

## Introduction

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Pathology is that branch of natural science which is concerned with the search for the cause and mechanism of disease. In this general sense the term applies to disease of all living organisms. Human pathology is primarily concerned with disease in man but does not exclude the insight which is gained from the study of disease in animals and plants. Fundamental facts of morbid life are revealed by exact observation and purposeful experiments on animals and plants.

The everyday word *disease* is an abstraction, and abstractions obviously cannot be the immediate object of natural science, which is necessarily founded upon observation of natural phenomena. The concept of disease has been established by extracting and totaling those characteristics of the sick which differ from the norm. In our observation of the sick and the healthy we study manifestations of life, and life presents itself to our senses as form and action. These manifestations are investigated with methods involving precise measurement. Anatomy-gross and microscopic is concerned with normal form. Physiology inquires into normal function. Life, however, is also experienced subjectively by the mind, and investigations of mind belong to the realm of psychology.

In pathology, as in all natural sciences, understanding must begin with observation and description. The earliest observations were concerned with obvious manifestations of abnormality of the patient during life-e.g., variations in the rate and quality of pulse or respiration, fever of varying type and intensity, abnormalities of excretion and secretion, and changes in bodily appearances and behavior.

Almost from the beginning of the era of pathologic anatomy there were minds which challenged the primacy of a descriptive doctrine as the ultimate goal of pathology. They questioned the identification of disease with morbid alteration, and they ridiculed the overestimation of anatomic diagnosis as the final aim in the search for the nature of disease. It is the eternal contribution of Rudolf Virchow to have recognized the inevitable sterility of a merely static appraisal of the structural alteration associated with disease. He also

formulated the principle which up to the present time has remained the axiom of research in pathology: to understand the inception and evolution of morbid states.

The pathologist concerned with the structural aspect of disease cannot confine himself to mere description. Pathologic anatomy originated as a branch of normal anatomy; it employed identical methods of gross and microscopic observation and description; but anatomic science advanced from mere description to an inquiry into the evolution of form. The concept of morphogenesis stimulated the development of embryology and comparative anatomy as components of normal anatomy. Pathologic anatomy utilizes the disclosures of these sciences in the interpretation of human monstrosities. Teratology and comparative pathologic anatomy have developed into an important field of biology; but beyond these special applications, the morphologic conception is a fundamental principle of pathologic investigation. Morphology rests upon the recognition that organic structure is constantly undergoing transformation. It is founded upon the comparison of different phases of organic life. Morphologic pathology compares normal with altered structure and correlates different states of pathologic lesions. It establishes relations between facts ascertained by observation, it correlates the morbid with the norm, and it teaches us that structural phenomena not only exist but that they pass through developmental stages. It introduces the dimension of time into the interpretation of static facts and it places them in the movement of life.

Life is manifested in structure and in function; the two cannot be dissociated. The maintenance of normal structure of living substance is guaranteed by the fundamental functions of assimilation and reproduction, and proper function is maintained by normal structure. This holds true for life in its most primitive as well as in its highest organization. A morphologic approach to structure implies a correlation between form and function. Thus, morphologic pathology guides us in visualizing aberration of function and makes structural change intelligible in terms of process. It leads us to the realization that pathology must strive for an understanding of the mechanisms of disease.

Biochemistry in its application to the analysis of organs and tissues is engaged in the search for the ultimate constitution of living matter without consideration of structure. Histochemistry, however, attempts to identify the chemical nature of morphologically separable units of cells and tissues. On the one hand, histochemistry employs the principle of anatomy-to separate separable things. In addition to conventional histologic technique it utilizes the most refined methods of separation, such as microdissection, ultracentrifugation, and electronic microscopy. On the other hand, it adapts certain methods of analytic and enzyme chemistry and of physics, such as ultraspectroscopy and x-ray dif

fraction, to the investigation of cells and intracellular substances. A combination of such methods has already promoted research in histology, embryology, cytology, and genetics. The pathologist concerned with the structural aspect of disease must realize that a fuller understanding of life, normal and abnormal, will be achieved only by recognition of the chemical and physical constitution of the living substance and its regulation by the laws disclosed by natural science. Such recognition ties morphologic pathology to biochemistry, biophysics, and to biology in general. Thus the pathologist must keep abreast of every advance in these sciences.

Pathology, conceiving of disease as life under altered conditions, tries to understand life in terms of a change in this interaction. Complex external and internal factors determine disease. It is the final object of pathology to recognize all fundamental factors in their action and interaction, in order to investigate causality in disease. Exact observation and correct correlation lead to inferences of causality which must be tested by experiment. The recognition of external factors as causes of disease does not complete the search. Oertel clearly states: "Any perfect causal explanation must include the complete and connected chain of all events which are responsible for phenomena, and these, moreover, must be in their proper position." In other words, etiology is not synonymous with pathogenesis. We must realize that the search for causality in disease must not stop with the recognition of external cause but must progress to

a demonstration of the mechanism by which the cause acts. Disease is the experiment of nature; we see only the results, while we are ignorant of the conditions under which the experiment has been performed. Step by step, pathology must unveil these conditions. It progresses from observation to correlation, from correlation to deduction, in order that rational experimentation may accomplish the final synthesis.

Disease manifests itself in alteration of form and function. An integrated knowledge of altered form and function is the ultimate aim of pathology and is the cornerstone of modern medicine. This integration requires not only a knowledge of facts but also a certain attitude of mind which must guide the future physician in the study of disease. This attitude of mind can be developed only if the student is trained to advance from exact observation to correlation of facts and from correlation to deduction.

Many methods used for the recognition of disease in the living are founded upon the knowledge of structural alterations in the dead. This accounts for the requirement that a textbook of pathology shall be devoted primarily to exact description and interpretation of structural anomalies observed in disease. No textbook of pathology with its spatial limitations can fully achieve this object. It can attempt to present in concise form the results of investigation; it can never give a full account of the long road which has led from the original observation of lesions to the understanding of their causation.