A TEXT ON SYSTEMIC PATHOLOGY

OTTO SAPHIR, M.D., Editor

Volume I

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Edited by

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PREFACE

A NUMBER OF textbooks of pathology exist and it may seem superfluous to encumber the field with yet another volume. But these texts, following tradition, are usually presented from the point of view of a university lecturer addressing second-year medical students who are assumed to have acquired a working knowledge of the basic sciences and to be ready for this new course. In these texts, the material is strictly divided into two main headings: general pathology and systemic pathology. The usefulness of such a presentation is unquestionable. However, if the text comprises only one volume, with one-third to one-half devoted to general pathology, it can necessarily present only the more important facts. While these may satisfy the ordinary needs of the student, he will be at a complete loss in a more complex situation. He will have difficulty in finding the exact information he needs, and his crowded curriculum makes a search through original sources almost impossible. Thus, one of the guiding motives for this undertaking was to provide students in medical schools with the more specialized information they may seek.

The hospital pathologist, busy with an ever-increasing routine, also needs readily available information to assist in solving perplexing problems. It should be provided by a colleague with many years of experience in a hospital where there is sufficient surgical and autopsy material, as well as facilities for complete work-up and follow-up of surgical patients. The pathologist in practice is, and should always be, interested in the fundamentals of general pathology. But, in given cases, his needs are immediate. He demands a forthright text. He needs day-by-day answers as well as help in preparing cases for clinical pathological conferences. It is hoped that this volume will help in unusual as well as in routine situations.

Laboratory tests for studying functional aberrations in various diseased organs have become quite numerous. The medical student, as well as the pathologist, is inclined to treat pathologic anatomy and the study of functions of diseased organs as separate entities. The error in this attitude is obvious. Pathology unrelated to the patient and to the study of abnormal function has no place in modern science. To stress this point of view whenever feasible and to make pathology "alive" was one of the main reasons for undertaking this task. Whenever indicated, references to clinical signs and symptoms and the course of the disease are made throughout the text.

Originally, it was planned that this text would be the work of a single author, and the advantage of having one viewpoint through the entire volume seemed to overshadow the obvious objection that the task might prove too difficult for one person. However, it became apparent that, in view of a heavy schedule of activities, it would be too long before the work could be accom-

plished, if ever. Contributors were chosen not only on the basis of their previous work but also because most of them had been affiliated with me in research or the academic field of pathology. This measure has assured a common broad concept and unity of presentation, but has not affected individual approaches and individual opinions. I am grateful for their contributions.

Opinions, certain deductions, explanations and classifications are occasionally at variance with accepted concepts set forth in textbooks and other publications. The views expressed here may, on occasion, seem unorthodox, biased, or even contrary to beliefs. My apologies to the *manes* of the great men who have made pathology a science but who have sometimes rigidly enshrined certain assumptions, making facts out of fads, thus often alienating the practitioners of clinical medicine. The views presented here are based on practical experience over the years, on facts gained as a result of sustained studies on a number of subjects, and on more than casual acquaintance with the pertinent literature and a critical evaluation of it.

It was thought it might be valuable as well as of interest to include a minor amount of biographical data in connection with eponyms and certain proper names. Four different standard sources were consulted, and occasional differences were found among them with regard to dates, etc. Although every effort was made to ensure accuracy, the reader may, then, note a few discrepancies in these data which were, unfortunately, unavoidable.

Grateful acknowledgment is due to my colleagues and friends who gave so generously of their time and knowledge in the reading and criticism of the manuscript. I am especially indebted to Drs. Max Appel, Francis Archer, Nathan Cohen, Dorothy Eshbaugh, Margaret Littman, Heinrich Necheles, Albert I. Rubenstone, William Saphir, Herbert Silverstone, Dora Stryzak and Stanley Weinmann. In the preparation of innumerable slides, the skill and loyalty of Miss Irene Goldberger greatly facilitated the work. The selfless cooperation of Mrs. Nancy Arnold was invaluable. I also wish to thank Mrs. Ira Frank for her unfailing interest and generosity. For the understanding and encouragement without which this book would not have been written, I want to express my deepest gratitude to Dr. Morris H. Kreeger, Executive Director of Michael Reese Hospital.

