HUMAN PATHOLOGY

A TEXTBOOK

BY

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WITH AN INTRODUCTION BY

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18 ILLUSTRATIONS IN COLOR AND 443, BLACK AND WHITE

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TO MY WIFE

PREFACE TO THE THIRD EDITION

As WITH biology in general, pathology is not static, and shows continuous change, growth and development. With new methods and new attacks, factual material is often altered or augmented and there is a constant ebb and flow of opinion and judgment. To meet changes of views as they are modified by the contributions of investigators in the special field, a textbook requires as frequent revision as circumstances will permit. The continued widespread use of this book by teachers, students and practitioners is a source of inspiration and gratification to the author, and provides the opportunity for improvement and modernizing which this third edition represents. The revision is considerably more extensive than was true of the second edition, and throughout the entire book every effort has been made to bring the material up-to-date.

There are completely new sections on edema, shock, rheumatic fever and diseases of the teeth. Doctor J. P. Quigley assisted in the preparation of the section of shock and although absolved from responsibility he has my gratitude. My thanks are extended to Professor Thomas J. Hill for the section on diseases of the teeth. The material on endocarditis has been largely rewritten, and the same is true of that on Bright's disease. Many other sections have been revised and there are innumerable minor corrections and changes. Careful attention has been given the references at the end of each chapter. Some of the older references have been deleted and more than six hundred new references inserted. Doctor Robert A. Moore has rendered invaluable aid in regard to this and other features. Sixteen new illustrations replace older cuts. The staff of the Department of Pathology of Western Reserve University and certain teachers of the subject in other universities have given many helpful criticisms. I am indebted to Doctor Harry Goldblatt for revision of the index and to Miss Catherine E. Lennon for faithful and conscientious work on the manuscript.

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PREFACE

THE history of pathology shows a gradual evolution from a subject based almost entirely on morphology to one so comprehensive that as H. R. Dean says, "to the pathologist—all medical things are pathology." From this point of view clinical medicine is applied pathology. At any rate, pathology is no longer merely the study of morbid form, although no evolution or development can divorce from it the fundamental importance of pathological anatomy. The purpose of this book is to present the morphological alterations incident to disease, in the light of modern views as to their functional significance. The subject matter is confined to human pathology, since the work is designed for students and practitioners of medicine, but general biology has been called upon to furnish data relevant to the origin, course and natural history of disease as it affects man. The features of morbid anatomy and histology are studied objectively and are looked upon as established facts. At the present time, explanations of disease and interpretations of its phenomena are often hypothetical and the attempt is made in the discussions to distinguish clearly between fact and theory. A working knowledge of normal anatomy and physiology and of bacteriology is prerequisite to a comprehension of pathology. These subjects are correlated with the processes and products of disease and, with the more important topics, the whole concept is employed as a basis for a brief introduction to the clinic. In summary this is a textbook of pathological anatomy and histology, related to the broader functional aspects of disease.

A textbook is only an introduction to the essentials of a subject. References may be given to the literature, but, in view of the rapid advances of biological and medical research, only by observation, investigation and well directed reading can the subject matter be kept abreast of the times. An important part of education is acquaintance with the names of those who have furnished its heritage. In the earlier chapters the names of investigators are given in the text infrequently and the student can get the references from the list at the end of each chapter. Later, however, as greater familiarity with the subject is assumed, the names are inserted more freely. In so far as possible references are made to journals easily accessible and in the English language. The bibliography is in no sense complete, but is so selected that by its use an introduction to the literature of pathology may be gained. The mode of reference is in general accord with that of the American Medical Association.

The conventional division into general and special pathology has been adopted as the result of a long teaching experience. It is believed that this arrangement is in harmony with the position of pathology in the medical curriculum and best serves to present the subject as an introduction to, and a

basis for, the clinical branches. For the advanced student and the practitioner it affords convenience of reference.

At the beginning of each chapter in general pathology the factual material is arranged in tabular form so as to give each topic its relative associations in the entire subject. This is regarded as of distinct pedagogic importance and in our experience has established its value. It may also serve as the basis of the problem method in the teaching of pathology, but before problems can be set it seems essential to provide a background of major and minor premises in the mind of the student.

Many of the illustrations were made under the direction of Doctor Simon Flexner for a book on pathology which he proposed to write. Manifold duties prevented him from completing a manuscript and the illustrations have been turned over to the author, who cordially acknowledges his gratitude. Thanks are due the Surgeon General of the Army and Major James F. Coupal for the use of photographs made at the Army Medical Museum, Washington, D.C. Other illustrations have been made from a rich material provided by association with several hospitals in this and other cities. The entire list of illustrations has been carefully selected and limited. Their purpose is to clarify the text rather than to provide a pictorial atlas.

