An impressionist landscape painting with a focus on light and color. The scene depicts a rocky, hilly terrain with patches of green and yellow vegetation. The brushstrokes are visible and textured, creating a sense of movement and atmosphere. The overall palette is dominated by earthy tones like greens, yellows, and browns, with some cooler blues and greys in the shadows and foreground.

**Verbal Finals:** Starting Thursday the VF is the full version (with insulin, digestion and absorption, p34). The final day to pass with a LA is this Friday, **April 4th**. Last day to pass with Luckie will be Thursday, **April 17th**.

**1. Pick up Name Folder**

- Pick up name folder and set it up at seat.

**2. Sit with your lab group.**

- laptops almost closed (avoid distracting)

**3. Clicker Attendance**

- Launch your Top Hat, and get ready to click.

An impressionist landscape painting featuring a large, dark, textured mountain peak on the right side. The sky is a mix of warm yellow, orange, and pink tones. The foreground is a textured expanse of blue, purple, and red. A white rectangular box with a thin black border is positioned on the left side of the image, containing the text "Laptops closed" in a bold, blue, sans-serif font.

**Laptops closed**

# Announcements

## 1. Exam II results

Part1= awarded for good effort (& early) 100-110%

Part2= earned by accurate answers 19-98%

(plus up to 10 BUMP points)

Resulted in an average score for our class= 79%

2. Exam in-class test returned at end of lab today.

EXAM2
109.00
106.33
105.33
104.33
102.00
102.00
98.67
97.67
97.33
96.67
96.33
94.00
93.67
88.00
87.33
85.67
83.33
79.67
77.33
76.33
75.67

**Budgeting homework time (60 min):** This is a professional Review paper that is 3700 words in length from an important medical journal so it will take some time to read, but if you have gained some understanding about genetics and diseases while working in the lab this semester you should be able to more quickly grasp most of what is discussed. If you struggle with the text, focus on each figure and determine what it is trying to explain. Scientists almost always first focus on the figures.

1. \_\_\_\_\_ **For Tuesday's lecture**, read Kenneth Polonsky's review paper on "The Past 200 Years in Diabetes" published in *New England Journal of Medicine* in 2012. This paper is provided at the back of your Course Pack. You do not need to take notes from all the written text, simply read for your own learning and to help you with your research.
2. \_\_\_\_\_ While reading, **focus mostly on the figures**. We will discuss these in class. Be prepared to state aloud what each figure is trying to explain or communicate.
3. \_\_\_\_\_ **Write out in your notebook** your explanation for Figure 2 and how that structure relates to what you learned about the biosynthesis of a protein back in the reading and lecture about *Endomembranes*. Describe how you predict the insulin protein is made DNA -> RNA -> protein and the path it takes via which organelles and what happens to it at each?

# The Past 200 Years in Diabetes

Kenneth S. Polonsky, M.D.

From the Department of Medicine, University of Chicago, Chicago. Address reprint requests to Dr. Polonsky at the Department of Medicine, University of Chicago, 5841 S. Maryland Ave., Chicago, IL 60637, or at [polonsky@bsd.uchicago.edu](mailto:polonsky@bsd.uchicago.edu).

N Engl J Med 2012;367:1332-40.

DOI: 10.1056/NEJMr1110560

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**D**IABETES WAS FIRST RECOGNIZED AROUND 1500 B.C.E. BY THE ANCIENT Egyptians, who considered it a rare condition in which a person urinated excessively and lost weight. The term diabetes mellitus, reflecting the fact that the urine of those affected had a sweet taste, was first used by the Greek physician Aretaeus, who lived from about 80 to 138 C.E. It was not until 1776, however, that Matthew Dobson actually measured the concentration of glucose in the urine of such patients and found it to be increased.<sup>1</sup>

Diabetes was a recognized clinical entity when the *New England Journal of Medicine and Surgery* was founded in 1812. Its prevalence at the time was not documented, and essentially nothing was known about the mechanisms responsible for the disease. No effective treatment was available, and diabetes was uniformly fatal within weeks to months after its diagnosis owing to insulin deficiency. In the intervening 200 years, major fundamental advances have been made in our understanding of the underlying causes of diabetes and the approach to its prevention and treatment (see timeline, available with the full text of this article at [NEJM.org](http://NEJM.org)). Although diabetes is still associated with a reduced life expectancy, the outlook for patients with this disease has improved dramatically, and patients usually lead active and productive lives for many decades after the diagnosis has been made. Many effective therapies are available for treating hyperglycemia and its complications.

