

# THE PANCREAS

## Principles of Medical and Surgical Practice

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*Edited by*

**Luis H. Toledo-Pereyra, M.D., Ph.D.**

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Chief, Section of Transplantation  
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## Foreword

Ever since Reginald Fitz made the medical profession aware of the importance of disorders of the pancreas, this organ has slowly yielded many additional clinical secrets. The editor has wisely invited comments by authorities who have contributed investigative as well as clinical observations on a variety of problems involving the pancreas. Their extensive clinical experiences certainly add authority to their contributions and reassure the reader seeking advice and guidance on a particular pancreatic problem.

This book provides the clinician, regardless of his or her field of interest, with an up-to-date review of the diagnosis and treatment of many problems involving the pancreas. The clinician can now outline masses by scans and visualize the ducts by endoscopic techniques. Such studies have raised the question of the role of pancreas divisum in the etiology of recurrent pancreatitis. Once again the sphincter of Oddi is being implicated in the etiology of pancreatitis. Sphincteroplasty has now been replaced by sphincterotomy with segmentectomy to improve drainage of both bile and pancreatic juice.

The original enthusiasm for total pancreatectomy in the treatment of cancer of the pancreas has not been sustained. The Whipple operation provides good results for carcinoma of the ampulla, but the long-term results for carcinoma of the pancreas probably do not exceed 25-30% five-year survivals. Chemotherapy and irradiation of the surgically exposed gland are being evaluated.

The new clinical syndromes resulting from a variety of hormones produced by islet cell tumors have stimulated interest in many fields. The clinician should be suspicious of these many islet cell tumor syndromes and utilize more fully the many immunoassays that are available for insulin, gastrin, vasoactive intestinal polypeptides, glucagon, somatostatin, and pancreatic polypeptides. Attempts at surgical removal of these tumors, including the gastrinoma, should be uniformly attempted. The islet cell tumor is commonly associated with other endocrine tumors.

Surgeons have become more aggressive in the management of trauma to the pancreas. Extensive resection of avulsed segments may be indicated.

One of the most exciting challenges for clinicians studying disorders of the pancreas is the possibility of controlling diabetes by surgical means, that



is, by the transplantation of a donor pancreas or islets. The editor of this book is an authority in this field whose contributions are clearly presented.

Although many advances have been made in the diagnosis and management of diseases of the pancreas, this organ remains one of the most challenging of all to the clinician. Earlier diagnosis of injuries and diseases of the pancreas combined with the principles of diagnosis and treatment outlined in this book should further improve the morbidity and mortality associated with disorders of this important retroperitoneal organ. The busy clinician will find that this book presents in a clear and interesting fashion not only the problems but the current approaches to their management.

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# Preface

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Our knowledge and understanding of pancreatic disease have increased considerably in the last decade. The introduction of more accurate diagnostic techniques (endoscopic retrograde cannulation of the pancreatic duct, computed tomography, ultrasound, biopsy, and recently nuclear magnetic resonance) have contributed to the early diagnosis of diseases of the pancreas. The improved medical and surgical management of pancreatic disease has led to a more acceptable prognosis in a great number of patients suffering from these conditions. Pancreatic cancer, however, remains a difficult disease to treat. Chemotherapy, radiation therapy, and/or surgery have not made the progress we had anticipated, although complications of pancreatic disease, including diabetes, are better understood and managed. New advances in pancreas and islet cell transplantation offer new possibilities for patients having end-stage pancreatic diseases of endocrine origin.

This book attempts to review in a systematic manner all medical and surgical aspects of pancreatic disease. The history, surgical anatomy, biochemistry, physiology, and pathology of the pancreas are clearly presented. All diagnostic means of establishing the presence of pancreatic disease are completely reviewed. The overall management of pancreatic disease in adults and children is analyzed in regard to traditional methods and recent findings. Finally, new therapeutic interventions are considered in light of the advances recently seen in the management of pancreatic disease.

The goals of this book are to offer the person studying pancreatic disease all necessary means of continuing his or her striving toward a complete understanding of the pathology of the pancreas; to present to the practicing physician the principles for the management of pancreatic disease; and to stimulate the student, resident, or fellow to continue to search for knowledge of pancreatic pathology, either medically or surgically.