It is a pleasure to express grateful appreciation of aid rendered by numerous friends. Maurice L. Richardson, M.D., Benjamin S. Kline, M.D., and Harry Goldblatt, M.D., have given freely of their time in criticism of the manuscript. Miss Catherine E. Lennon, who has prepared the index and repeatedly typed the manuscript, has been an invaluable and faithful assistant. Mr. J. C. Harding, Librarian of the Cleveland Medical Library, has kindly checked the references. The drawings have been made by Mr. Louis Schmidt and Mr. E. F. Faber. Several friends, notably Wade H. Brown, M.D., Louise Pearce, M.D., and Stanley Cobb, M.D., authorities in their fields, have criticised certain parts of the manuscript. The author absolves all of these from responsibility for statements in the text but extends his warmest thanks for their interest and help.

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INTRODUCTION

PATHOLOGY is admittedly one of the fundamental subjects, if not the basic subject, of the medical curriculum. The reasons for this are perhaps obvious, because medicine in the last analysis deals with the consequences of disturbed function or altered structure of the organs and tissues, which induce the symptoms collectively termed disease. Therefore, without an understanding of pathology we can have but an imperfect, and at most empiric, notion of the essential nature of disease.

Moreover, disease itself is not a fixed or static condition; it appears in a great variety of forms and degrees of intensity, of which some progress towards restitution or recovery, and others towards dissolution or death. Hence disease is not a state, but a process ever changing its manifestations, until one or the other terminal stage is reached.

This process includes those modifications arising merely from the aging or senescence of the body in the ordinary course of the development and decline of the individual, as well as the action and reaction of the organs and tissues to many kinds of injurious influences engendered without, and perhaps even within the body. Although parasites are responsible for many disturbances of function and structure, the number and variety of injurious agencies far exceed the limits of parasitic activity and embrace purely physical and chemical effects, to whose action even the injury induced by parasites may come to be ascribed.

The reactive and reparative phenomena, on which restitution and recovery from injury depend, include many general biological or physiological processes, as of growth, immunity, and the like, making the complete exposition of the foundations of pathology a subject so vast as far to exceed the limits of a single volume or manual.

The present volume provides a well considered and successful compromise with regard to the almost endless number of topics demanding inclusion in a textbook on pathology. The work covers the fields of general pathology, pathological or morbid anatomy, pathological histology, functional or pathological physiology, and the general subjects of bacteriology and immunology. Greater detail in the special topics of physiology, parasitology, and immunology may be sought in textbooks devoted particularly to those branches of learning.

The presentation adopted is adequate and proceeds from the general to the particular. The discussion of debated or intricate subjects is sufficient to permit of definite understanding of the points at issue. The subject matter is remarkably complete and the text is lucid; while the illustrations, whether drawings or photographs, are precise and appropriate. In brief, the textbook presents the broad subject of pathology, as now conceived and taught in this country and in Europe, in a manner suitable for the medical and

biological student, as well as for the practitioner of medicine desiring to keep abreast with the ever enlarging subject of pathology. The references to special articles and treatises at the end of the chapters are well chosen, and they contain properly a preponderance of publications in English. The typography, illustrations, and bookmaking reflect credit on the publishers, just as the matter itself is of high credit to the author.

Doctor Karsner has made a notable addition to the English literature on pathology, and the prospective reader is to be congratulated on having available an authoritative and timely manual adapted equally for use as a textbook and a work of reference.

SIMON FLEXNER.

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PART I—General Pathology

A TEXT BOOK OF HUMAN PATHOLOGY

CHAPTER I

GENERAL PHENOMENA OF DISEASE

Introduction.—Health is that state in which the organism is in complete harmony with its environment. Disease includes a variety of conditions leading to a disruption of this harmony, but by common usage excludes congenital anomalies and certain acquired deformities. Disease represents the sum of the action of the cause, and the effects produced by the cause, plus all the retrogressive, progressive, morphological and physiological processes set up in the individual. Pathology is the study of the cause, processes and effects of disease. It therefore concerns itself with the nature of disease. As a matter of practical fact, pathology is concerned with predisposing and exciting causes and with alterations of form and function incident to disease. Essentially, this means the study of etiology, pathological morphology and pathological physiology, the latter including general physiology and biochemistry. It must therefore be assumed that the student has a working knowledge of embryology, normal cytology, histology and anatomy, physiology, biochemistry, bacteriology and protozoölogy. Without this knowledge of the normal, studies of the abnormal rest on an insecure foundation.

