygenated (Perutz), the "Murayama thesis" of sickling as an interaction of hydrophobic bonds between deoxygenated sickle-cell haemoglobin molecules seems less original than this book might suggest. Indeed it has been proposed by others before in some detail. It may be noted in passing that we know nothing about the location of the complementary site which bonds the β s chain in deoxy haemoglobin, and although an $\alpha_2\beta_2$ tetramer is required for sickling, it is not essential that the β -chain bonds to the α -chain as pictured on pp. 26-27.

Urea breaks hydrophobic bonds at a 6-molar concentration which is equivalent to more than 30,000 mg/100 ml of blood. Yet the authors do not seem surprised that the optimal level for active treatment is 300-400 mg/100 ml, and that even oral therapy is reported to be successful in preventing sickle-cell crises. Even so, considerable diuresis can result and in one of the few case descriptions urine output reached a level of 1,000 ml an hour. Considering the difficulties caused by regulating the water and salt metabolism and the need to administer urea dissolved in invert sugar by a central venous catheter, one wonders whether the game is worth the candle. The really lethal crises in sickle-cell anaemia are the sequent-

ration crises and the aplastic episodes, and less so the painful infarctive events. The first two require immediate blood transfusion, and does the third really justify the heroic measures suggested by the authors?

Nevertheless, there is much of interest in this book, and it is worth recording that the contrast between the concentration of urea needed for dissolving hydrophobic bonds and the observation of improvement of sickle-cell anaemia with much lower concentrations of urea stimulated other workers to discover that the small amounts of cyanate which are present in urea solutions are adequate to inhibit sickling by binding with the NH_2 terminals of the polypeptide chains of the haemoglobin S molecule. As this is an unspecific blockage of NH_2 terminal groups of proteins in general, it is of course, doubtful whether it can develop into a practical therapy. One wonders whether the elegant demonstration by Muravama that well-dialysed sickle-cell haemoglobin does not sickle unless a small molecular factor from the dialysate is added refers to 2:3 diphosphoglycerate. This compound is known to encourage sterically the deoxy conformation of haemoglobin.

The book is lavishly edited, beautifully illustrated, and written in a triumphant and elated style. One hopes, however, that this will not mislead the undiscerning reader.

H. LEHMANN

Adverse Effects of Drugs

Iatrogenic Diseases. P. F. D'Arcy, Ph.D., and J. P. Griffin, Ph.D., M.B. (Pp. 208; £3.50.) Oxford University Press. 1971.

Although the title leads one to expect that this book deals with all the ills doctors inflict upon their patients, the aspects covered are only those in which drugs have been implicated. This is a good book, written with a pleasant and easy style that is a great credit to its authors, especially when it is remembered that the subject treated does not lend itself to stylish writing. Sadly, the trouble with books, even good ones, is that they never get read by the people most in need—in this case all the many doctors in and out of hospital who put little thought into their prescribing and who have never taken the trouble to learn enough about the drugs they use or about the added risks of multiple drug treatment.

The format is a new approach to drug

adverse effects. They are presented according to the system involved—heart, lungs, liver, and so on, and not, as in the standard reference volume in this field, according to classes of drug. While uniformity of style is preserved with only two authors the inherent disadvantage is that in this field there are bound to be subjects in which neither author is particularly expert. Thus, although all the topics covered are carefully reviewed and most of the conclusions drawn are correct, there are sections in which there is some uncertainty and in which the balance is poor. The section on cardiac dysfunction is substandard, and experts studying other sections will find omissions and some mistakes. But many sections, notably those on blood dyscrasias and diabetogenic effects, are quite excellent. The two introductory chapters, dealing with epidemiological aspects and drug interaction, are weak—basically because the material is not well

organized and relates poorly to the chapter titles and subheadings. With a little block dissection much the same material could be rebuilt to give distinct sections on epidemiology of drug adverse effects (including surveillance systems) and the mechanisms of drug induced disease (including interactions).

To have assembled so much information in so readable a form is an undoubted achievement. *Iatrogenic Diseases* is well referenced and indexed, and will be useful to all prescribing doctors. At its reasonable price it will be a valuable piece of sideroom or consulting room equipment. Medical undergraduates and physicians studying for higher examinations will also find it useful. Any second edition will be better still if the introduction is tidied up and if something can be done about the subject sections in which the authors themselves lack experience.