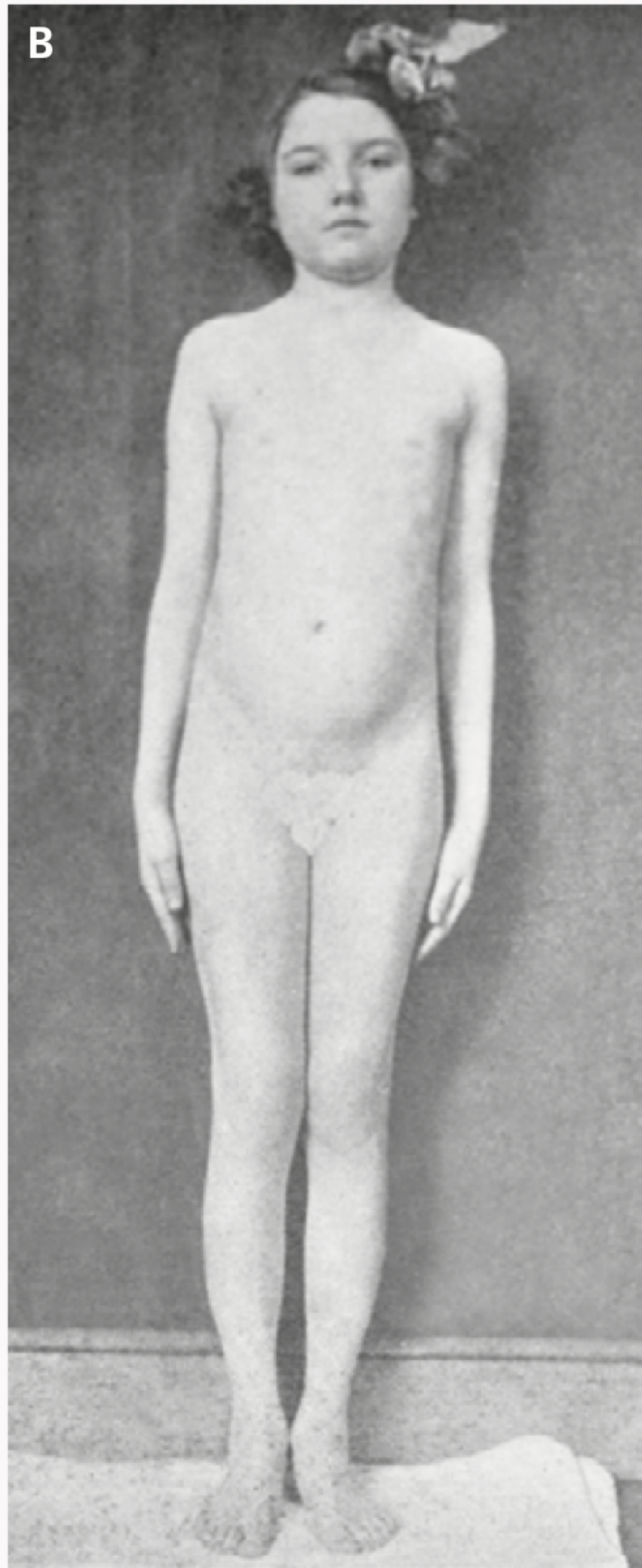
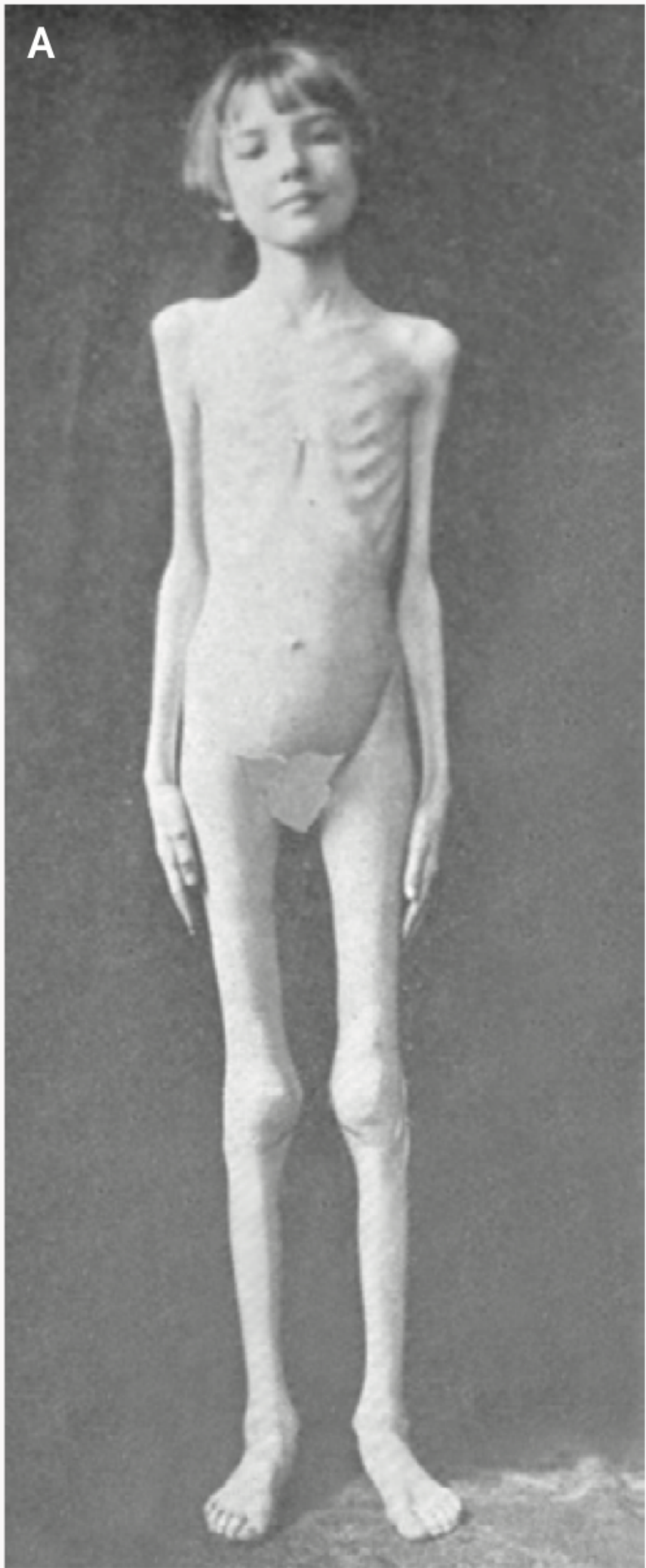


