

The Hepatic Circulation

and Portal Hypertension

CHILD

The Hepatic Circulation

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TO MY WIFE
MARGARET

PREFACE

AS ORIGINALLY CONCEIVED, this book was to have been limited to a consideration of the normal and pathological anatomy and physiology of the portal venous system. It was my intent to discuss the clinical aspects of this unique venous circulation and to review the many related experimental studies which have been made upon it, not only in laboratory animals but in man as well. In this fashion, it was hoped to bring together in one volume a useful body of information concerning this poorly understood blood vascular system.

Early in the development of the manuscript, I realized that one of the three circulations of the liver could not be separated logically from the other two. Consequently the scope of this volume was broadened to consider not only the portal venous system, but also the intimate circulatory dynamics of blood flowing to and from the liver. In accepting the responsibilities of this more ambitious effort, I have drawn freely upon the investigations of others. It is my sincerest hope that those who find their names in this volume will not take offense. The subject of the liver and its related vascular structures, I have discovered, constitutes a large research and clinical field sorely taxing the abilities of any one essayist. To those, therefore, who have kindly permitted me to reflect their views and to reproduce certain of their illustrations I am most particularly indebted.

It is my hope that, as published, this volume will enable the basic scientist to appreciate some of the clinical problems which confront the physician and surgeon in their efforts to manage successfully patients with hepatic disease and related disorders. Conversely, I believe that clinical scientists may benefit from a broader understanding of the fundamental problems involved in any disease process. Briefly stated, the major objective in writing this book is to help close the gap in time which always seems to exist between discoveries of the basic sciences and their clinical application to disease.

Insofar as the original studies contained in this volume are concerned, I must pay tribute to the resident system by which young surgeons are trained. Since its introduction into this country over a half century ago by Dr. William Stewart Halsted, this system of surgical training has always maintained as one of its major tenets a

period of time devoted to laboratory investigation. Only by early association with the disciplines of research may an awareness be aroused of the important relationship existing between the surgical experimental laboratory and progress in clinical surgery. To the several resident surgeons, past, present and future, who have contributed to this volume I must express my gratitude and appreciation. Without their help, their many inspirations, and their tireless efforts, this book would never have been written. In this day of faltering and indecision with regard to residency training programs in surgery, I would urge that the ideals of Dr. Ha'sted be kept more strongly in mind than ever before.

To my teacher and recent chief, Dr. Frank Glenn, I would express especial thanks, not only for his encouragement and help in the preparation of this volume, but also for the privilege of working in the laboratories of surgical research at Cornell Medical College and upon the surgical wards of the New York Hospital. To the memory of my professors, Dr. George J. Heuer and Dr. William DeWitt Andrus, I would pay important tribute, for they were surgeons, skilled in their art, convinced of the place of research in surgery, and loyal beyond measure to the ideals of resident training in surgery. For the friendship of Dr. N. C. Foot and Miss Margaret Boise I am and ever shall be grateful.

I should be remiss indeed were I not to express my appreciation to Miss Louise Cross for her work upon the text and its bibliography; to my secretary, Miss Nan Wilkinson, for her cheerful and discerning efforts in behalf of the manuscript and its many revisions; to the W. B. Saunders Company, for their generous support and resourcefulness in publishing this volume; and to the National Institutes of Health for their many grants-in-aid without which this volume would have been impossible.

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and
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CHAPTER 1

Introduction

FROM time to time in the development of the art and science of surgery, new therapies are devised and old ones undergo important revisions. Currently, the relationship between diseases of the liver and its several circulatory systems is the subject of surgical interest and attack. Portal hypertension, although its existence had been suspected for many years, has recently been accurately defined. It has also assumed a position of clinical importance, for today significant elevations in portal pressure can be reduced to harmless levels.

