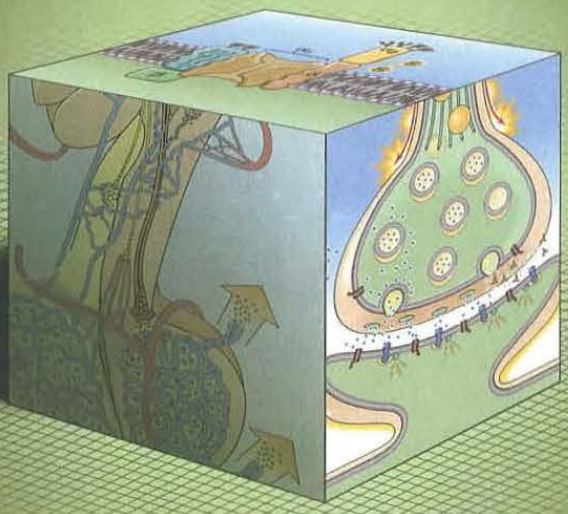
Walter F. Boron ▪ Emile L. Boulpaep

MEDICAL PHYSIOLOGY



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MEDICAL PHYSIOLOGY

A Cellular and Molecular Approach

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The Curtis Center
Independence Square West
Philadelphia, Pennsylvania 19106

MEDICAL PHYSIOLOGY ISBN 0-7216-3256-4

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The Publisher

Library of Congress Cataloging-in-Publication Data

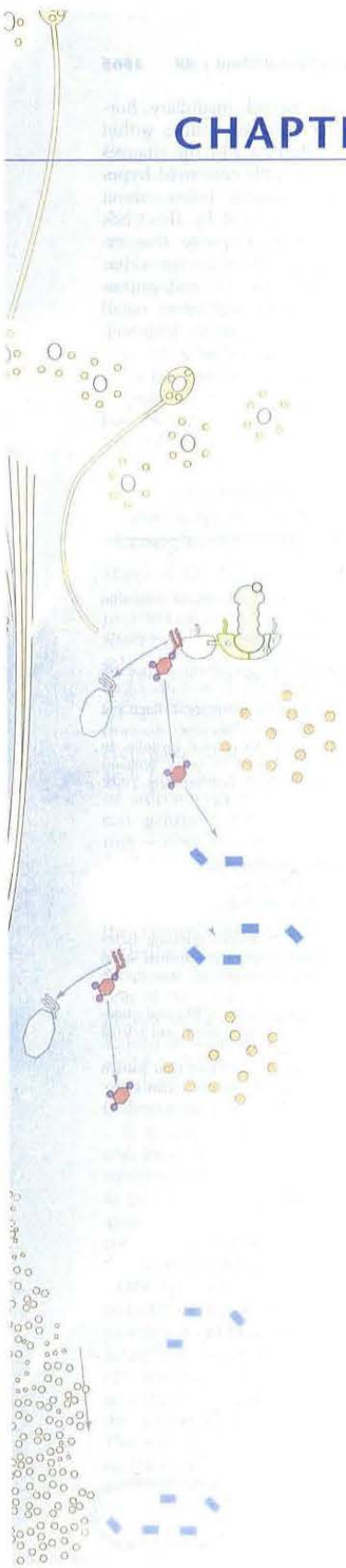
Boron, Walter F.
Medical physiology / Walter F. Boron, Emile L. Boulpaep—1st ed.
p. cm.
ISBN 0–7216-3256–4
1. Human physiology. I. Boulpaep, Emile L. II. Tile
[DNLM: 1. Physiology. QT 104 B7356M 2003]
QP34.5 .B65 2003
612—dc21 00–051597

Acquisitions Editor: William R. Schmitt
Developmental Editor: Melissa Dudlick
Publishing Services Manager: Frank Polizzano

PI/DNP

Printed in China

Last digit is the print number: 9 8 7 6 5 4



CHAPTER 50

The Endocrine Pancreas

Eugene J. Barrett

The Islets of Langerhans Are Endocrine and Paracrine Tissues

The pancreas contains two types of glands: (1) exocrine glands, which secrete digestive enzymes and HCO_3^- into the intestinal lumen (see Chapter 42), and (2) endocrine glands, called the "islets of Langerhans."

The normal human pancreas contains between 500,000 and several million islets. Islets can be oval or spherical and measure between 50 and 300 μm. Islets contain at least four types of secretory cells—α cells, β cells, δ cells, and F cells—plus various vascular and neural elements (Fig. 50–1 and Table 50–1). **β cells** secrete insulin, proinsulin, C peptide, and a newly described protein, amylin. β cells are the most numerous type of secretory cell within the islets; they are located throughout the islet but are particularly numerous in the center. **α Cells** principally secrete glucagon, **δ cells** secrete somatostatin, and **F cells** (also called pancreatic polypeptide cells) secrete pancreatic polypeptide.