Causes of Disease.—The study of the causes of disease is called etiology, and forms an important basis for all work in preventive, diagnostic and curative medicine. Causes may be classified in a variety of ways, such as point of origin within or without the body, and the nature of the agent whether physical, chemical, mechanical, bacterial, or animal, but the most important classes are predisposing and exciting. Predisposing, remote, distant or preparatory causes are those which produce a tendency to acquire disease or prepare the body for the action of the direct cause. Exciting, proximate, determining, immediate or direct causes are those which incite the actual disease processes. Any cause may be classified as general, when it affects large numbers; individual, when it operates on a single organism; or special, when it leads to a special type of disease. Our brief discussion will proceed

on the basis of this last classification including in each group the predisposing and direct action of the factors discussed. A comprehensive discussion is to be found in Roger's book.

General Causes.—These are concerned especially with the environment, such as temperature, air, water, soil, etc. Man, being a warm blooded animal, has a practically constant normal body temperature maintained by the mechanism of thermotaxis, which operates to preserve the level of body temperature in the face of changing environmental temperature. Extremes are better met if the air be relatively dry. High temperatures may, by failure of the body to maintain adequate radiation, directly produce such conditions as heat exhaustion or thermic fever. Dry heat is found by Murphy and his collaborators to increase the number of lymphocytes in the blood, and animals treated by heat are said to exhibit increased resistance to tuberculosis and to transplantable cancers. Local burns are caused by dry and moist heat, x-rays, radium, electricity, caustics and war gases, and vary from erythema to tissue destruction. The three most common causes of death following severe burns are shock, toxemia and exhaustion (Pack and Davis). Extremes of heat and cold produce depression of general activity and cold may lead to crowding in ill ventilated places thus increasing exposure to infections. Cold may so reduce circulation in distal parts as to lead to death of those parts or necrosis, which when infected with putrefying bacteria becomes gangrene. Local application of freezing mixtures may have the same effect.

CLIMATIC CONDITIONS deal particularly with heat, cold and humidity, the last emphasizing the effects of the former. Sayres and Harrington find that high temperature reduces capacity for work, but is less effective if the humidity be low. Movement of the air tends to counteract the ill effects of high humidity except when external temperatures are above 37° C. Summer season, for a variety of reasons, predisposes to diseases of the intestinal canal, and winter to diseases of the respiratory tract, rickets, etc. It is possible that summer may induce low vasomotor tonus, so that hyperemia of internal viscera ensues. Bacteria flourish on foods in the summer, and introduced into a hyperemic intestinal canal may have a favorable field for establishing infection. Cold, if long continued, may be well borne, but if intermittent so as to produce chilling may lead to hyperemia of internal parts. The investigations of Mudd and his collaborators clearly indicate that such is the case, and if so, local resistance is perhaps reduced.

It is well known that LIGHT is of importance to the maintenance of health. It is not altogether clear whether these effects are due to long wave lengths, or short wave lengths and it is also probable that simultaneously other influences operate. Brown, Pearce and Van Allen show that diffuse sunlight is one of the factors which maintain mass relationships of organs and functional activity. Pearce and Brown demonstrate a correlation between light and experimental tumor growth. We have shown that short wave lengths combat the poisonous effects of uranium. Chick, Hess and many others have studied the influence of short wave lengths in the prevention and cure

of rickets. It is impossible in the scope of this book to cover a subject so widely investigated and the reader is referred to such articles as those by Sellards, by Bering, by Clark, by Bovie and by Laurens.

Roentgen Rays and Radium.—The progressive advances in production of radiations, since the discovery of x-rays, the isolation of various rays for study, the difficulty of establishing units of dosage and the uncertainty of biological reactions have resulted in accumulation of data that cannot be precisely evaluated. The following summary of our present information is general and subject to change as exact observations are contributed. Excessive irradiation produces effects upon the body which may be acute or chronic, local or general. Important general effects including especially prostration and gastro-intestinal disturbances may follow, after a latent period of several days, massive and deep irradiation. The severity is generally greater following x-ray than radium exposures, especially those of the abdomen. The available evidence incriminates protein disintegration products, particularly proteose. The source is not known but the sensitiveness of lymphoid structures to irradiation suggests that their destruction may contribute. Intestinal ulceration occurs in experimental animals but is not constant in man. Protein metabolism is increased, and with many variations the blood sugar is generally increased. Blood and urine chlorides are reduced.