Otto Saphir, M.D.

CONTENTS

I. THE HEART

By Otto Saphir, M.D.

ALTHOUGH it was originally intended to discuss the various heart diseases from the point of view of their location, this plan was not followed through. Alterations of the endocardium affecting also the myocardium are treated as disease entities rather than as changes occurring in special locations. Degenerative diseases, vitamin deficiencies, changes due to chemicals, tumors, etc., are likewise discussed as involving the *whole* heart

rather than its individual structures. Contrary to other texts, these diseases will be taken up separately. Other alterations are mentioned as found predominantly in the endocardium, myocardium, or pericardium. This was thought to be a more practical approach as well as space-saving.

Degenerative Changes

Cloudy swelling of the myocardium is often associated with acute infectious diseases, severe anemias and poisonings. The heart muscle is softer than normal, and on section is grayish with obscured outlines of individual muscle bundles, the cut surface appearing parboiled. Microscopically, the cytoplasm of the muscle fibers is granular, and sometimes minute eosinophilic droplets are seen throughout the sarcoplasm (hydropic degeneration). While these changes may resemble those occurring post mortem, one does not see such other postmortem changes as spotty autolysis of the myocardium, of the valvular endocardium and of the aortic intima characterized by a dirty reddish discoloration. Severe cloudy swelling may go on to necrosis of individual muscle fibers, as often observed in diphtheria. In such instances, masses of sarcoplasm with complete loss of their striations seem to have been separated from the surrounding sarcolemma and appear as crumbled masses.

Sometimes the term myocardosis is used to denote noninflammatory disease of the myocardium. It is favored principally by the clinical physician in lieu of the old term "myodegeneratio cordis," which implies the presence of any kind of change leading to weakening or insufficiency of the myocardium. There are also those who use "myocardosis" principally for changes other than myocarditis, as those occurring in infections and degenerative disease. Thus, cloudy swelling, fatty degeneration, etc., are included in this term. While it is true that by "osis" is meant a "morbid process," it also means "abnormal increase" and therefore is sometimes misleading. Besides, the term includes so many anatomic conditions of the myocardium that its usage is not recommended, especially since it is not yet generally accepted.

In **hyaline degeneration** (HYALOS, Gr., *glass*) the individual muscle fibers seem to have been transformed into hyalinized fibers, however still retaining their individual shape. The fibers are highly eosinophilic and have lost their nuclei. Such changes resemble Zenker's (waxy) degeneration of striated muscle fibers. Hyaline degeneration is often found in regions of old myocardial infarcts, particularly in the adjacent endocardium and about infarcted papillary muscles. Hyaline muscle fibers with parts of their sarcoplasm replaced by large vacuoles have been described in the beri-beri heart. Hyaline deposits (hyalinosis) are common in any type of old myocardial scar, whether the result of myocardial infarcts or of inflammation. Aschoff bodies often heal with fibrosis and hyalinization. The tips of the papillary muscles are often whitish and completely hyalinized. This is particularly common in advanced age, and may be the result of coronary arteriosclerosis, the region most remote from the source of vascular supply being first and principally affected. The hyalinized endocardium appears pearly white. Hyalinization is very common in heart valves which are the seat of an old endocarditis; it may also be found in the adjacent mural endocardium brought about by abnormal blood currents and pressure changes, with resulting circumscribed chronic inflammation, fibrosis and eventual hyalinization.

Basophilic (mucoid) degeneration occurs frequently. Among 75 consecutive autopsies it was found by Scotti[291] in 71 per cent and was noted most commonly in patients over 40 years old. It consists of basophilic masses within the sarcoplasm and appears to be mucinous in nature, probably a mucoprotein or acid mucopolysaccharide. Its cause is not known, but it is more pronounced in instances of myxedema (Brewer[41]) where miliary foci of basophilic degeneration are supposedly characteristic. It also occurs often in hearts that contain an abundance of lipochrome pigment. Scotti[291] found that certain vascular lesions, particularly coronary atherosclerosis, were frequently present in persons who had basophilic degeneration of the myocardium.