*A timeline is  
available at  
[NEJM.org](http://NEJM.org)*

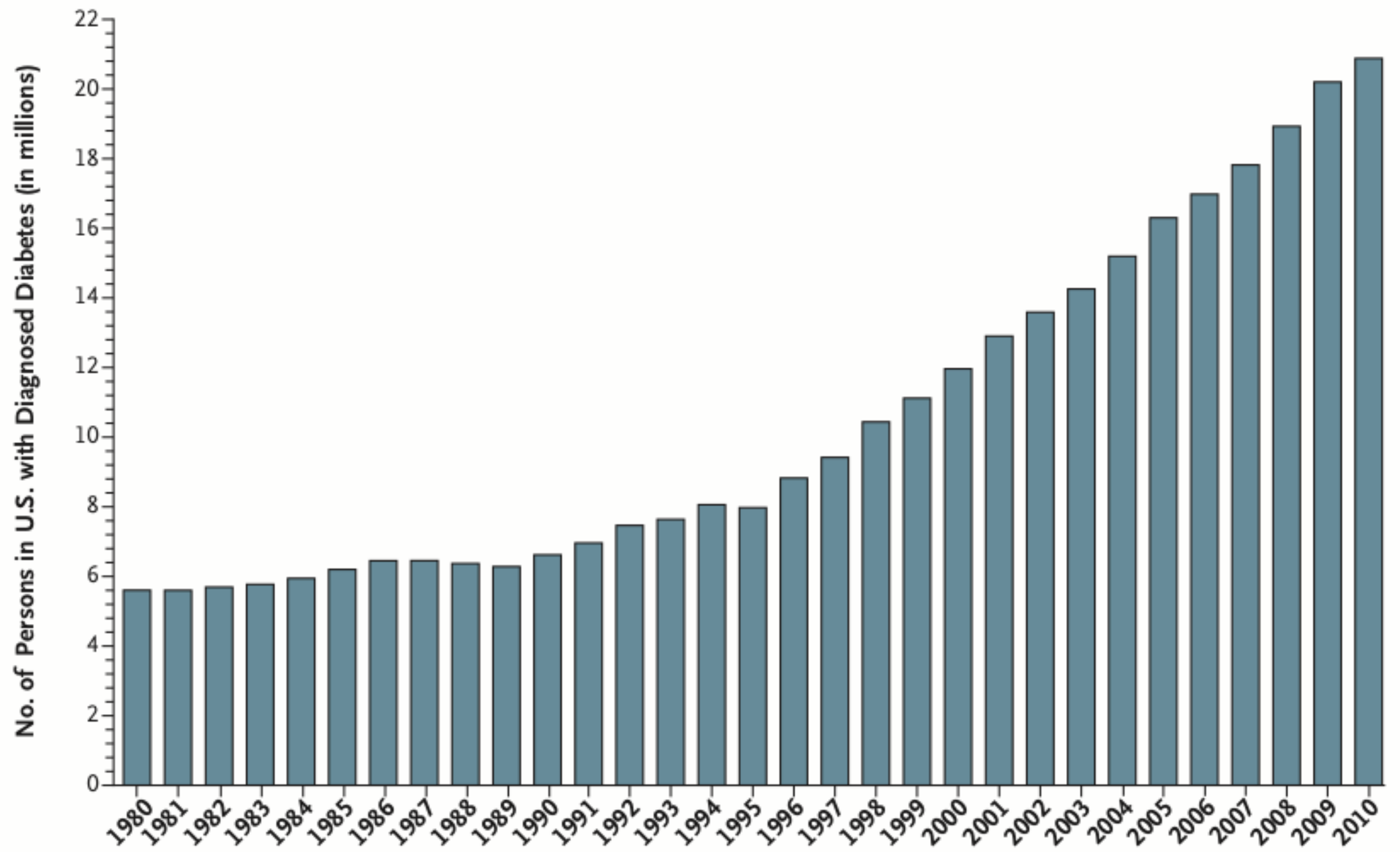


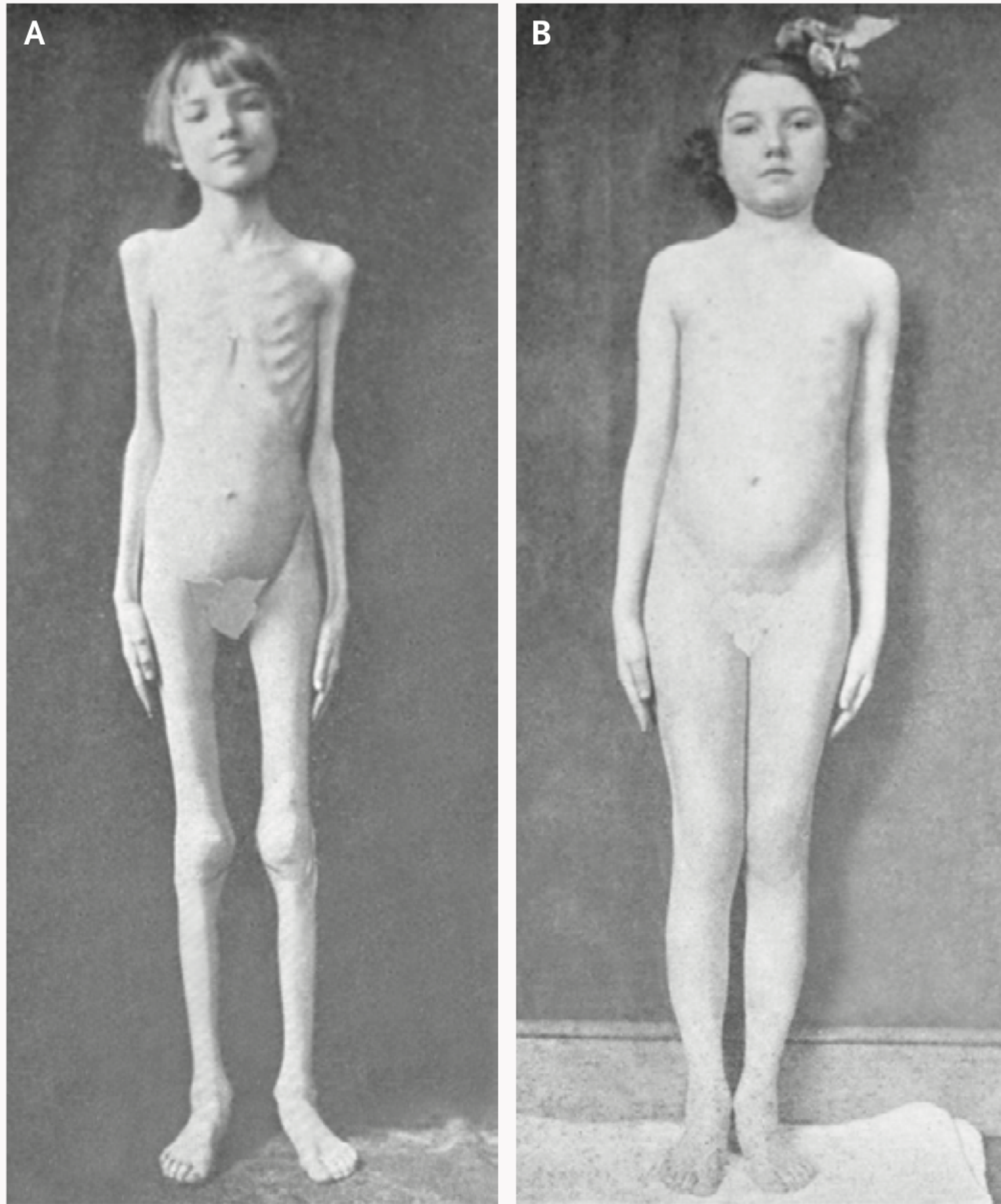
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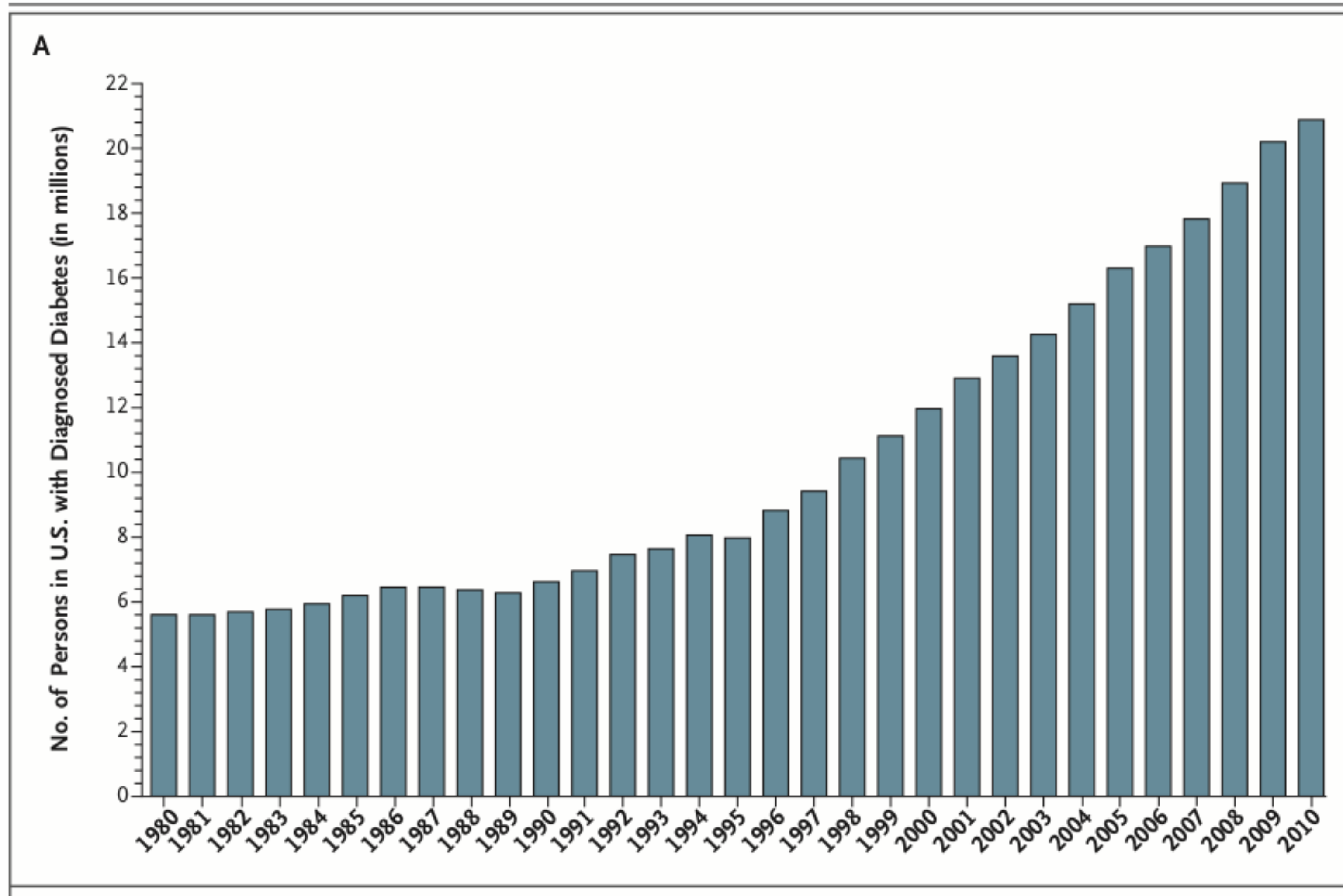
**A**





