

THE YEAR BOOK
of PATHOLOGY *and*
CLINICAL PATHOLOGY

(1962-1963 YEAR BOOK Series)

EDITED BY

WILLIAM B. WARTMAN, B.S., M.D.

*Morrison Professor of Pathology, Northwestern University;
Director of Laboratories, Passavant Memorial Hospital;
Senior Attending Pathologist, Chicago Wesley Memorial Hospital;
Consulting Pathologist, Children's Memorial and Veterans
Administration Research Hospitals, Chicago.*

YEAR BOOK MEDICAL PUBLISHERS

INCORPORATED

35 EAST WACKER DRIVE • CHICAGO 1

TABLE OF CONTENTS

The designation *1962-1963 Series* is used in this volume to indicate publication during the "series year," which began in September, 1962.

PATHOLOGY

Who Killed Cock Robin? <i>by</i> CARL A. DRAGSTEDT	7
General Pathology	19
The Biochemical Lesions in the Development of a Fatty Liver, <i>by</i> K. R. REES	19
The Cell Surface or Is It a Membrane?	28
Lymphocytes	44
Mature or Pluripotential Cells?	44
Runt and Secondary Diseases, Graft Destruction	48
Time-Ordered Secretion of Gamma Globulin— The Thymus	52
Inflammation and Infection	55
Cellular Aspects	55
Proteins, Lysosomes and Ribosomes	60
Antigen-Antibody Reactions	66
Sarcoid Tissue and Sarcoidosis	70
Radiation Injury	72
Toxic Substances	76
Cancer— <i>with the assistance of</i> EDWIN T. NISHIMURA	81
General Features	81
"Ex Africa semper aliquid novi"	89
Growth of Neoplastic Cells and Tissues; Metastasis	92
New Methods	100
Cardiovascular System	105
The Myocardium and Valves	105
Blood Vessels	113
Hemopoietic System	117
Infection in Leukemia and Lymphomas	117
Lymphomas and Thymus	121
Toxoplasmosis of Lymph Nodes	130
Respiratory System	132

Alimentary System	143
Tumors with Functional Effects	143
Polyps and Benign Tumors	147
Cancer	154
Inflammation	159
Vascular Lesions	167
Liver and Bile Ducts	171
Urinary System	182
Kidney Function	182
The Juxtaglomerular Complex	185
Nephrosis and Related Conditions	190
Chronic Pyelonephritis	199
Miscellaneous Kidney Conditions	203
Urinary Bladder	207
Female Genital System and Breast	209
Male Genital System	221
Endocrine Glands	226
Carotid Body and Glomus Jugulare	226
Adrenal	230
Thyroid	232
Parathyroid	240
Musculoskeletal System	244
Nervous System	252
The Eye	260
Skin	266

CLINICAL PATHOLOGY

Clinical Chemistry— <i>with the assistance of</i> EDWARD FITZSIMMONS	279
Laboratory Control	279
Inborn Errors of Metabolism	284
Liver Function	288
Enzymes	293
Proteins	303
Steroids and Lipids	311
Electrolytes	322
Urinary Constituents	333
Diagnostic and Technical Methods	344

TABLE OF CONTENTS

5

Hematology— <i>with the assistance of</i> JOHN M. BUDINGER . . .	356
Erythropoiesis and Anemia	356
Leukemia	369
Coagulation Disorders and Fibrinolysins	376
Bone Marrow and Spleen	394
Blood Groups	398
Transfusions	409
Clinical Microbiology— <i>with the assistance of</i>	
HERBERT M. SOMMERS	417
Factors of Patient Resistance	417
Infections in Hospitals	420
Bacteriology	424
Mycobacteria, Named and Not Named	436
Viruses	445
Serology	454
Fungi	457
Parasites	469

THE YEAR BOOK *of* PATHOLOGY *and* CLINICAL PATHOLOGY

(1962-1963 YEAR BOOK Series)

EDITED BY

WILLIAM B. WARTMAN, B.S., M.D.