Fatty changes in the myocardium are very common. These are usually classified as fatty

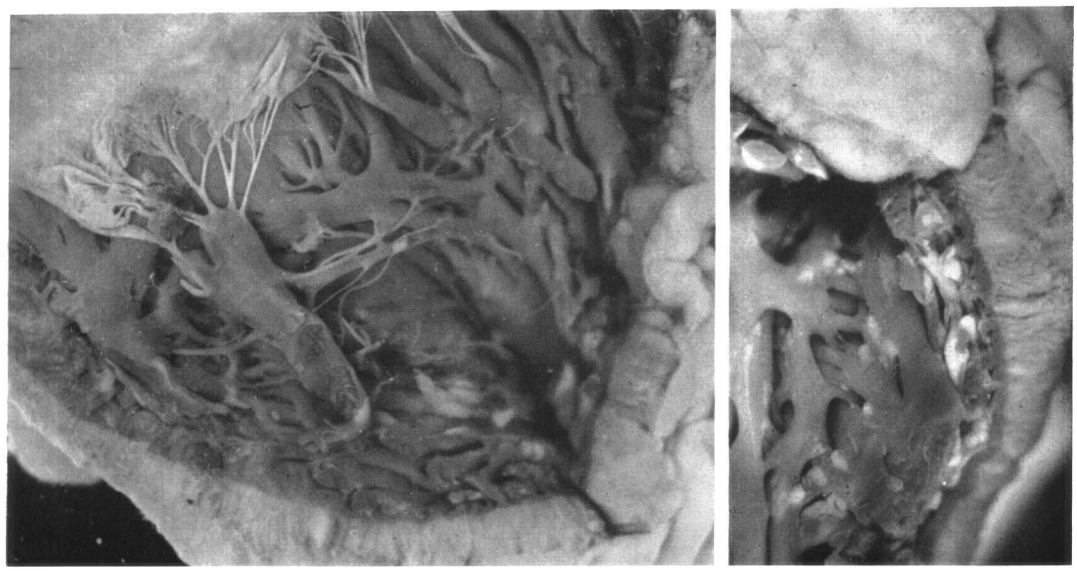
degeneration or fatty infiltration, although the two processes are entirely different entities.

Fatty degeneration of the myocardium occurs principally in cases of general or more localized hypoxia, in acute infectious diseases and poisonings. It is thus seen in severe anemias from any cause, in instances of nutritional disturbances such as occur with severe coronary arteriosclerosis, especially in the vicinity of myocardial infarcts. It is common in diphtheria, in various septic conditions and poisonings such as phosphorus and chronic arsenical poisoning, and is likewise seen in chronic alcoholism. There are those who advocate the possibility of a transient lipemia, possibly brought about by those agents which also cause fatty changes in the liver (see lipotropic substances, etc., Liver, Vol. II). The outstanding change is the appearance of minute fat droplets in the sarcoplasm which are not visible under normal conditions. This "becoming visible" has been termed phanerosis (PHANEROS, Gr., *manifest*, i. e., becoming visible). The chances are, however, that the fat droplets are carried to the heart by the blood stream (rather than having been there in an obscure form), and now, because of certain alterations, become visible.

The size of the heart is not influenced by fatty degeneration. The myocardium as seen through the endocardium is pale yellowish, or ill-defined larger or smaller yellowish areas in no characteristic locations may be seen throughout. In other instances, and particularly in the various anemias, the changes are most pronounced in the papillary muscles and columnae carneae, where fatty degeneration is seen in the form of more or less parallel yellow streaks, the so-called tiger stripes ("tiger" or "thrush-breast" heart). This configuration of the fatty degeneration is probably linked with the distribution of vessels in the papillary muscles and the fact that the fatty degenerated muscle fibers are located at a distance from these vessels. Microscopically, a number of small fat droplets are seen in the sarcoplasm, often arranged in parallel rows, which obscure the striations and eventually also the nuclei of the muscle fibers. The individual fat droplets remain isolated and do not fuse. An interesting fact is the observation that while fatty degeneration is confined to the sarcoplasm of the myocardial fibers, clumps of fatty globules may be expelled from the fiber and become located in the interstitial tissue (Linzbach[190]).