The cells within an islet receive information from the world outside the islet. These cells also can communicate with each other and influence each other's secretion. We can group these communication links into three categories:

1. **Humoral communication**. The blood supply of the islet courses outward from the center of the islet toward the periphery, carrying glucose and other secretagogues. In the rat—and less strikingly in humans—β cells are more abundant in the center of the islet, whereas α and δ cells are more abundant in the periphery. Cells within a given islet can influence the secretion of other cells as the blood supply courses outward through the islet carrying the secreted hormonal product of each cell type with it. For example, glucagon is a potent insulin secretagogue, insulin modestly inhibits glucagon release, and somatostatin potently inhibits the secretion of both insulin and glucagon (as well as the secretion of growth hormone and other nonislet hormones).
2. **Cell-cell communication**. Both gap and tight junctional structures connect islet cells with one another. Cells within an islet can communicate via gap junctions, which may be important for the regulation of both insulin and glucagon secretion.
3. **Neural communication**. Another level of regulation of islet secretion occurs via innervation from both the sympathetic and the parasympathetic divisions of the autonomic nervous system (ANS). Cholinergic

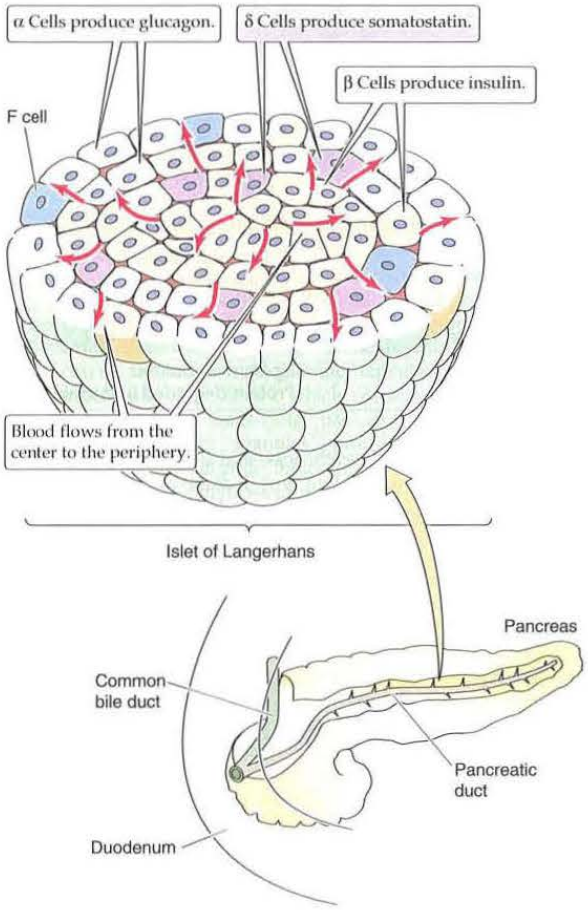


FIGURE 50–1. Islet of Langerhans.

stimulation augments insulin secretion. Adrenergic stimulation can have either a stimulatory or inhibitory effect, depending on whether β-adrenergic or α-adrenergic stimulation dominates (p. 1065).

These three communication mechanisms allow for a tight control over the synthesis and secretion of islet hormones.

INSULIN

The discovery of insulin was among the most exciting and dramatic events in the history of endocrine physiology and therapy. In the United States and Europe, insulin-dependent diabetes mellitus (IDDM), or type 1 diabetes, develops in about 1 in every 600 children in their lifetime. However, the prevalence is only about 1 in 10,000 in eastern Asia. Before 1922, all children with diabetes died within 1 or 2 years of diagnosis. It was an agonizing illness; the children lost weight despite eating well, became progressively weaker and cachectic, were soon plagued by infections, and eventually died of overwhelming acidosis. No effective therapy was available, and few prospects were on the horizon. It was known that the blood sugar was elevated in this disease, but beyond that, there was little understanding of its pathogenesis.

In 1889, Minkowski and von Mering demonstrated that removing the pancreas from dogs caused hyperglycemia,

TABLE 50–1

PRODUCTS OF PANCREATIC ISLET CELLS

CELL TYPE	PRODUCT
α	Glucagon
β	Insulin Proinsulin C peptide Amylin
δ	Somatostatin
F	Pancreatic polypeptide

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