Abdominal ascites due to cirrhosis of the liver has long been regarded as secondary to splanchnic congestion. Numerous unsuccessful efforts have been made surgically to relieve patients of this troublesome manifestation of hepatic disease. During recent decades, however, biochemical studies have indicated that large amounts of fluid collecting within the abdominal cavity may more properly be related to metabolic deficiencies or abnormalities. Consequently, direct surgical attacks upon ascites fell for a time into disfavor and were discarded one by one. Within the past few years, however, interest in the surgical treatment of ascites has been revived through a more comprehensive understanding of intrahepatic circulatory relationships. Intractable collections of abdominal fluid have apparently responded to hepatic arterial ligation.

Although from time to time a few surgeons have suspected that man could survive sudden occlusions of his portal vein, it has been proved only within the past few years that this large vein could be resected were it found invaded by a malignant tumor. Another one of the proverbial *noli me tangere's* of surgery, then, has come within the scope of direct surgical attack. So great a stimulus to investigation have diseases of the hepatic vasculature proved, that in recent years a host of heretofore undreamed of experimental techniques have been developed to further knowledge concerning this complex organ. How many of these may prove to be important clinically cannot yet be estimated.

In spite, however, of these many advances in the physiology of

hepatic circulation and in spite of many improvements in the medical and surgical treatment of hepatic diseases and their various manifestations, much yet remains to be learned. The many factors concerned in hepatic regeneration have yet to be clarified. What role the lymphatics of the liver play in the normal economy of the organ and how these are adversely affected by disease is poorly understood today. The physiology of the hepatic artery in health and disease is as yet far from clear. Why can this vessel and its branches be successfully resected in some animals and not in others? Why is hepatic arterial ligation fatal in men whose livers are normal, yet apparently compatible with life when the liver is the site of cirrhosis? That elevated levels of portal pressure can be lowered by shunts fashioned between the portal and systemic circulations is today a matter of record. Yet the operations required are long, difficult, and hazardous. Such major efforts have these proved to be that surgeons over the world have sought to devise some less formidable and yet equally effective operation. Furthermore, as far as can be determined, mere reduction of portal pressure does not improve liver function in any way. Those who advocate hepatic arterial ligation, however, do appear justified in claiming that at least they are making some effort toward improving the status of the liver itself.

In spite of the great number of laboratory and clinical investigations which have been directed toward interpreting intrahepatic circulatory dynamics correctly, many problems concerning the interrelationships of the portal vein, the hepatic veins, the hepatic artery, and the intrahepatic lymphatics remain unsolved. In addition to the large number of details which must still be learned about the liver and its blood and lymph vessels, there exists today much confusion and little clarity concerning the large body of facts and observations on this subject which have accumulated over the years. What new information will be forthcoming in the future is a matter of conjecture; the problem at hand concerns what is known today of the normal liver, its complicated vascular systems, and the various diseases in which its vessels are implicated.

As the large number of essays upon the blood vessels of this organ are reviewed, numerous contradictions of seemingly basic facts can be found. The observations of one author cannot be correlated with those of another. Experiments reproducible in one laboratory are found not to check with those in another. To what, then, can all these apparent discrepancies be attributed? In all probability, they can best be ascribed to the innumerable methods of investigation which have been employed. Not only have investigative techniques varied, but, in addition, the livers of any number of different animals have been studied and efforts made to reduce these to a common

denominator. When drugs, hormones, and toxic substances have been used in the course of an investigation, their dosages and methods of administration have been found to be widely divergent. When dyes, particulate matter, or colloids have been injected into one or more of the hepatic vessels, particle size and injection pressures have varied extensively. In some studies, injections have been made during life, while in others specimens have been prepared for study after death. In this great diversity of investigative effort, then, can probably be found a valid explanation of the many discrepancies in information on hepatic hemodynamics which exist today.

These problems and others, the significance of which is probably quite unsuspected today, have provided the stimulus for the preparation of this monograph. If it successfully portrays some of the important aspects of hepatic physiology as this is understood today and serves to interest a few in the many problems which remain unsolved, it will have accomplished its purpose.