In **fatty infiltration,** the subepicardial fat tissue is increased and there apparently is an invasion of the adjacent myocardium by fat tissue. This occurs often in obesity but is sometimes seen in the undernourished, and it is frequently found in association with fatty livers. Since under normal conditions there is more fat in the region of the anterior wall of the right ventricle, fatty infiltration is first and foremost noticeable in this region. The excess fat deposited subepicardially adjacent to the myocardium of the right ventricle causes pressure atrophy and eventual disappearance of neighboring muscle fibers, which soon are replaced by fat. This process repeats itself when more and more fat is deposited. Eventually, much of the entire thickness of the right ventricle may thus be replaced by fat. Grossly, early fatty infiltration is seen along the section made for the opening of the tricuspid valve. In more severe instances, it seems as if the subepicardial fat tissue, comparable to a malignant tumor, had invaded the adjacent myocardium. Yellow, slightly elevated areas are often beneath the endocardium of the right ventricle. If much of the myocardium of the right ventricle is replaced by fat, the terms fatty heart or lipomatosis or adipositas of the heart are used. Fatty infiltration likewise involves the left ventricle and the atria, especially the right atrium. Within the left ventricle it appears as circumscribed, slightly elevated and elongated yellow areas often following the ramifications of the bundle of His. In the right atrium, fatty infiltration may involve the sinus and the atrioventricular node. Microscopically, the presence of fat tissue deep within the myocardium adjacent to atrophic muscle fibers is characteristic. Often, islands of atrophic muscle fibers or fibers undergoing autolysis are found completely surrounded by fat, indicating that some time ago muscle fibers must have been present where there is now fat tissue.

Fatty degeneration per se does not seem to interfere with cardiac function. In a number of instances, however, the same causes which



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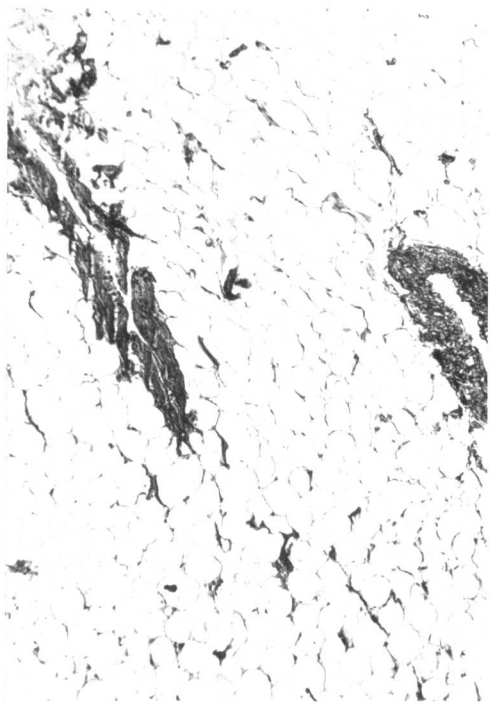
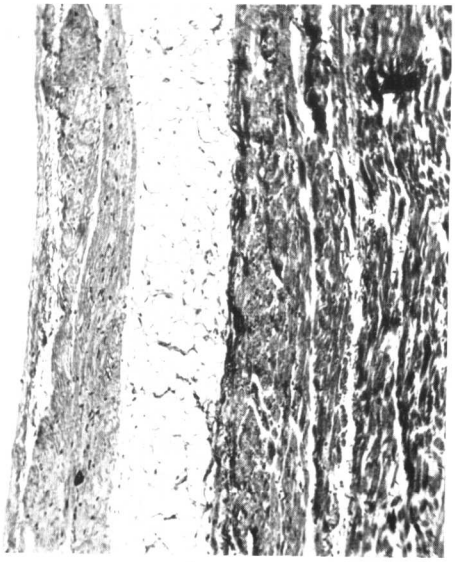
1. Fatty infiltration of the heart, right ventricle.
2. Fatty infiltration of the heart, right ventricle. Note the extension of the subepicardial fat tissue into the myocardium. There is also fat in the subendocardial layer.



