



X	Z	R	R ₁	R ₂	Mp. °C	Calcd. %			Found. %		
						C	H	N	C	H	N
CH	N	NHCOCH ₂ Cl	H	H	290-291	59.87	4.11	12.70	60.14	4.14	13.00
CH	N	NHCOCH ₂ CH ₂ Cl	H	H	144-145	61.41	4.73	11.94	61.46	4.73	11.71
CH	N	NHCO(CH ₂) ₃ Cl	H	H ^a	114-115	62.74	5.27	11.27	62.78	5.39	11.16
CH	N	H	NHCOCH ₂ Cl	H	280-282	59.87	4.11	12.70	60.04	4.14	12.68
CH	N	H	NHCOCH ₂ CH ₂ Cl	H	134-135	61.41	4.73	11.94	61.60	4.84	12.24
CH	N	H	NHCO(CH ₂) ₃ Cl	H	122-123	62.74	5.27	11.27	62.70	5.55	11.10
CH	N	NHCOCH ₂ Cl	H	CH ₃ ^b	162-165	61.41	4.73	11.94	60.90	4.65	11.68
CH	N	NHCOCH ₂ CH ₂ Cl	H	CH ₃	145-146	62.74	5.27	11.27	62.48	5.05	11.02 ^c
CH	N	NHCO(CH ₂) ₃ Cl	H	CH ₃	143-144	64.00	5.75	10.66	63.69	5.90	10.45
N	CH	NHCOCH ₂ CH ₂ Cl	H	H ^d	139-140	61.41	4.73	11.94	61.44	4.96	11.92
N	CH	NHCO(CH ₂) ₃ Cl	H	H ^d	115-118	62.74	5.27	11.27	62.73	5.20	11.29
N	CH	NHCO(CH ₂) ₄ Cl	H	H	139-141	64.00	5.75	10.66	63.81	5.60	10.66

^a Gave 5-aminoisoquinoline on reaction with HN(CH₂CH₂OH)₂. ^b Gave 3-methyl-5-aminoisoquinoline on reaction with HN(CH₂CH₂OH)₂. ^c Anal. Calcd: Cl, 14.26. Found: Cl, 14.20. ^d Gave 5-aminoquinoline on reaction with HN(CH₂CH₂OH)₂.

ω -chloroacyl chlorides with the appropriate aminoheterocycle. It was hoped to convert these to alkylating agents similar to those prepared by Elderfield and LeVon³ from 8-aminoquinolines but in several preliminary experiments these amides were readily hydrolyzed in reactions with N,N-bis((2-hydroxyethyl)amine and the route was abandoned.

Experimental Section⁴

Preparation of Amides.—The appropriate aminoquinoline or aminoisoquinoline was treated with the appropriate ω -chloroacyl

- (2) (a) Clarkson College of Technology. (b) University of Miami.
 (c) To whom inquiries should be addressed at Clarkson College of Technology.
 (3) R. C. Elderfield and E. F. LeVon, *J. Org. Chem.*, **25**, 1576 (1960).

chloride under the conditions of Elderfield and LeVon,³ the conditions of DiGangi,⁵ or more conveniently in CH₂Cl₂ or CHCl₃ to give after neutralization the amides listed in Table I.

***p*-N,N-Bis(2-chloroethyl)aminobenzoyl Derivative of 5-Aminoquinoline.**—Use of *p*-[N,N-bis(2-chloroethyl)amino]benzoyl chloride and 5-aminoquinoline in the above sequence gave a 53% yield of solid, mp 169–172°. This compound exhibited no antineoplastic activity against Walker carcinosarcoma 256 at 25 mg/kg.

Anal. Calcd for C₂₀H₉Cl₂N₃O: C, 61.86; H, 4.93; N, 10.82; Cl, 18.26. Found: C, 61.82; H, 5.00; N, 10.82; Cl, 18.21.

(4) Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points are taken in capillaries and are corrected.

(5) F. E. DiGangi, *J. Am. Pharm. Assoc.*, **44**, 136 (1955).

Book Reviews

The Epidemiology of Tropical Diseases. By OSCAR FELSENFELD. Charles C Thomas, Publisher, Springfield, Ill. 1966. xiv + 488 pp. 16.5 × 24 cm. \$14.75.