Local effects upon the skin appear to be due largely to soft rays. Erythema appears in from a few days to about three weeks. Degeneration and destruction of the basal cells of the epiderm, followed by flattening of the papillae, and degeneration of sweat glands, sebaceous glands and hair follicles with depilation may be observed. Repeated exposures may cause hyperkeratinization, acanthosis and indolent ulcers. Epidermoid cancers may develop with or without preceding ulcers. This is especially true upon the fingers and the dorsum of the hand.

Experimentally a lymphocytosis may occur, the only real evidence of a stimulating effect of irradiation upon cells, and although Wood and others disagree, Murphy attributes resistance to cancer in part to this change. X-ray workers may show a leucopenia, especially of the polymorphonuclear neutrophiles. Conversely leucemia has been attributed to repeated exposure. Profound anemia of aplastic type is also thought to be due to x-rays (Wegelin). There is no doubt that radium may produce a similar anemia. This has been observed frequently in painters of luminous dials. Radio-active substances accumulate permanently in the body and from a position in the reticulo-endothelial system of bone marrow exhaust the hematogenic tissues. The bone may be rarified and fractured. Bone sarcoma may occur presumably due to the continued action of alpha rays not screened out by the skin. (See Martland)

Viscera may be damaged by deep x-ray and by radium. Parenchymal degenerations may be followed by necrosis because of direct injury and of vascular thrombosis and fibrosis. Intestinal ulceration, in this category, may be complicated by dense peritoneal adhesions. A genuine chronic nephritis

has been produced in animals and has been reported in man. That the lungs may become fibrotic is not finally established. Injury to the myocardium is variable. The gonads are especially sensitive. Degeneration of spermatogenic cells is followed by their death and disappearance. The Sertoli cells may become swollen and proliferate; the interstitial cells are not affected. The Graafian follicles disappear but there is little or no effect upon corpora lutea or supporting tissues.

In the treatment of tumors, the short penetrating rays are of especial importance. The "law" of Bergonié and Tribondeau, that immature and dividing cells are destroyed more readily by irradiation than are mature cells, is applied in determining radio-sensitivity of tumors. Application of this law is not without exception and Ewing points out that other factors such as situation, accessibility, vascularity, infection, general health, etc., may play an important part. Nuclear disintegration and deformation, cytoplasmic destruction, multinucleated giant cells, phagocytosis of cells and nuclear fragments, vascular thrombosis and productive endovasculitis, and surrounding granulation and fibrosis, are observed. The relative importance of direct effect of the rays upon the cells and of vascular occlusion is not settled. Murphy attaches much significance to increase in number of lymphocytes in the blood as a factor in resistance to tumor growth but Wood and others oppose this view. The destructive effects of irradiation have been attributed to beta rays and secondary gamma rays and also to liberation of negatively charged particles resulting from atomic disintegration (Wood) but Jacobsen's studies with high voltage cathode rays indicate that the destruction is due to cathode rays liberated in the tissues by irradiation. Experimentally, nuclear effects in germ cells, with disturbance of genes, may produce serious effects upon progeny (Muller, Weinstein, Curtis). In tissue cultures small doses depress mitosis temporarily and large doses more durably (Kemp and Juul).

Radium is bactericidal, principally by the action of beta rays, but x-rays are not definitely bactericidal except in the presence of fluorescence (Newcomer). Short wave-length rays produce deterioration of immune bodies in vitro. The reader is referred to comprehensive articles by Colwell and Russ, by Warren and by Rolleston.

Ultraviolet rays have much the same general effects as the milder doses of x-ray and radium. Sunlight, through the action of the ultraviolet rays produces sunburn and in those sensitized by the presence of porphyrins in the body, discussed in the chapter on pigments, may produce more serious lesions. Ultraviolet rays are said to increase metabolism, to stimulate blood forming organs, to increase a resistance to infection and to be bactericidal. It is well established that the shorter wave length ultraviolet rays, by direct or indirect (irradiated ergosterol) action, exert a favorable effect upon the retention of calcium and phosphorus and consequently are of use in both the prevention and cure of rickets. (See Clausen)

The influence of photodynamic substances and catalyzing agents is discussed by Bering, Clark, Kinney and by Hauptmann.

Sound is of little importance in pathology except as it may lead to, or increase the intensity of, psychoneuroses. It is said to induce deafness in such occupations as boiler making by producing a chronic fibrosis of the tympanic membrane.

Death from electric shock is due either to respiratory paralysis or ventricular fibrillation, without significant anatomical lesions (see Jaffe). Smaller quantities may produce severe burns, due to electrolytic destruction of tissues and cells.