*Morrison Professor of Pathology, Northwestern University;
Director of Laboratories, Passavant Memorial Hospital;
Senior Attending Pathologist, Chicago Wesley Memorial Hospital;
Consulting Pathologist, Children's Memorial and Veterans
Administration Research Hospitals, Chicago.*

YEAR BOOK MEDICAL PUBLISHERS

INCORPORATED

35 EAST WACKER DRIVE • CHICAGO 1

THE PRACTICAL MEDICINE YEAR BOOKS

► There are sixteen YEAR BOOKS in various fields of medicine and one in dentistry. Publication of these annual volumes has been continuous since the first one appeared in 1900. The YEAR BOOKS make available in detailed abstract form the working essence of the cream of recent international medicoscientific literature. Selection of this material on vital advances in clinical management and research is made by distinguished editors who critically review each year more than 120,000 articles published in the world's foremost journals.

Medicine: PAUL B. BEESON, M.D.; CARL MUSCHENHEIM, M.D.; WILLIAM B. CASTLE, M.D.; TINSLEY R. HARRISON, M.D.; FRANZ J. INGELFINGER, M.D.; PHILIP K. BONDY, M.D.

General Surgery: MICHAEL E. DE BAKEY, M.D., with a section on *Anesthesia*, by STUART C. CULLEN, M.D.

Drug Therapy: HARRY BECKMAN, M.D.

Obstetrics & Gynecology: J. P. GREENHILL, M.D.

Pediatrics: SYDNEY S. GELLIS, M.D.

Radiology: JOHN FLOYD HOLT, M.D.; WALTER M. WHITEHOUSE, M.D.; HAROLD W. JACOX, M.D.; MORTON M. KLIGERMAN, M.D.

Ophthalmology: WILLIAM F. HUGHES, M.D.

Ear, Nose & Throat: JOHN R. LINDSAY, M.D.; with a section on *Maxillo-facial Surgery*, by DEAN M. LIERLE, M.D., and WILLIAM C. HUFFMAN, M.D.

Neurology, Psychiatry & Neurosurgery: ROLAND P. MACKAY, M.D.; SAM BERNARD WORTIS, M.D.; OSCAR SUGAR, M.D.

Dermatology: RUDOLF L. BAER, M.D.;

Urology: WILLIAM W. SCOTT, M.D.

Orthopedics & Traumatic Surgery: H. HERMAN YOUNG, M.D., with a section on *Plastic Surgery*, by NEAL OWENS, M.D.

Endocrinology: GILBERT S. GORDAN, M.D.

Pathology & Clinical Pathology: WILLIAM B. WARTMAN, M.D.

Cancer: RANDOLPH LEE CLARK, M.D.; RUSSELL W. CUMLEY, Ph.D.

Cardiovascular & Renal Diseases: W. PROCTOR HARVEY, M.D.; JOHN W. KIRKLIN, M.D.; ALEXANDER S. NADAS, M.D.; OGLESBY PAUL, M.D.; VICTOR E. POLLAK, M.D.; T. JOSEPH REEVES, M.D.; ROBERT W. WILKINS, M.D.; IRVING S. WRIGHT, M.D.

TABLE OF CONTENTS

The designation *1962-1963 Series* is used in this volume to indicate publication during the "series year," which began in September, 1962.

PATHOLOGY

Who Killed Cock Robin? <i>by</i> CARL A. DRAGSTEDT	7
General Pathology	19
The Biochemical Lesions in the Development of a Fatty Liver, <i>by</i> K. R. REES	19
The Cell Surface or Is It a Membrane?	28
Lymphocytes	44
Mature or Pluripotential Cells?	44
Runt and Secondary Diseases, Graft Destruction	48
Time-Ordered Secretion of Gamma Globulin— The Thymus	52
Inflammation and Infection	55
Cellular Aspects	55
Proteins, Lysosomes, and Ribosomes	60
Antigen-Antibody Reactions	66
Sarcoid Tissue and Sarcoidosis	70
Radiation Injury	72
Toxic Substances	76
Cancer— <i>with the assistance of</i> EDWIN T. NISHIMURA	81
General Features	81
"Ex Africa semper aliquid novi"	89
Growth of Neoplastic Cells and Tissues; Metastasis	92
New Methods	100
Cardiovascular System	105
The Myocardium and Valves	105
Blood Vessels	113
Hemopoietic System	117
Infection in Leukemia and Lymphomas	117
Lymphomas and Thymus	121
Toxoplasmosis of Lymph Nodes	130
Respiratory System	132