ROBERT WOOD

SELECTED NEW TITLES

Clinical Anxiety. Malcolm Lader, D.P.M., and Isaac Marks, D.P.M. (Pp. 202; £2.20.) Heinemann, 1972.

The Operating Theatre of Old St. Thomas's Hospital. (Pp. 24; 15p.) Guy's Hospital, 1971.

The Geriatric Amputee: Principles of Management. Committee on Prosthetic-Orthotic

Education 1968-1969. Chairman, Herbert E. Pedersen. (Pp. 82; £3.50.) National Academy of Sciences, Washington, 1971.

The Penguin Medical Encyclopedia. Peter Wingate. (Pp. 463; 60p.) Penguin Books, 1972.

Transactions of the Ophthalmological Society of the United Kingdom. Vol XCI Session 1971.

(Pp. 956; price not given.) Churchill Livingstone, 1972.

Clinical Renography. K. E. Britton, M.R.C.P., and N. J. G. Brown, M.A. (Pp. 198; £5.) Lloyd-Luke, 1971.

The Blood Vessels of the Kidney. Julia Fourman, M.B., and D. B. Moffat, F.R.C.S. (Pp. 161; £3.75.) Blackwell, 1971.

Community Medicine

This month sees the retirement of the editor of *Community Medicine*, G. L. C. Elliston. The journal was founded in 1908 as *The Medical Officer* by Sir George Elliston, who was succeeded as editor by his son in 1954. *Community Medicine*, one of the journals in the Macmillan group, is published weekly price 25p. Its new editor is to be Miss Shirley Lewis, formerly of the *Guardian*.

Medical Books in Bangladesh

Many hospitals and research libraries in Bangladesh suffered losses of journals during the recent hostilities according to the librarian of the Dacca Institute of Postgraduate Medicine. Any donations of medical journals for the period 1948-70 should be sent to the librarian for further distribution at the Institute of Postgraduate Medicine, Dacca, Bangladesh. All will be acknowledged.

Society of Apothecaries Award

At a lively dinner on 7 March the Worshipful Society of Apothecaries of London presented its gold medal in therapeutics for 1972 to Dr. Denis P. Burkitt, "in recognition of his outstanding work which has led to a greater understanding of the nature of certain forms of neoplasia."

£20,000 Gift for Guy's

A gift of £20,000 has been received by Guy's Hospital Medical School from the Herbert E. Dunhill Trust with a promise of a further £20,000 for the endowment of a fellowship in dermatology. This will be called the Dunhill Dermatology Research Fellowship.

Professor A. J. Haddow

We much regret an error in the photographs published last week (p. 809) with our announcement of the election of the new Fellows of the Royal Society. The photograph published over the name of Professor A. J. Haddow was in fact of Sir Alexander Haddow, and we apologize to both for the embarrassment caused them. A correct photograph of



[Scottish Press]

Professor A. J. Haddow appears above.

People in the News

Lord Greenwood of Rossendale has accepted an invitation from the Secretary of State for the Environment to be chairman of the Local Government Staff Commission for England. The commission is being set up to help and advise local authorities and their staffs during the reorganization of local government. Though the commission cannot be formally established until the Local Government Bill becomes law the Secretary of State is intending that work may begin in advance of legislation.

Major-General R. J. Gray, late R.A.M.C., has been appointed deputy director, medical services, H.Q. Southern Command.

COMING EVENTS

North Teesside Group of Hospitals.—Details and copies of the programmes of lectures, meetings and consultants' ward rounds, to which all doctors are invited, may be obtained from the postgraduate clinical tutor, North Teesside Group of Hospitals, Hardwick, Stockton-on-Tees, Teesside. (Tel. Stockton 62122.)

Obstetric Anaesthetists Association.—Meeting 11 April, St. Thomas's Hospital. Details from Dr. Felicity Reynolds, Department of Pharmacology, St. Thomas's Hospital, London S.E.1. (Tel. 01-928 9292.)

Ophthalmological Society of the United Kingdom.—Annual congress, 11-13 April, Edinburgh. Details and application forms from the society, at the Royal College of Surgeons of England, 35/43 Lincoln's Inn Fields, London WC2A 3PN. (Tel. 01-405 3474.)