Only an insignificant number of American medicinal scientists and physicians are working in the field of tropical diseases, in spite of the fact that almost 500,000 Americans have been sent into jungles where they lie in foxholes, wade through vector-infested streams, and eat food that would be condemned as unsanitary in their home land. The reason for this apparent lack of interest is, quite simply, money. The U. S. Public Health Service must marshal its funds wisely for the health of the nation, and in the now increasingly rare intervals of "peace," tropical diseases present no major health hazard to most Americans. Most of the pharmaceutical industry sees little financial incentive in producing drugs that the impoverished underdeveloped countries in tropical regions could ill afford. This is a deplorable state of affairs both from a human and scientific point of view. Disregarding our inherent humanitarian impulses to help our fellow men to rid themselves of disease, we appear to be condemned by circumstances and by unwise policies to send wave after wave of our best young males to fight in tropical countries for many years to come. This alone should call for a major public and private effort to sponsor research in tropical diseases. Scientifically, huge unexplored areas lure the medicinal and medical investigator to apply to them experiments in fundamental science and clinical art.

The textbook by Felsenfeld makes a valuable contribution to this neglected field and should be required reading for any com-

mittee that toys with plans for research on tropical maladies. It can be read profitably by epidemiologists and by laymen. The infectious process, including routes and vectors of infections, start off the book and lead next to control measures by sanitation and immunization. The next four major sections are devoted to detailed discussions of the epidemiology of bacterial, mycotic, parasitic, rickettsial, and viral diseases encountered in hot, humid belts; some of these infections overlap with conditions prevalent in North America as well. The final section of the book deals with noncommunicable diseases of nutritional and occupational origin, malignancies, dental and cardiovascular disorders, and addiction and mental diseases. Here again the tropics hold no privileged position, and much of what the author has observed there would apply to domestic conditions.

The book is clearly written, well printed, and thoroughly readable. There is an adequate subject index, and at the end of each section a list of references to books, recent monographs, and reviews.

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ALFRED BURGER

Developmental and Metabolic Control Mechanisms and Neoplasia. A Collection of Papers Presented at the Nineteenth Annual Symposium on Fundamental Cancer Research, 1965, at The University of Texas M. D. Anderson Hospital and Tumor Institute. The Williams and Wilkins Company, Baltimore, Md. 1965. x + 514 pp. 16 × 23.7 cm. \$16.00.

The symposium on which this book is based is one of a continuing series dedicated to the application of new principles of biological research to the problem of cancer. Each is devoted to a general topic. This book, like others before it, reflects the fact that this symposium on cellular control mechanisms is a research symposium dealing with a newly developing research area. Except for the direct relationship to cancer research, these meetings are not unlike the Cold Spring Harbor Symposia on Quantitative Biology. In fact, the 26th Cold Spring Harbor Symposium in 1961 on Cellular Regulatory Mechanisms provides excellent background material for the reader of this volume.

At the molecular level, research progress in nucleic acid synthesis, protein synthesis, and the genetic code has been remarkable and now almost permits an explanation of the reproduction of certain simple viruses in molecular terms. It is not yet true to say this of bacteria or higher organisms because of insufficient information concerning the control of gene expression and metabolic function.

Since cancer can be considered as a disorder of the regulation of growth, studies on developmental and metabolic control mechanisms in both normal and malignant cells are obviously of paramount importance to cancer research. The stakes are high: if the process of malignant transformation involves the control rather than the structure of the genes, an understanding of the regulatory mechanisms involved might even make possible the reversal of this change. One may argue that it is premature to attack the cancer problem at this level. However, the book does attempt to make immediate application of present knowledge to the baffling problem of neoplastic cellular growth, differentiation, and control, and the symposium planners and contributors are to be congratulated for their efforts.

The book is presented in five sections and includes 25 papers composed by a total of 37 authors, who are well qualified in their various fields of competence. In a witty and challenging first section, Erwin Chargaff presents the Bertner Foundation Award Lecture, entitled "On Some of the Biological Consequences of Base-Pairing in the Nucleic Acids." This is followed by sections on Biosynthesis and Control Mechanisms (8 papers), Molecular Basis of Early Development (8 papers), Molecular Basis of Later Development and Control (3 papers), and, finally, Comparative Studies of Control Mechanisms in Normal and Neoplastic Tissues (5 papers).

This reviewer does not feel that a mechanical listing of the title and authors of each paper presented in this volume will materially aid the reader of this book review in evaluating the book or in deciding for himself whether to read it. Rather, an attempt will be made in this review to discuss the philosophy of the field and the value of the book against the background of accumulated knowledge in genetic and cancer research.