Atmosphere is of importance particularly as concerns pressure, moisture, movements and composition. The optimum pressure for all functions is about fifteen pounds to the square inch. Increases in pressure are well borne for short periods but fatigue appears early. The great danger is of sudden release of pressure, which may produce "caisson disease." Gases are under essentially the same pressure in the body as in the atmosphere, so that sudden release of pressure may produce bubbles in the body fluids and tissues. The bubbles are of greatest importance in the nervous system, where temporary or permanent disease of the tissue may occur. Low atmospheric pressures are observed at high altitudes and especially concern mountain dwellers and aviators. Schneider points out that although high altitudes condition low pressure, decreased temperature and humidity, increased sunshine and electrical alterations, "it is recognized that the controlling element in the physiological reactions is the diminished partial pressure of oxygen and the consequent imperfect aëration of the arterial blood." The acute symptoms, simulating drunkenness, due to sudden elevation or active exercise before acclimitization, are temporary and easily recovered from. Chronic anoxemia leads to ready fatigue, to an increase in the number of circulating erythrocytes, and although the point is controversial as yet, probably to reduced hydrogen ion concentration of the blood. The moisture of atmosphere is of importance in that increased humidity often leads to ready fatigue and decreased bodily exercise. Humidity also favors bacterial growth. The presence of large bodies of water tends to equalize atmospheric temperatures. The movements of air are of importance in relation to chilling of the body surface and also in blowing insect carriers of disease over wider areas than they could otherwise travel.

The composition of the atmosphere other than as mentioned above concerns particulate content and gases. The particulate content of importance includes bacteria, either in dried form or in minute droplets of sputum or other secretion, protein dusts and inert dusts. Thus, infection may be directly transmitted in the air. Protein particles, such as pollens, epidermis and hairs of animals, may produce asthma, coryza and other reactions in those who are hypersensitive. Inert particles such as carbon, marble, iron, silica are considered in reference to diseases of the lungs in the chapter on pigmentation. The normal gases of the atmosphere may vary in relative amounts and other gases may be present. The latter may be either harmless or directly injurious, as for example carbon monoxide with its production of carbon monoxide hemoglobin, or nitrogen tetroxide (Wood) and other gases such as the war

gases, which may directly cause or predispose to pulmonary inflammations. Numerous other lesions may be produced by atmospheric impurities and are important particularly in industrial medicine. Decrease of carbon dioxide is of little significance, but increases are important physiologically (Scott) and may lead to serious pathological disturbances. Oxygen is present in the air in approximately optimum concentration, although wide ranges are possible with preservation of health. Martin, Loevenhart and Bunting find little change until oxygen is reduced to 12 per cent. or less, when important pathological changes occur. We have found experimentally that long exposure to atmospheres containing 80 per cent. or more oxygen induces a pneumonia.

Huntington in an analysis of the geographic distribution of the influenza epidemics of 1918 points to the necessity for further study of how the human subject and the invading organisms are influenced by the atmosphere. Apparently only the weather is of significance in the variations in virulence of the epidemic in different localities.

Water, as it occurs in atmosphere, has been referred to. Water, as obtained for drinking and washing, as well as its availability for forestation and vegetable growth generally is of the greatest importance in maintenance of health. Its capacity for carrying the exciting causes of certain infectious diseases such as typhoid fever, cholera and dysentery are well known. Sedgwick and MacNutt have observed that in several cities the purification of water has been followed not only by a decrease of water-borne diseases such as typhoid fever and diarrheas, but also of acute respiratory diseases and pulmonary tuberculosis. The death rate minus the typhoid component is generally decreased. The chemical composition of water may perhaps predispose to disease and there are claims that hard waters may lead to abnormal calcification in the body, but this is not proven. That hard waters produce goiter is probably not true. The work of Marine and Manley indicates that the absence of another chemical constituent, namely, iodin, is probably a most important factor in the development of goiter (see chapter on Ductless Glands).

It will be seen that much of the material discussed above deals with hygiene, and for more complete discussion of these subjects as well as the influence of dwelling, crowding, soil, etc., the reader is referred to the texts on hygiene and sanitation.

Individual Causes.—These include age, sex, heredity, constitution, and such personal factors as food, clothing, occupation and psychic influences.

Age may be roughly divided into prenatal life, infancy, childhood, youth, early middle life, middle life and old age. Ballantyne and others discuss conditions of prenatal life, which include such factors as physical condition and nutrition of the mother, disturbances in placenta, fetal membranes and umbilical cord, abnormalities of embryonal and fetal development. At birth the infant is subjected to traumatic influences, to infection during labor and to sudden change in environment. In infancy, food offers important predisposing and direct causes of disease; infections from the immediate family, more particularly the mother, may occur. The infant may possess certain