Alimentary System	143
Tumors with Functional Effects	143
Polyps and Benign Tumors	147
Cancer	154
Inflammation	159
Vascular Lesions	167
Liver and Bile Ducts	171
Urinary System	182
Kidney Function	182
The Juxtaglomerular Complex	185
Nephrosis and Related Conditions	190
Chronic Pyelonephritis	199
Miscellaneous Kidney Conditions	203
Urinary Bladder	207
Female Genital System and Breast	209
Male Genital System	221
Endocrine Glands	226
Carotid Body and Glomus Jugulare	226
Adrenal	230
Thyroid	232
Parathyroid	240
Musculoskeletal System	244
Nervous System	252
The Eye	260
Skin	266

CLINICAL PATHOLOGY

Clinical Chemistry— <i>with the assistance of</i> EDWARD FITZSIMMONS	279
Laboratory Control	279
Inborn Errors of Metabolism	284
Liver Function	288
Enzymes	293
Proteins	303
Steroids and Lipids	311
Electrolytes	322
Urinary Constituents	333
Diagnostic and Technical Methods	344

TABLE OF CONTENTS

5

Hematology— <i>with the assistance of</i> JOHN M. BUDINGER	356
Erythropoiesis and Anemia	356
Leukemia	369
Coagulation Disorders and Fibrinolysins	376
Bone Marrow and Spleen	394
Blood Groups	398
Transfusions	409
Clinical Microbiology— <i>with the assistance of</i>	
HERBERT M. SOMMERS	417
Factors of Patient Resistance	417
Infections in Hospitals	420
Bacteriology	424
Mycobacteria, Named and Not Named	436
Viruses	445
Serology	454
Fungi	457
Parasites	469

PATHOLOGY

Who Killed Cock Robin?*

The Martyred Scientist

CARL A. DRAGSTEDT, M.D., Ph.D.

In view of the deadly question posed by the title of this article, I would like to begin with the following excerpt from Dr. Treloar's treatise⁵ entitled "The Enigma of the Cause of Death":

Assertions that selected diseases are the "great killers of mankind" are common in high places. National societies promoting campaigns for funds to study those diseases contend for each death to be assigned to the disease of their special interest; thus will their claims for priority in charitable donation gain the desired weight provided by statistical evidence. Vital statisticians routinely respond in such ways as fall within their province to "fix the blame," or, in more formal language, to secure with scientific accuracy, from the medical profession, coroners, or others, a specification of the cause of each death. Pursuit of this objective is certainly laudable from all conventional viewpoints, but in so conforming one may become a victim of habit rather than an alert pursuer of well reasoned objectives. . . . It is a false proposition that each death is a response to a single cause. . . . As a result of this, the selection of one cause for tabulation purposes has itself become a major problem for us, leading to much juggling of terms, rules, and instructions to the distress of the medical profession as well as the statisticians. Efforts in recent years to solve the problems of tabulation and interpretation of assignment of multiple causes represent an attack on a basic problem and clearly indicate that causation of death is not considered singular.

This article deals with a different sort of death, but I hope to show that there is again the same sort of enigma as to the cause of death, that it also is an affair of multiple causation. The death referred to is the decline and cessation of important creative work on the part of a research scientist. . . .

It is my hope that the detailed protocol of a scientific death might illustrate and delineate this multiple causation hypothesis and at the same time indicate that the cause of such deaths is not so mysterious after all. I refer to the death of that well-known scientist Cockrell Robinson, known quite generally as Cock Robin.

*Reprinted, with permission, from *Clinical Pharmacology and Therapeutics*, 3:721-729, 1962. This article originally appeared in *Perspectives in Biology and Medicine*, 5:364-376, 1962.

Cock Robin came to the medical school of Chihuahua University as an assistant professor with a medium background in physiology and pharmacology. It was his good fortune to launch his researches in an area which proved exceedingly fertile. There ensued a shower of reports which attracted considerable attention since they dealt with problems which were tangential to the interests of a number of anatomists, physiologists, pharmacologists, and biochemists. . . . Robin's shower of reports, with which he aroused the academic world, was more than equaled by the deluge of things which happened to him. . . .