"Forensic Aspects of Drug Abuse."—One-day conference, 14 April, Manor Hall, Clifton, Bristol, organized by Bristol University and the Royal College of Psychiatrists. Attendance is restricted to members and affiliates of the college and those concerned in the field of forensic psychiatry or the law. Details are obtainable from Dr. I. Pierce James, Glenside Hospital, Bristol BS16 1DD. (Tel. 0272 653285, extn. 28.)

"Chronic Myeloid Leukaemia."—International symposium, 15-16 April, Bologna, sponsored by the Italian Society of Haematology. Details from the secretary, Dr. M. Baccarani, Haematology Division, Istituto di Patologia Medica II, Ospedale S. Orsola, 40138 Bologna, Italy.

St. John Ambulance Annual Medical Conference.—"Fun and Games—the Risks to Life and Limbs in Sports and Leisure," 21-23 April, Nottingham University. Application forms and details from the conference secretary, H.Q. St. John Ambulance, 1 Grosvenor Crescent, London S.W.1. (Tel. 01-235 5231.)

SOCIETIES AND LECTURES

For attending lectures marked * a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Tuesday, 4 April

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 11.15 a.m., discussion by Mr. J. B. Blaikley: Large Bowel Lesions and the Gynaecologist. (Admission by ticket only, obtainable from the secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.3.)*
ST. ANN'S GENERAL HOSPITAL.—At St. Ann's Road, London, N.15, 1 p.m., Dr. H. D. Friedberg (Wisconsin Medical College): Aspects of Bundle Branch Block.

Wednesday, 5 April

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4.30 p.m., Dr. A. C. Allison: Immunological Enhancement versus Tolerance.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—6 p.m., Mr. W. M. Mee: Paediatric Surgical Problems for the General Surgeon.*

Thursday, 6 April

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. R. S. Murley: Variations on the Theme of Hiatus Hernia.*
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—6.30 p.m., Mr. J. C. M. Currie: The Place of Surgery in the Management of Intractable Pain.*

Friday, 7 April

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Mr. R. C. Farrow: The Management of Common Fractures and Their Complications.*
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—6.30 p.m., Mr. E. L. Trickey: Diagnosis and Management of Bone and Joint Infections.*

UNIVERSITIES AND COLLEGES

CAMBRIDGE

M.D.—J. Hedley-Whyte.

SHEFFIELD

The title of professor associate in surgery has been conferred on Mr. F. J. P. O'Gorman.

The title of professor associate in medical physics has been conferred on Dr. Harold Miller.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the President's Council of the Royal College of Surgeons of Edinburgh held on 17 March the following were admitted as Fellows:

M. M. Ahmed, M. M. Ayoub, M. A. M. Ayoub, P. E. Cleary, Santimoy De (Mrs), R. J. J. Crane, S. M. Desai, P. T. C. Docherty, W. J. Guillum-Scott, R. M. Heddie, M. A. Jabbar, I. A. Khwaja, D. E. Lyons, R. M. McFadden, M. ChB University of Edinburgh 1966, Dolly Mary Man Gue (Mrs), A. G. Murphy, M. A. Nanjiani, S. K. Sachdev, P. A. Tan, Suke Min Then, N. J. Warden.

ROYAL COLLEGE OF PSYCHIATRISTS

The following have been admitted as members:

S. A. Abell, I. Abey-Wickrama, J. A. Abramczuk, P. L. Agulnik, P. Ainsworth, E. R. Alexander, N. Ali, D. L. Aspinall, R. B. E. Badawi, F. P. Bahadur, V. F. A. Bailey, L. M. Barber, J. Barcroft, G. J. Barnes, C. G. Barrow, J. L. Barton, T. S. Bedi, E. H. B. Bennie, F. J. Beren, T. A. Betts, H. Bevan-Jones, D. J. Bevington, S. Bhanji, R. G. Bird, H. R. Board, M. J. Bowman, R. K. Brahma, T. G. Brennan, J. K. Brockbank, P. W. Brooks, T. J. R. Bruce, N. Buhrich, A. S. Burman, G. B. Burnett, J. J. Byng-Hall, M. E. S. Byrnes, G. J. Calvert, A. A. Campbell, W. C. Canning, P. A. Carney, E. L. Cay, D. D. Chisholm, A. B. Christie, M. R. Collieson, D. R. Collyer, J. R. Colville, J. F. Connolly, A. I. Cooklin, I. B. Cookson, A. F. Cooper, P. E. Copus, J. R. Cornwell, T. J. Crow, R. L. Cundall, J. J. Cuthill, J. R. T. Davidson, R. J. Doig, J. H. Dowson, R. J. Draper, I. G. Dresser, M. T. Duff-Miller, D. L. F. Dunleavy, D. Eaves, J. Egan, A. A. El-Gaaly, H. Etkin, L. E. J. Evans, W. Falkowski, B. Fenn, M. A. S. Field, A. J. Forrest, E. M. Fottrell, O. S. Frank, A. H. C. Freed, E. G. Gallagher, R. M. Galloway, A. M. G. Gath, A. L. Gay, G. Gross, E. F. Guirguis, N. M. Gyaneshwar, M. A. Halim, K. Hamadah, J. Handley, J. N. Haworth, J. M. Heron, R. M. Hester, S. W. Hettiaratchy, M. K. Hinchliffe, S. R. Hirsch, T. A. Holding, B. L. Houghton, L. K. V. Howell, S. C. Jain, F. E. James, R. E. S. James, D. M. Jenkins, D. Johnson, D. A. W. Johnson, E. C. Johnstone, D. L. Julier, E. M. Kapp, T. Kay, G. D. A. Kearney, A. M. P. Kellam, M. J. Kelleher, J. M. Kellett, P. M. Kelly, M. J. Kember, R. I. Kennedy, D. A. Kent, B. M. King, H. I. Knutzelius, S. V. Korgaonkar, F. Lappin, D. W. Laurie, B. Law-Yone, N. D. G. Leslie, P. S. Lewis, C. A. Lund, J. S. Lyon, R. G. McCreadie, R. McCurley, F. M. A. McDougall, A. W. T. McDowall, F. C. McEvert, R. D. McFarlane, E. MacLay, G. P. Maguire, S. A. Mahmud, M. T. Malcolm, B. M. Male, B. Malekpour, N. S. Marks, M. S. Markus, J. C. M. Mason, M. B. Matthews, L. G. Measey, J. Meilak, N. D. Minton, C. J. Molodyski, F. A. Moore, H. G. Morton, R. C. S. Moss, C. Q. Mountjoy, D. I. P. Nasser, J. R. Noble, C. Nolan, P. N. Nott, H. F. Oakeley, M. D. O'Brien, S. F. O'Connell, P. O'Farrell, J. Olsen, J. O'Melia, R. J. O'Riordan, R. B. F. Orr, K. B. O'Sullivan, D. S. Paine, J. M. Pallett, R. L. Palmer, J. M. Penman, K. S. Perinpanayagam, R. I. Perkins, G. M. Petrie, A. L. Phanjo, J. Picton-Jones, R. T. Pinto, D. C. R. Pitcher, T. Pitt-Aikens, J. Ponchia, P. E. Potter, O. H. Proctor, S. Qaragholi, I. B. Raafat, M. S. Rasalam, L. W. Rasiah, L. G. Ratnasabapathy, D. G. Reid, M. G. Revill, J. R. Robinson, J. W. Rollins, F. G. Rooth, M. A. Salih, G. A. Sampson, W. A. Saunders, J. Savej, N. P. Sebaratnam, S. H. Shaw, N. K. Shrubshall, U. A. Siddiqui, G. Singh, J. Singh, T. H. Singh, O. M. J. M. Sirisena, S. K. Sishta, M. M. Slack, S. M. Smith, A. G. Saddy, S. T. Sohal, B. Spears, D. Storer, G. Stores, J. C. Sturge, E. M. Sutherland, R. P. Swinson, S. Syed, A. J. Taylor, H. K. Teo, R. Thavazothy, H. J. Tollinton, D. A. Toms, M. Valvis, A. N. Varma, R. M. Veall, R. Viswanathan, E. J. A. Vogler, G. H. Warrick, H. C. Weaving, N. H. Weir, P. G. F. West, R. Whyte, Y. V. Wiley, D. D. R. Williams, A. M. Wilson, C. R. M. Wilson, S. Woolcott, S. M. N. Zaidi, M. Zakauddin.

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