**Figure 1. Effects of Insulin Therapy.**

These photographs from 1922, in a case described by Geyelin,<sup>11</sup> show a young girl with insulin-deficient diabetes before treatment with insulin (Panel A) and after treatment (Panel B).



# The Past 200 Years in Diabetes

Kenneth S. Polonsky, M.D.

From the Department of Medicine, University of Chicago, Chicago. Address reprint requests to Dr. Polonsky at the Department of Medicine, University of Chicago, 5841 S. Maryland Ave., Chicago, IL 60637.

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Copyright © 2012 Massachusetts Medical Society.

**D**IABETES WAS FIRST RECOGNIZED AROUND 1500 B.C.E. BY THE ANCIENT Egyptians, who considered it a rare condition in which a person urinated excessively and lost weight. The term diabetes mellitus, reflecting the fact that the urine of those affected had a sweet taste, was first used by the Greek physician, Aretaeus of Cappadocia, in the 4th century A.D. However, urine

## So what causes Diabetes??

Diabetes was a recognized clinical entity when the *New England Journal of Medicine and Surgery* was founded in 1812. Its prevalence at the time was not documented, and essentially nothing was known about the mechanisms responsible for the disease. No effective treatment was available, and diabetes was uniformly fatal within weeks to months after its diagnosis owing to insulin deficiency. In the intervening 200 years, major fundamental advances have been made in our understanding of the underlying causes of diabetes and the approach to its prevention and treatment (see timeline, available with the full text of this article at [NEJM.org](http://NEJM.org)). Although diabetes is still associated with a reduced life expectancy, the outlook for patients with this disease has improved dramatically, and patients usually lead active and productive lives for many decades after the diagnosis has been made. Many effective therapies are available for treating hyperglycemia and its complications.



A timeline is  
available at  
[NEJM.org](http://NEJM.org)