The Department of Surgery of our institution offered an environment which was conducive for the development of this work. The help from members of the Transplantation and Surgical Research sections of our institution is greatly appreciated, particularly the editorial assistance of D. A. Gordon.

*Luis H. Toledo-Pereyra*

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# 1 History of Pancreatic Surgery

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Charles G. Child III

## **ANATOMY**

## **PHYSIOLOGY**

**Exocrine Pancreas**

**Endocrine Pancreas**

## **PATHOLOGY**

## **EARLY PANCREATIC SURGERY**

**Pancreatic Trauma**

**Pancreatic Cysts**

**Annular and Aberrant Pancreas**

**Pancreatic Lithiasis**

## **ACUTE AND CHRONIC PANCREATITIS**

**Acute Pancreatitis**

**Chronic Pancreatitis**

## **PANCREATIC TUMOR**

## **ENDOCRINOLOGY**

## **OTHER BENIGN AND MALIGNANT**

## **TUMORS OF THE PANCREAS**

**Cancer of the Body and Tail**

**Pancreaticoduodenal Cancer**

**Palliation**

**Local Excision**

**Pancreaticoduodenectomy**

## **PANCREATIC TRANSPLANTATION**

Long before physicians could give any serious thought to surgery of the pancreas, this abdominal organ had to be discovered, some insight into its functions obtained, and knowledge of its injuries and diseases acquired. Early anatomists made the initial contributions, physiologists the next, and finally, with the development of the microscope, pathologists were able to define some of the diseases with which the pancreas is afflicted.

## **ANATOMY**

In about 300 B.C., Herophilus of Chalcedon (1), regarded by many as the father of anatomy, first described the human pancreas. Four hundred years later Ruphos of Ephesus (2) named this important abdominal organ the *pancreas* (παν, all; χρεας, flesh). Galen (3) recognized the pancreas in his voluminous writings and dogmatically identified it as a cushion for the

stomach. He called it the callicreas (καλλοσ, good; χρεασ, flesh). This designation, never a popular one, was used for a short time but abandoned in the Middle Ages. In early English writings the pancreas is often called the *sweetbread* (4).

During the next 1,200 years, few references to the pancreas are found. Mondino of Luzzi (5) described the organ and some of its ducts in 1275. In 1540 Vesalius (6) provided the first complete description of the pancreas and its more important anatomical relationships. In 1641 Moritz Hoffman (7) discovered the pancreatic duct in a rooster and is supposed to have told his friend Johann Wirsung about it. In any event the main pancreatic duct in man was described in detail by Wirsung (8a,b) in 1642 and the accessory duct by Santorini (9) in 1724. In 1729 Augustus Walther (10) wrote about the vascular relationships of the pancreas, and in 1728 Vater (11) described his famous papilla. In 1887 Oddi (12) recorded the complex musculature of the sphincter bearing his name, and in 1879 Gage (13) elaborated on the function of the ampulla of Vater and the pancreatic ducts in the domestic cat.