CHAPTER 2

Historical Background

ALMOST from the beginnings of recorded time, the liver has been the object of much speculation, study, and experimentation. By the ancients it was accorded a position of first importance in bodily function. They thought that in the liver the blood mixed with the chyle and from there spread out through the entire body. In addition, they accorded the liver a prominent position in many religious rites, particularly those concerned with animal sacrifice and soothsaying.

Galen regarded the liver as the focus of animal heat and as an organ intended for the formation of blood and for the origin of the veins. By his pretense to omniscience, Galen successfully held up any advance in true knowledge of the liver until the sixteenth century. Audacious indeed was Vesalius when at the age of twenty-nine he described the course of the veins, the various relationships of the liver, and the true anatomy of the heart. Not only did Vesalius change the entire course of medical thought by exposing the errors in Galen's speculations, but he also paved the way for clarification of the hepatic circulation. Accurate knowledge, however, of the portal and hepatic veins and the hepatic artery had to await the epoch-making discovery of the circulation of the blood by Harvey in 1628. This, together with the perfecting of the microscope, really marks the origin of modern appreciation of hepatic anatomy and physiology.

In 1640, fourteen years before Glisson's classical description of the hepatic capsule appeared, Waleus pointed out that there were as many branches of the hepatic artery as there were branches of the portal vein or bile ducts and that these structures all lay in close proximity encased in a common sheath. Glisson in 1654 elaborated the vascular nature of the stroma of the liver, and suggested that its primary usefulness was for the support of its weight. Glisson also clearly demonstrated by an experiment that portal blood passed through the liver and into the vena cava. At a dissection in London, he filled a large ox bladder with water and a little milk. This reservoir was fitted with a pipe which in turn was tied into the portal

vein near the liver. On squeezing the bladder, the milky water passed through the liver, entered the vena cava, and thence entered the right sinus of the heart. As more of the milk-tinged water was passed through the liver, the organ lost its red color and became pale. This observation led Glisson to conclude that portal blood bathed not only the large hepatic vessels, but the capillaries as well. Glisson also noticed that numerous small arteries penetrated the substance of the liver. In conjecturing at some length as to their function, his curiosity was perhaps the first to be aroused on the various functions performed by the portal vein and hepatic artery: Why, he asked, did an organ so richly supplied with portal blood actually need an arterial circulation?

Wepfer in 1664 and Bidloo in 1685 both recognized that the liver was composed of multiple small bodies. In 1685 Malpighi also established the fact that the human liver, as well as that of shellfish, lizards, ferrets, mice, squirrels, and oxen, appeared to be composed of a number of hexagonal lobules attached to the vessels of Glisson's capsule. These, interestingly enough, Wepfer described as glandular in function and he termed them acini.

In 1694 William Salmon translated Diemerbroeck's popular book, "The Anatomy of Human Bodies," into English, and for the first time gave the English-speaking peoples a complete picture of the anatomy of the liver. That the era of speculation was fast giving way to the new medical science of observation and experimentation is reflected in Diemerbroeck's comments on the old and the new. He wrote in 1672, "Concerning the Office of the Liver there are various Opinions, of which the Ancientist and the most revered is from Galen who saith that Sanguinification is compleated in the Liver, and that it is the true and primary sanguifying or blood making bowel. But this Opinion, after the discovery of the Circulation of the Blood has been wholly abolished; since it is found that the Blood is only made in the Heart. . . . Malpighi, who has examined the substance and inner parts of the liver most accurately by his microscope, . . . has observed many things unheard of, and hitherto altogether undiscovered. . . . But Malpighi, by reason of these new Golden Inventions seems unwilling to call the liver a Bowel for the future, but rather a conglomerated or clustered glandule; yet I beseech him to grant us this liberty, that we may still, for a while call it a Bowel lest by too sudden a change of the name we should render our discourse obscure. . . . In the meantime, the condition of the unfortunate liver is to be lamented; as being that which formerly was call'd the Principal Bowel and by Galen seated in the highest Throne of Sanguinification and there has been worshipped for many Ages by the common consent of Physic; yet that in these our times it should be torn and