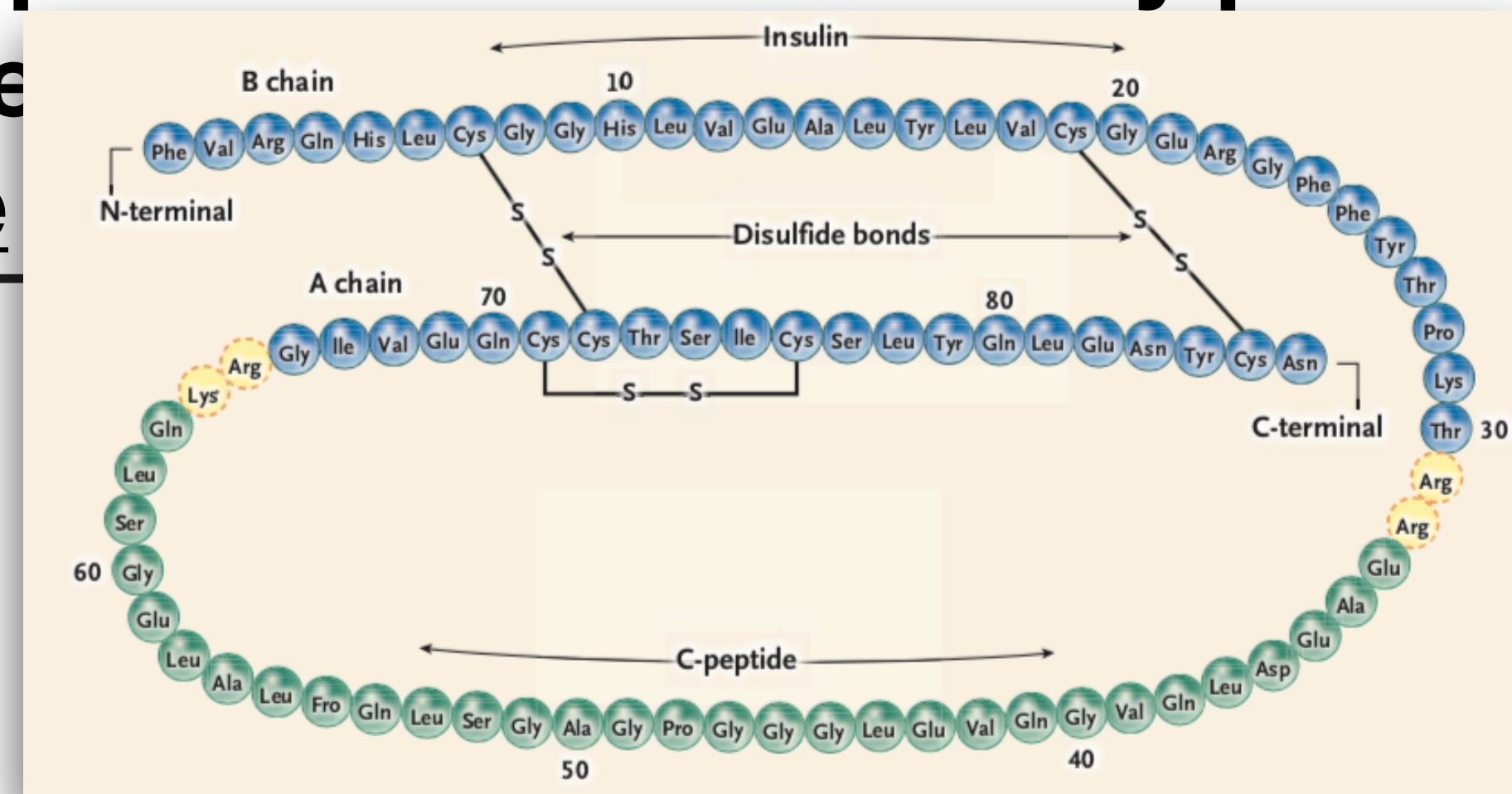
Type 1?

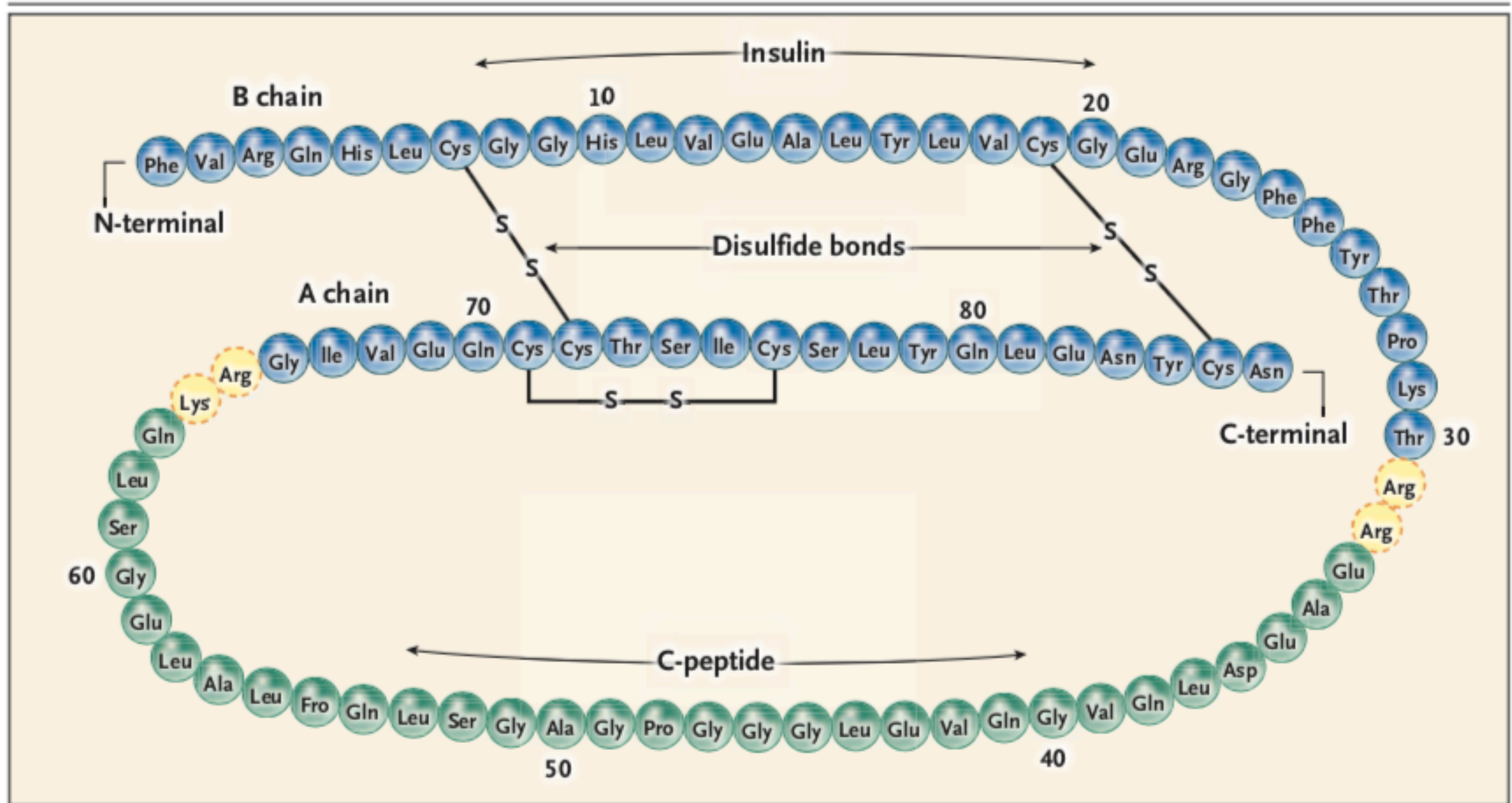
Type 2?

**“So what causes Diabetes?”**  
(failure at generation or action of insulin)

Type 1 diabetes occurs predominantly in young people and is due to selective autoimmune destruction of the pancreatic beta cell, leading to insulin deficiency.