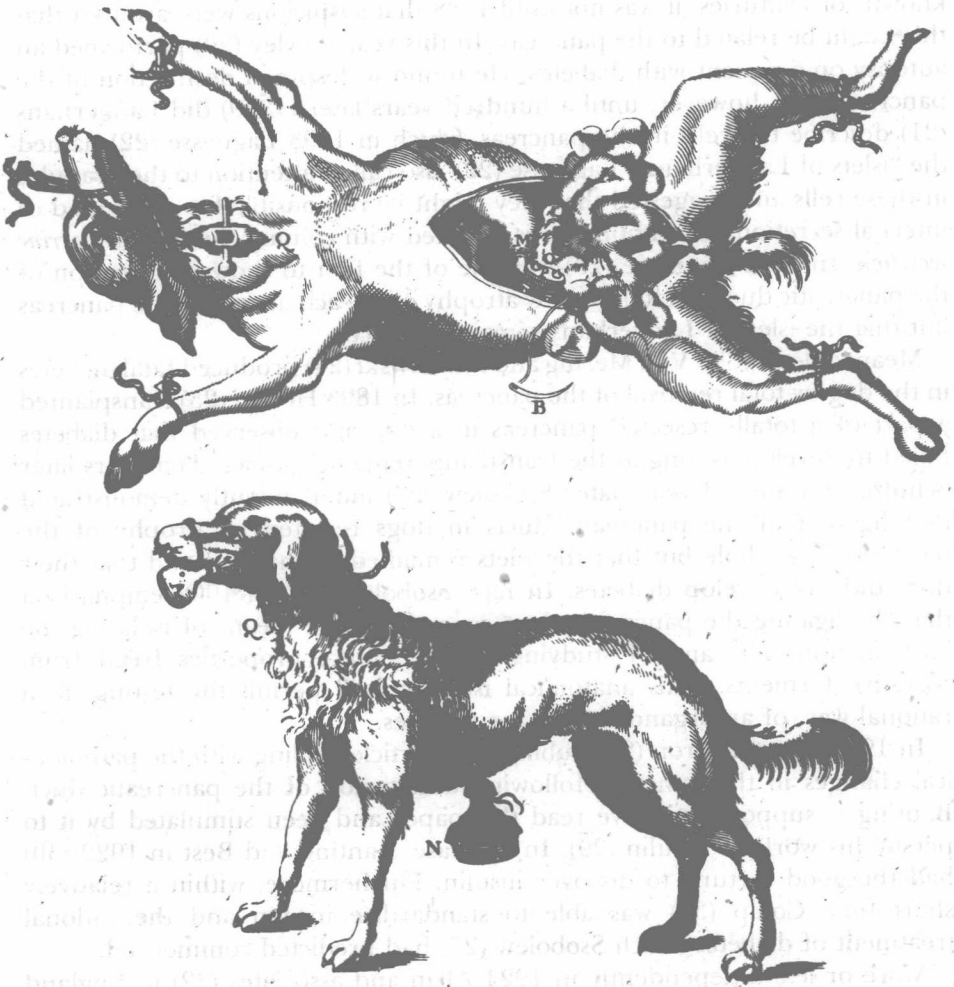
## PHYSIOLOGY

### Exocrine Pancreas

With the gross anatomy of the pancreas reasonably well understood it was inevitable that early physiologists should become curious about the function of this mysterious abdominal organ. To this end the earliest observations are those of de Graaf (14). In 1664 he cannulated the pancreatic duct of a dog with a duck's quill. This he brought out through the animal's abdominal wall and collected in a leather bottle the fluid that dripped from the quill. In Figure 1-1 is reproduced de Graaf's illustration of this classic experiment. Although de Graaf speculated on the digestive function of pancreatic juice, his observations were inaccurate and his deductions largely in error. In 1683 Brunner (15) removed much of the pancreas in dogs. He noted that some of his animals developed great thirst and urinated excessively. Brunner did not, however, link these observations with diabetes. Almost two centuries later Claude Bernard (16) made the first important discoveries about the functions of the external, or exocrine, pancreatic secretion. He demonstrated that this emulsified fatty foods, converted starch to sugar, and had a solvent action on protein.

As early as 1875, Haidemann (17) noticed the effect of vagal stimulation on the pancreas. This early observation on the physiology of the pancreas was later confirmed by Pavlov (18). This famous physiologist then reported that vagal stimulation promoted the discharge of pancreatic enzymes but did not increase the flow of pancreatic juice. Very early in the twentieth century Bayliss and Starling (19) published extensive accounts of pancreatic secretion and announced their discovery of secretin. These men paved the way for





**Figure 1-1** De-Graaf's (14) original illustration showing cannulation for collection of saliva and pancreatic secretion. (Brunschwig A: *The Surgery of Pancreatic Tumors*. St Louis, CV Mosby Co, 1942.)

development of contemporary understanding of the role of the exocrine pancreas in digestion.

### Endocrine Pancreas

While some early investigators were concerned with the more or less obvious external secretion of the pancreas, others were beginning to suspect that this gland had yet another function. Although the disease diabetes had been

known for centuries, it was not until 1788 that suspicions were aroused that this might be related to the pancreas. In this year Cawley (20) performed an autopsy on a patient with diabetes. He found widespread destruction of the pancreas. Not, however, until a hundred years later (1869) did Langerhans (21) describe the cells in the pancreas, which in 1893 Laguesse (22) named the "islets of Langerhans." Laguesse (22) also called attention to the granules in these cells and suggested that they might be responsible for some kind of internal secretion. In addition he is credited with coining the term *endocrine secretion*. In 1902 Laguesse (23) was one of the first to show that ligation of the pancreatic duct was followed by atrophy of the acinar cells of the pancreas but that the islets of Langerhans remained intact.