In the introductory paper, Dr. Chargaff discusses past and present concepts of base pairing and, without attacking the messenger RNA concept *per se*, advocates a more critical approach to acceptance of this concept, with respect to the identity, stability, and function of many of the RNA fractions now classified as mRNA.

In the next three sections, a number of topics are discussed: the enzymology of genetic and biosynthetic control mechanisms; mechanisms of nucleic acid, protein, and virus synthesis; the function of histones, activator and repressor proteins, sRNA, and structural cellular organization as separate control elements; feedback control mechanisms by metabolites; regulatory enzymes; the operon concept and the repressor hypothesis; and hormone regulation of gene action.

In the last section, the relationship of control mechanisms to cancer research is drawn in more detail. Many of the foregoing subjects are discussed in terms of neoplastic growth and, in addition, there are included discussions on a theory of neoplastic growth based on altered template stability, the observed deletion of a negative feedback system from a malignant tissue, and studies on the hybridization of somatic cells.

Most of the experimental work presented is based on bacterial systems. Control mechanisms exist in bacteria for the regulation of protein synthesis and enzyme action, and an understanding of such bacterial control mechanisms is a logical first step to the understanding of similar mechanisms in higher organisms. However, information on control mechanisms that will be of direct significance to cancer research will come only from direct observations on normal and neoplastic mammalian cell systems. The regulatory mechanisms of differentiated organisms are not only far more complex than those of bacteria, but they are not

necessarily the same. Higher organisms may therefore be expected to possess certain regulatory mechanisms not found in bacteria. Major differences between the metabolic processes of bacterial and mammalian cells are becoming apparent. (For example, it may be mentioned that mammalian mRNA fractions are more stable than those of bacteria, and that histones, which are now generally accepted to be regulatory proteins controlling some of the functions of mammalian cell genes, do not exist in bacterial cells.) This very important point is recognized for the most part, but not unanimously, by the various authors of the book.

This book is not written as an integrated review of the field. Since it is essentially a collection of the edited text, slides, and discussion of each paper presented at the symposium, it suffers from the disjointedness characteristic of such compilations of individual presentations. It suffers further from nonuniformity of manuscript format in that some papers have formal summaries, whereas others do not. A volume of this kind would be greatly improved by the inclusion of a summary for each paper. Furthermore, another significant deficiency is that there is neither an over-all summary or evaluation of the entire symposium nor summary of any of the five general symposium sections. Finally, this kind of compilation of a new and explosively developing area is really outdated prior to publication. However, the book does serve as a reasonable estimate of the state of the field as of the time of the symposium and, accordingly, is of value both to investigators directly involved in the field and to those individuals desiring a status report.

The book is not intended for the beginner in molecular biology. Molecular biology has now advanced to the stage at which investigators and reviewers in the field no longer feel obliged to begin at the beginning in introducing their subjects. For this reason, some acquaintance with the origins of the field and with recent developments will be helpful, if not necessary, to the reader.

In conclusion, this reviewer recommends the book as a worthwhile and valuable contribution to a newly developing field. It is well suited for the research investigator or the graduate student, but not for the undergraduate or the casual reader.

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The Story of Health. By ANNE and GERALD HOWAT. Foreword by F. A. E. CREW. Pergamon Press, Oxford; Long Island City, N. Y. 1967. viii + 118 pp. 21 × 13.3 cm. 26 Illustrations. 1 £ 75 sh (\$13.30).

This little booklet traces the development of medicine from the age of dinosaurs to the present decade. It is addressed to the British reader, age 10-13. The twelve short chapters are followed by thoughtful questions such as "Why is water an important commodity? Why must it cost money," or "Tell the story of the discovery of penicillin." Such major lights as Hippocrates, Vesalius, the Curies, Pasteur, Ehrlich, Crawford Long, and Koch are mentioned but the index also contains the names of such medical personalities as Disraeli and Winston Churchill. One cannot escape the conclusion that ancient civilization may have been a prelude to medicine in far-off lands, but that we owe our present longevity, hygiene, and physical happiness to British discoveries in the health sciences. Of the latter, chemistry does not fare too well as an adjunct to medicine: only 4.5 pages are devoted to drugs, vitamins, etc., and of these one-half page is given to digitalis (Withering), and one-half page to avitaminoses and their early observers (Captain Cook, James Lind of the Royal Navy) and to the dietary regulations of the Ministry of Food.

The average American will probably get a better picture of medicine by watching the medical interludes on the "Today" show than by reading this book. Medicinal chemists may want to give it to their off-spring to nudge them in the direction of a career in medical science at an early age.

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