Cock Robin was appointed to the editorial board of the *Journal of Pharmacology*. He naively thought that this would require no extra time on his part since he would merely read in advance of their publication the same manuscripts he usually read when published. What a disillusionment! He was soon enmeshed in lengthy arguments with a number of authors as to the reliability of their data, their profligate use of tables, graphs, and illustrations, their employment of statistical procedures, their grammatical errors, and so on. For example, he wrote at least 50 letters explaining to various prospective authors that "hypothecate" means to deposit as security for a loan and is not to be used where "hypothesize" was intended. There were many instances, of course, in which he concealed the opinion that the statement in question should have been hypothecated rather than allowed to see the light of publication. He discovered that some investigators who had achieved a good reputation as to the clarity of their articles must have owed a good bit of that respect to the retread job done by some editor. It was not long until he also resorted to rewriting some entire manuscripts as being less time consuming than the lengthy criticisms and instruction otherwise called for.

Robin was appointed to the Council on Drugs of the American Medical Association and to its Subcommittee on Nomenclature. This committee has the task of preparing monographs describing new drugs for publication in the society journal. Incidental to this major function, it participates in the naming of new drugs. A new drug, of course, is christened by its commercial sponsors with a name which is copyrighted and is called its proprietary or trade name. Since the patent governing the manufacture of the new drug expires in

17 years, while the copyrighted name has a greater permanency, there is a necessity for a nonproprietary name by which it may be called by such concerns as may choose to produce and market it when the patent expires. This is its common or generic name, and should the drug be important enough to merit inclusion in *The United States Pharmacopeia* or the *National Formulary*, it becomes its official name. The Council on Drugs has assumed the function of negotiating a suitable generic name with the proprietary concern and of arbitrating this with representatives of the Pharmacopeia, the British Pharmacopoeial Commission, the French Codex, and the World Health Organization, with the hope that confusion may be lessened and international recognition be achieved for a single name. It is obvious that the ownership company is unlikely to suggest, and is even reluctant to accept, a generic name which is anywhere near as short, euphonious, or easy to remember as its trade marked name. To illustrate, let us suppose that X company has copyrighted the name Bam for the chemical substance β -tetrahydronaphthylamine hydrochloride. It would probably suggest some relatively minor abridgment of this unwieldy chemical name as a generic name. The nomenclature committee would counter with some much shorter name. Its ardor in the matter of brevity, however, is tempered by the ever present hazard that a really short name may well be the slang term for garbage, horse manure, or fornication in Hindi, Turkish, or some other language unfamiliar to the committee, and dictionaries are of little help in this dilemma. In due course, some compromise is agreed upon, but meanwhile the fecund chemical departments of the drug houses have spawned many candidates for christening.

Robin was appointed to the Pharmacology Study Section of the National Institutes of Health. In 1940, before the war, the total Federal contribution to the national support of medical research was around \$3,000,000. By 1955, that of the Department of Health, Education, and Welfare alone had grown to \$64,000,000, and by 1960, that of just the extramural program of the National Institutes of Health was \$293,000,000. The major mechanism for the disbursal of these huge sums of money is through the National Institutes of Health, a division of the Department of Health, Education, and Welfare. The Institutes maintain hospitals and laboratories in

which a substantial amount of direct research is conducted. In addition, the Institutes foster medical research through a variety of "extramural" programs consisting of training grants, research grants, and fellowships. No disparagement is intended by reporting that the local staff members refer to the extramural program as the outhouse program. This indirect support is now many times greater than its direct effort. The mechanisms set up by the Institutes to direct the distribution of this money rely heavily upon hundreds of scientific advisers, recruited from scientific institutions from all parts of the country and organized into National Advisory Councils and Study Sections.

Some of the money voted by Congress for the support of medical research is earmarked for cancer, arthritis, mental health, and so on. This is partly because certain legislators have almost as much zeal to become known as the friend of the deaf, the blind, or the halt as they do to become known as the friend of the veteran. This allocation to specific categories imposes less handicap upon the Institutes than you might think since there is so much overlap of interest in the fundamental and basic areas of research. In any event, decisions are made to appropriate certain sums for fellowships to prospective investigators, other sums as training grants to institutions so that the latter may attract and train bright young people as investigators, and still other sums to support specific research projects. Some ground rules as to age, training, experience, and so on are drawn up, and invitations are then extended for applicants to state their qualifications and their hopes. While all the administrative machinery is in the hands of the salaried staffs of the Institutes, all of the decisions as to who gets what and how much are made by these scientific advisers who are not on the government payroll and should be immune to any congressional or other political pressure. I would like to emphasize this because I believe it is a matter of some comfort to all who are taxpayers. Each scientific adviser, in his capacity as section member or council member (the latter group, by the way, acting as a review body for the work of the former), has hundreds of applications, with their accompanying reprints, letters of recommendation, and other supporting documents, to study and appraise. This is a brief description of the job which came to Robin.