Meanwhile in 1890 Von Mering and Minkowski (24) produced fatal diabetes in the dog by total removal of the pancreas. In 1893 Hedon (25) transplanted a part of a totally resected pancreas in a dog and observed that diabetes failed to develop as long as the transplants remained intact. Ten years later Schulze (26) and 12 years later Ssobolew (27) independently demonstrated that ligation of the pancreatic ducts in dogs resulted in atrophy of the pancreas as a whole but that the islets remained unchanged and that their dogs did not develop diabetes. In fact, Ssobolew (27) in 1902 emphasized that "by ligating the pancreatic duct, we now have a means of isolating the islets anatomically and of studying their chemical properties freed from digestive ferments. This anatomical isolation will permit the testing, in a rational way, of an organotherapy for diabetes."

In 1920 Moses Barron (28) published an article dealing with the pathological changes in the pancreas following obstruction of the pancreatic duct. Banting is supposed to have read this paper and been stimulated by it to pursue his work on insulin (29). In any case, Banting and Best in 1922 (30) had the good fortune to discover insulin. Furthermore, within a relatively short time Collip (31) was able to standardize insulin and the rational treatment of diabetes which Ssobolew (27) had predicted commenced.

More or less independently in 1924 Allan and associates (32) in England and Fisher (33) in the United States reported that depancreatized dogs did not thrive on insulin alone. The health of their animals was improved by feeding them raw pancreas or by the regeneration of pancreas at the stump of the excised gland. In 1936 Dragstedt and his associates (34) demonstrated a fat-metabolizing hormone in raw pancreas which, in addition to insulin, permits healthy survival of dogs without a pancreas and prevents liver damage in these animals. Later this was called lipocaic (35). These several observations led to appreciation of the importance of supplementing the diet of a patient who has had his pancreas removed—certainly following total pancreatectomy and many times after subtotal removal of most of the gland. Today there are available many potent pancreatic extracts for dietary augmentation following Whipple operations of either the subtotal or total variety.

## PATHOLOGY

That early physicians chanced upon a variety of diseases of the pancreas after pancreatectomy in their postmortem dissections is reflected in the writings of Diemerbroeck (4). In 1694 this chronicler of the contemporary lore of medicine and pathology wrote that the pancreas or sweetbread was a flat oblong gland attached to the duodenum. He further noted that "in some sickly people the pancreas exceeds its usual bigness and is often full of corruption—that sometimes little stones breed within it—that if the sweetbread juice is too scanty, too mild, or too insipid, it causes a weak efforvescency, obstructions, atrophies, and extraordinary binding of the body." Diemerbroeck (4) also recognized a pancreatic abscess in a "merchant of Leyden who swooned away and at length went into fits; in whose carcass all other parts being safe, only the sweetbread was found putrefied with an aposteme." In Figure 1-2 are reproduced a few paragraphs on the pancreas from Diemerbroeck's original publication of 1694 (4).

Giovanni Morgagni (1682–1771) (36) is credited with being the first to identify cancer of the pancreas. He described in detail the autopsy of a woman whose pancreas was enlarged, hard, and gristly. He also described a

**Table 1-1** Records of Pancreatic Disease at Guy's Hospital, 1884–1897

Primary malignant disease of pancreas	31
Cirrhotic congested or hard pancreas	26
Small atrophic pancreas	19
Growth adherent to pancreas	13
Secondary growths in pancreas	11
Fatty pancreas	9
Dilated pancreatic duct	
(In some cases in which the pancreas was otherwise diseased the duct was dilated, but the cases have not been counted twice over.)	
Tubercle of pancreas	4
Mechanical damage to the pancreas	4
Ulcer of stomach adherent to pancreas	4
Calculi in pancreas	3
Suppuration of pancreas	3
Cysts of pancreas (including one case of hydatid)	3
Hemorrhage into pancreas	3
Lymphadenoma of pancreas	1
Cavity in head of pancreas	1
Ulcer of duodenum adherent to pancreas	1
Kidney adherent to pancreas	1
Action of acid on pancreas	1
Total	142

SOURCE: White H: *Guy's Hospital Rep* 54:17, 1897. London, John Churchill.