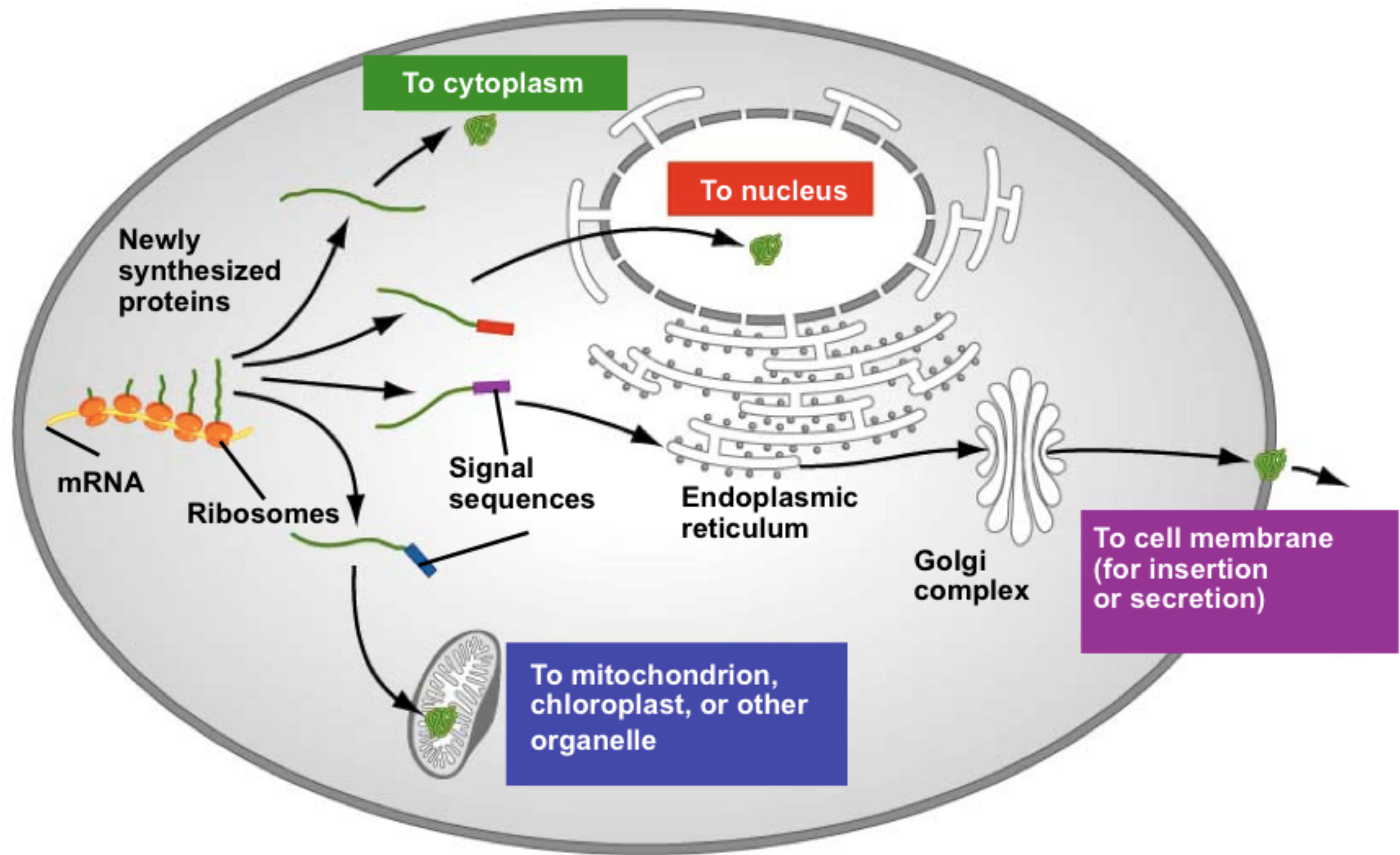
Himsworth first proposed in 1936 that many patients with diabetes have insulin resistance. We now know that insulin resistance is a characteristic of type 2 diabetes