3. Fatty infiltration of the right ventricle. Note the lone remaining, but atrophic, myocardial fibers.

lead to fatty degeneration are also responsible for the death of the patient. Fatty degeneration is a reversible process, and if the patient recovers from the original disease, the myocardium also returns to normal. On the other hand, fatty infiltration causes permanent damage to the myocardial fibers. And yet it often seems remarkable to find at autopsy severe fatty infiltration with replacement of much of the myocardium by fat in patients who have shown no evidence whatsoever of impaired function. However, fatty infiltration is sometimes of importance in explaining unexpected death where only small pulmonary emboli or small foci of bronchopneumonia are found. Only rarely, in our opinion, is it the sole cause of death. Fatty infiltration involves principally the right ventricular wall, where various regions are replaced by fat. Such a right ventricle does not have the reserve power of a normal one, and anything that would raise the right intraventricular pressure, even only very temporarily, might cause it to fail. It is sometimes possible to explain various changes in heart rhythm by fatty infiltration of the atrial nodes. We have seen such a case which clinically showed paroxysmal tachycardia with the Wolff-Parkinson-White syndrome. There are rare cases on record of rupture of the right ventricle solely due to fatty infiltration, attesting to its detrimental effect.



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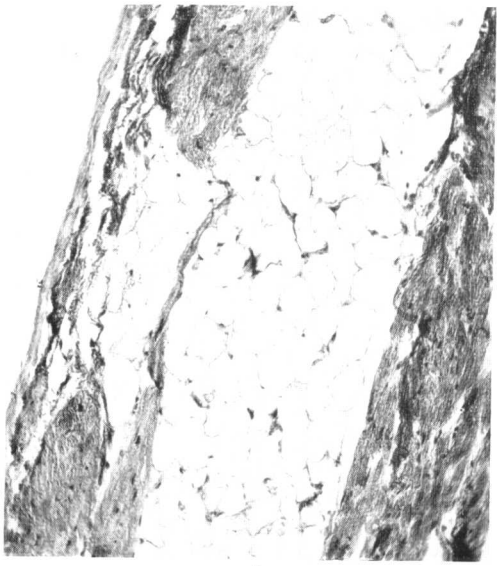

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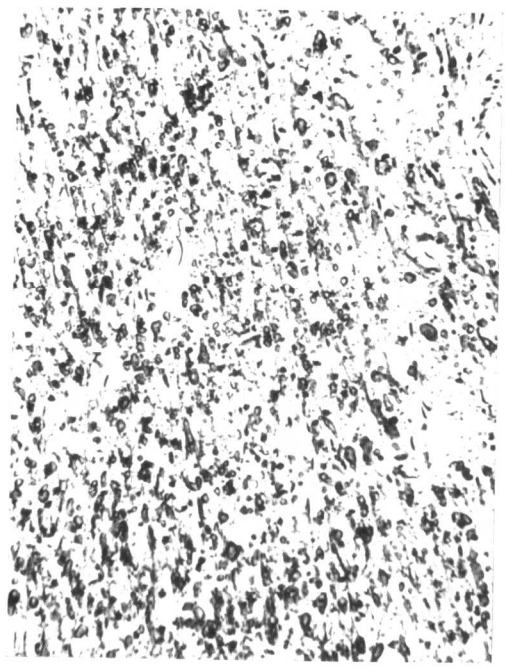
4. Fatty infiltration in region of the left bundle branch.

5. Fatty infiltration in the region of the left bundle branch. Note compression and atrophy of conduction fibers.

However, in spite of the fact that severe fatty infiltration is common, rupture of the heart is very rare (see Donat[76]). On the other hand, we have sometimes observed rupture of the heart due to recent myocardial infarcts where there also was marked fatty infiltration.

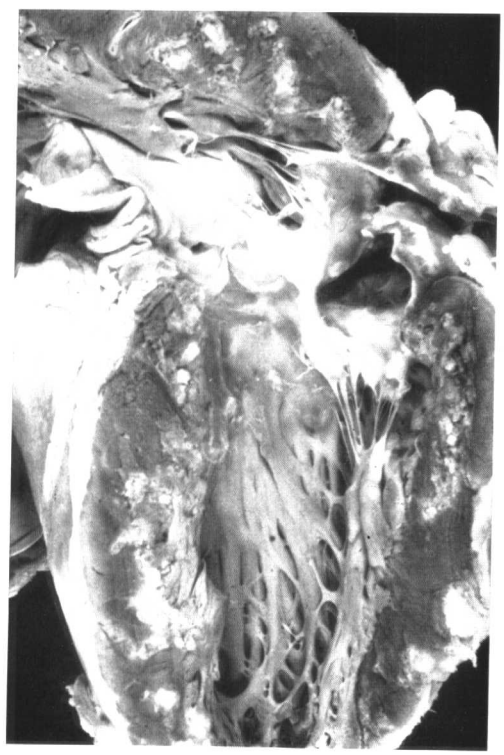
Fatty degeneration also affects the endocardium. It is often seen in the region of the ventricular surface of the anterior leaflet of the mitral valve in children and adults. Microscopically, minute fat globules are noted within the lining endocardial cells and also intercellularly. This may be combined with a moderate degree of connective tissue proliferation.