Robin was elected to the Revision Committee of *The United States Pharmacopeia*. . . . The Revision Committee has the unique distinction of having its decisions achieve legal status although the men who prepare them have no official government position. . . . The original book, and its subsequent revisions, achieved such high scientific status and was so free of criticism that there was never any justification or excuse for the government to take over this function on the one hand, while the pharmacopeial personnel were so proud of the record and so jealous of their prerogative of maintaining a small island where John Q. Citizen was pre-eminent on the other that this quasilegal position may well continue indefinitely. . . . The question naturally arises, why does an academic man accept or take on one of these jobs? The answer is clear. There is no disputing the fact that for the most part they represent honors or at least some sort of recognition of ability on the part of the individual, and the latter is seldom immune to this sort of flattery. Should he be reluctant to accept in view of the fact that they are unremunerative, frequently vexatious, and always time consuming, he is reminded of the fact that they are indirectly a tribute, or at least an advertisement, to his university which he ought to recognize and encourage. Everytime some national committee or editorial board and so on is named, the academic genealogy of its members is cited. The public relations departments of universities keep records of such items since this constitutes the sort of publicity so useful to them in their fund-raising operations. It also provides a means of ranking and comparing the staffs of various institutions. Those of you who doubt this statement must have been deaf to the gnashing of teeth which went on at many campuses after President Kennedy began picketing the new frontier with the Harvard Alumni Association.

Sometime during the course of the above events, the administration at Chihuahua University took cognizance of what was going on and promoted Robin to an associate professorship. This promotion and his increased stature as a research scientist were recognized by his fellow faculty members in the customary manner. In the center of the campus stands the Hexagon Club, a "three-story building of impressive, if mongrel architecture, complete with canopy to the curb and coat of arms." It is the faculty club, although a few

nonfaculty men are permitted membership. Although both breakfast and evening meals are served to a few lonesome widowers and bachelors, the heart of the day is lunchtime, when several hundred members converge upon it, to eat, to visit, and perhaps to enjoy a game of bridge, canasta, or billiards. Dominating the large dining room is the Hexagon Table, at which the savants gather—those who have won Nobel prizes or would have won them if there were more to go around. No brash young faculty member ever approached this table except by special invitation from one of the anointed. This now happened to Robin, and he ate there on a number of occasions. Although he was envied greatly by all his contemporaries, he would have preferred to eat with his close friend, Alpheus Blimp. Blimp was a graduate of Chihuahua University who as an undergraduate cheerleader had composed its most inspiring cheer. It went like this: Chi hua hua, Chi hua hua, Chi hua hua hua; go she wah, go she wah, go she wah wah. Blimp was rewarded for this sterling accomplishment by a position in the English department. Although he had begun on the bottom rung of the academic ladder, he was now an assistant professor, popular with everyone because of his unfailing good humor and notable for having no ulcers or other badges of academic frustration.

Robin's promotion was noted and acted upon by two other individuals. In the first place, Robin's wife, Mrs. Robinson, promptly went out to Uppity Hills, signed up for a large wooded lot, and got a contractor to build a house much too big for their needs and for their means. To conserve money, the upstairs was left in an unfinished condition for Robin to complete. And to bring in some extra money, Mrs. Robinson prodded him into working up a popular science lecture called "Why Science?" which he could give to church, PTA groups, and similar organizations for a modest stipend.

In the second place, the Dean took note of Robin's increase in rank by assigning him assorted academic responsibilities. Robin was made chairman of the curriculum committee. Every spring the Dean attends the annual meeting of the Association of American Medical Colleges, hears the Dean of X institution rant enthusiastically about some new integration course or correlation course or some horizontal or vertical course (whatever they mean!) newly flourishing at X institution, and wants the curriculum committee to see what