While under normal conditions the myocardial fibers contain a moderate amount of glycogen, it is greatly increased in von Gierke's, or glycogen-storage disease (E. R. von Gierke, German pathologist, 1877—1945). (For changes in the type of glycogen stored, particularly as to its solubility, see Liver, Vol. II.) The glycogen is unusual in that it does not readily break down after death. **Glycogen infiltration of the heart** is part of a systemic disease, involving also the liver and the kidneys. Sometimes the changes in the latter organs are relatively slight, while the myocardium is predominantly involved — "cardiomegalia glycogenica" (MEGALIA, MEGAS, Gr., *large*). Glycogen-storage disease affects only infants and children.



6. Glycogen infiltration: Best's carmine preparation.

The heart is markedly enlarged in this condition. A number of instances in the older literature referred to as "idiopathic hypertrophy" of the heart were large hearts due to glycogen infiltration. The heart is firm and reddishgray, and the myocardium appears rather homogeneous and glassy. Microscopically, the muscle fibers are very much broader than normal, with distinct striations and with many small glycogen droplets appearing in the routine hematoxylin-eosin preparations as minute vacuoles. These can be easily identified as containing glycogen by special staining methods. As intimated before, glycogen can still be demonstrated even several years after the heart has been fixed in formalin. (For older literature see Van Creveld.[323] See also the section on Liver.) Of interest in this connection are the findings of Mowry and Bangle,[229] who discovered considerable amounts of myocardial glycogen in 19 of 33 unselected infants. Six of these had amounts similar to two patients with glycogen-storage disease; three of the six had hypertrophic hearts. This may indicate that glycogen-storage disease is perhaps more common than is usually thought, or that excessive amounts of glycogen may occur occasionally in otherwise normal infants and, being of transitory nature, do not justify per se a diagnosis of glycogen-storage disease.



7. Calcification of the heart.

For changes in the heart in diabetes mellitus, see page 97.

There are cases reported as "nodular glycogenic degeneration" of the heart, which sometimes are misinterpreted as congenital rhabdomyomas (see Leach[179] and Kidder,[165] and also page 109).

Calcification of the heart is not rare in the region of the aortic and mitral valves and in the pericardium, incident to various pericarditides, especially tuberculosis. In the myocardium itself, however, it is more unusual. It is classified as dystrophic (DYS-, Gr., prefix implying *ill, hard, bad;* TROPHE, *nourishment*) or metastatic calcification. In the former, calcium is deposited in tissues and cells which are the seat of disease, while metastatic calcification means deposition of calcium mobilized from natural depots.

Dystrophic calcification is found in old infarcts and at any site where hyalin has been present for some time. On several occasions we have seen just below the membranous septum a small area of calcification within an old infarct which was responsible for complete heart block. At autopsy of a sixteen year old boy we found such severe calcification of large areas of the myocardium of both ventricles that the heart had to be opened with a saw. Microscopically, there were areas of ossification as well. For all practical purposes the heart was a "stony heart." The uninvolved muscle fibers were markedly hypertrophic. There was a history suggestive of diphtheria, and the implication was that the necrosis of muscle fibers preceded the subsequent calcification.

Foci of calcification are occasionally observed within the walls of old cardiac aneurysms. However, recent small septic infarcts in the myocardium, as occurring in acute bacterial endocarditis and endocarditis lenta, may likewise show calcification.

Dystrophic calcification is very common in old valvular heart disease following fibrosis and hyalinization. However, it may occur