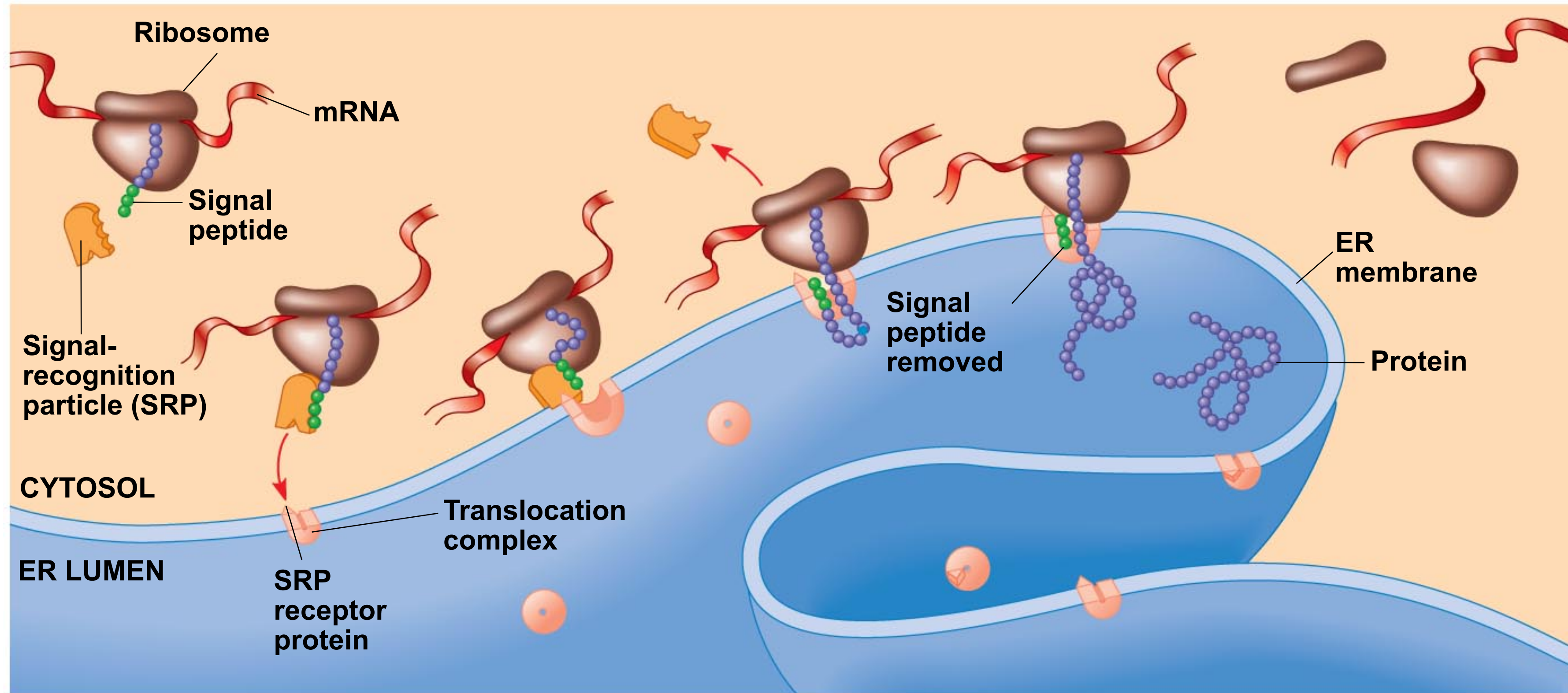


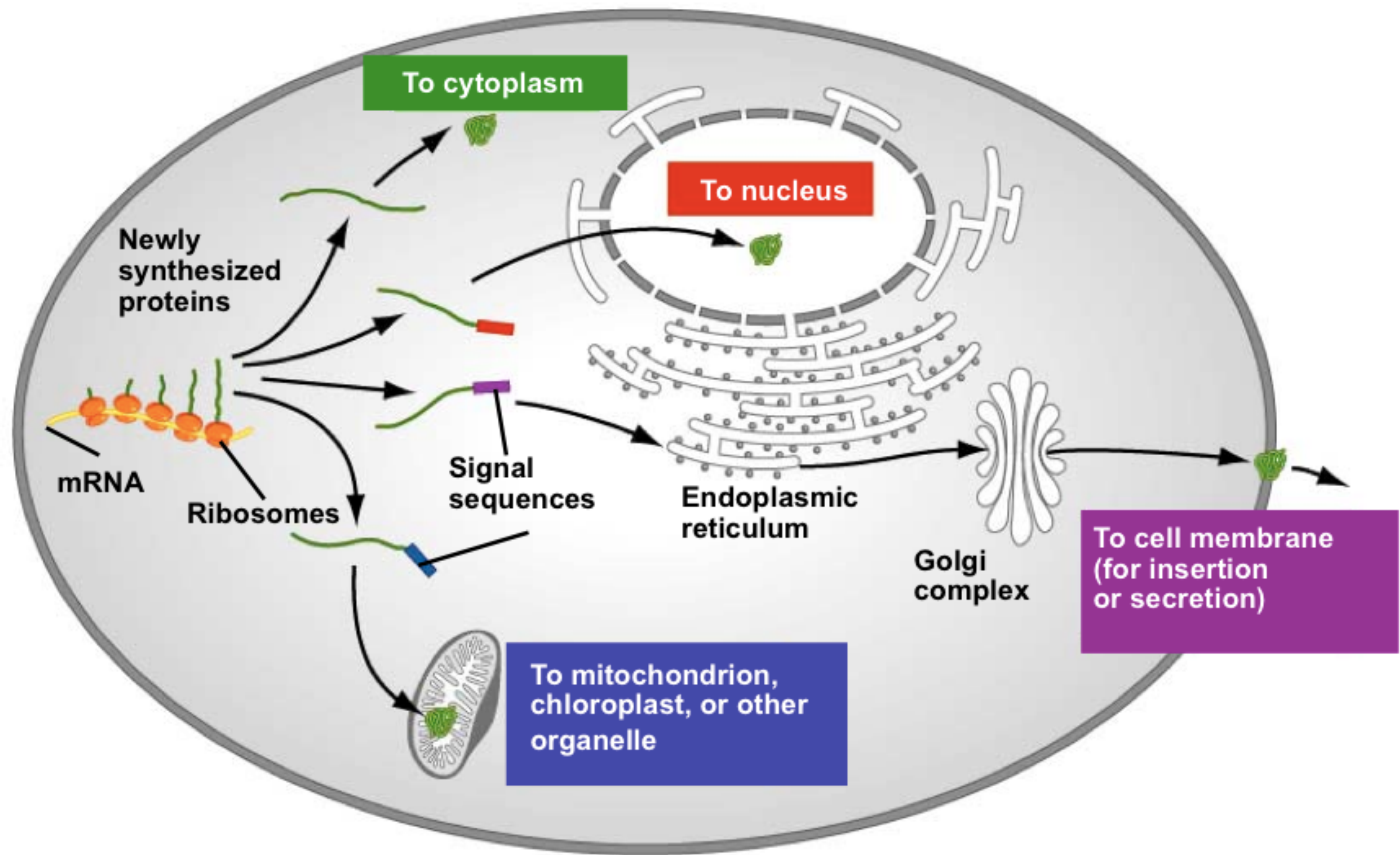


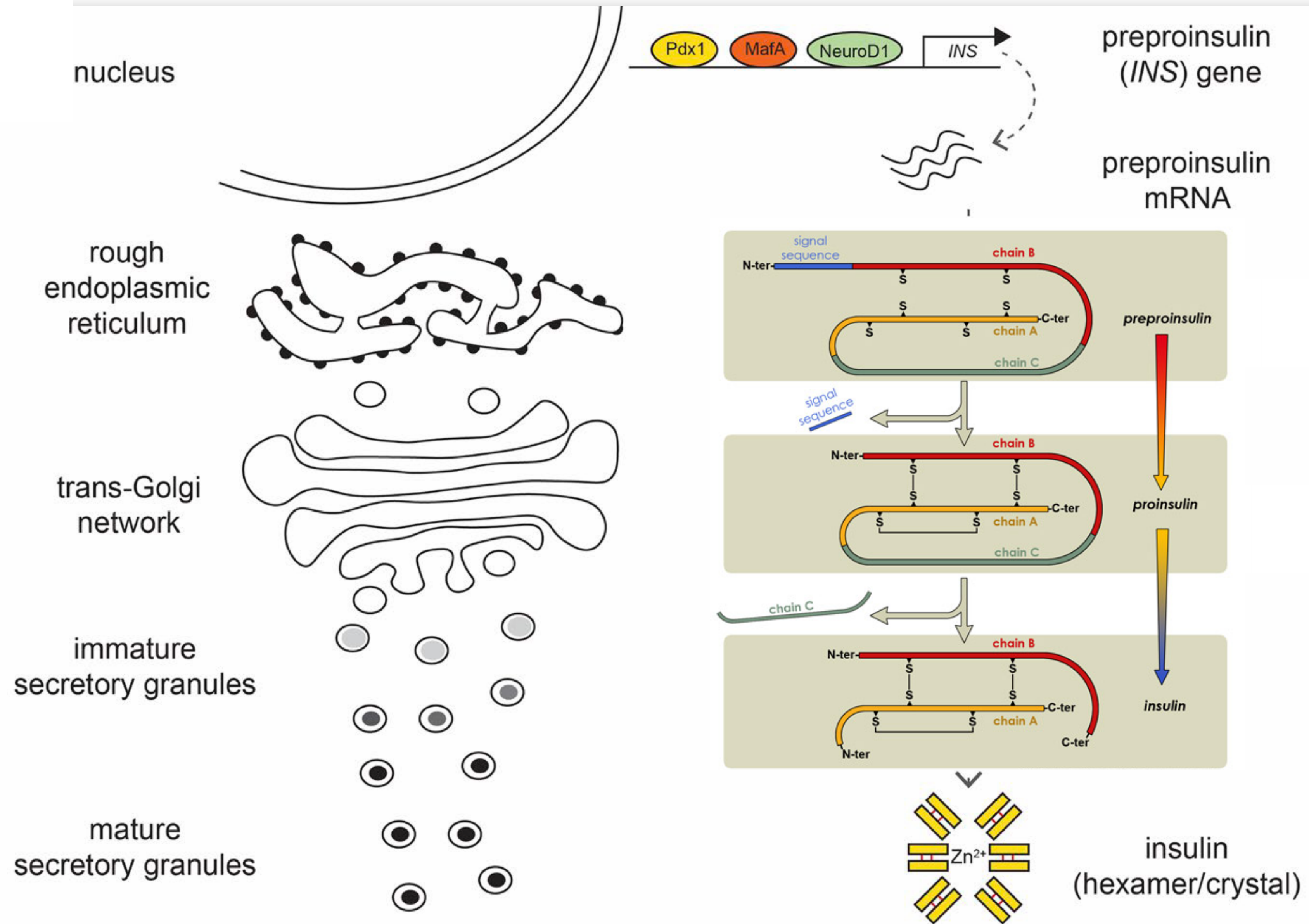
**Figure 2. The Structure of Human Proinsulin.**

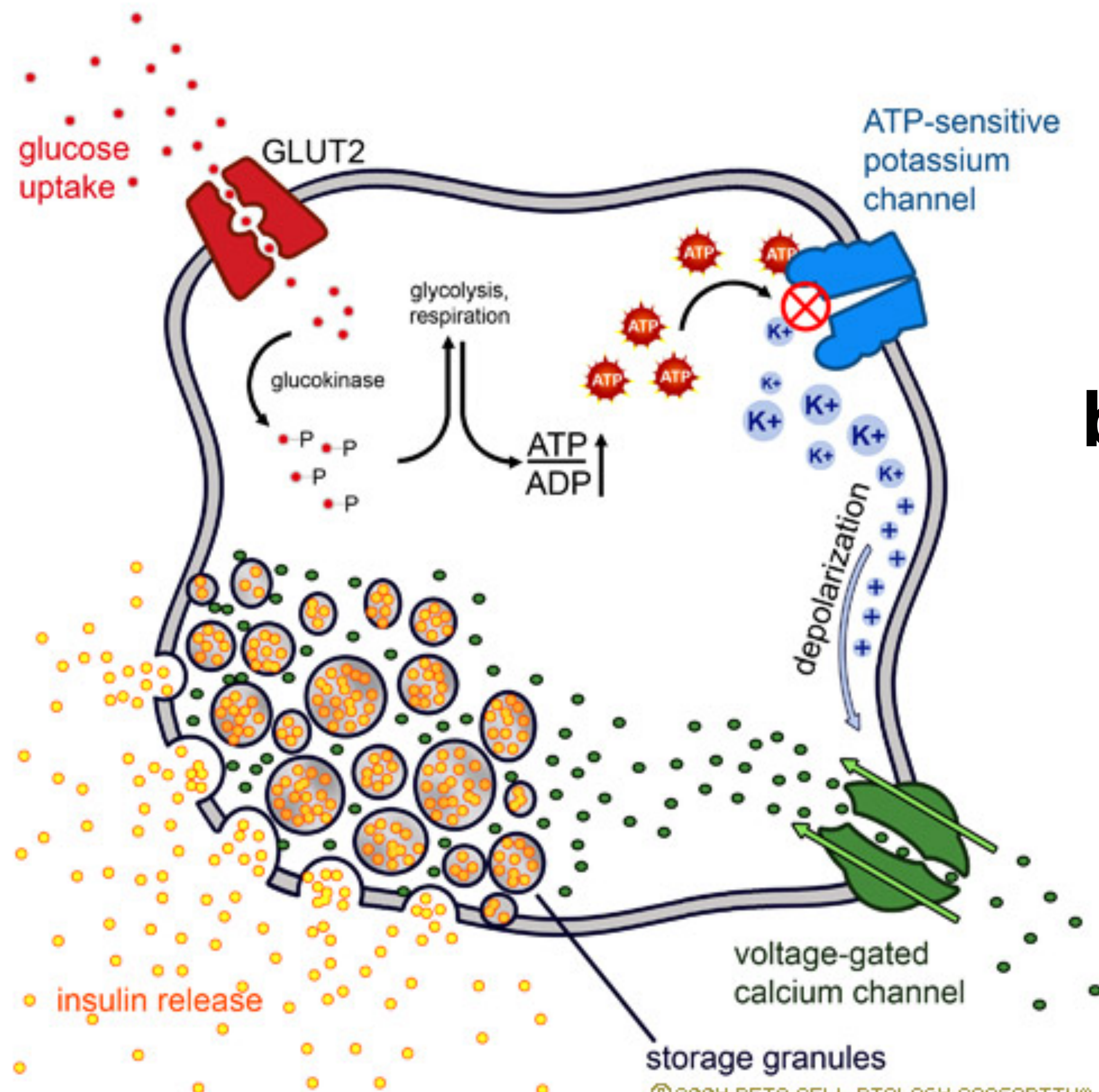
Proinsulin is converted to insulin by proteolytic converting enzymes that remove the connecting peptide (C-peptide) and the lysine-arginine (Lys-Arg) and arginine-arginine (Arg-Arg) sequences of dibasic amino acids, leaving the mature insulin molecule, which consists of A and B chains connected by disulfide bonds.









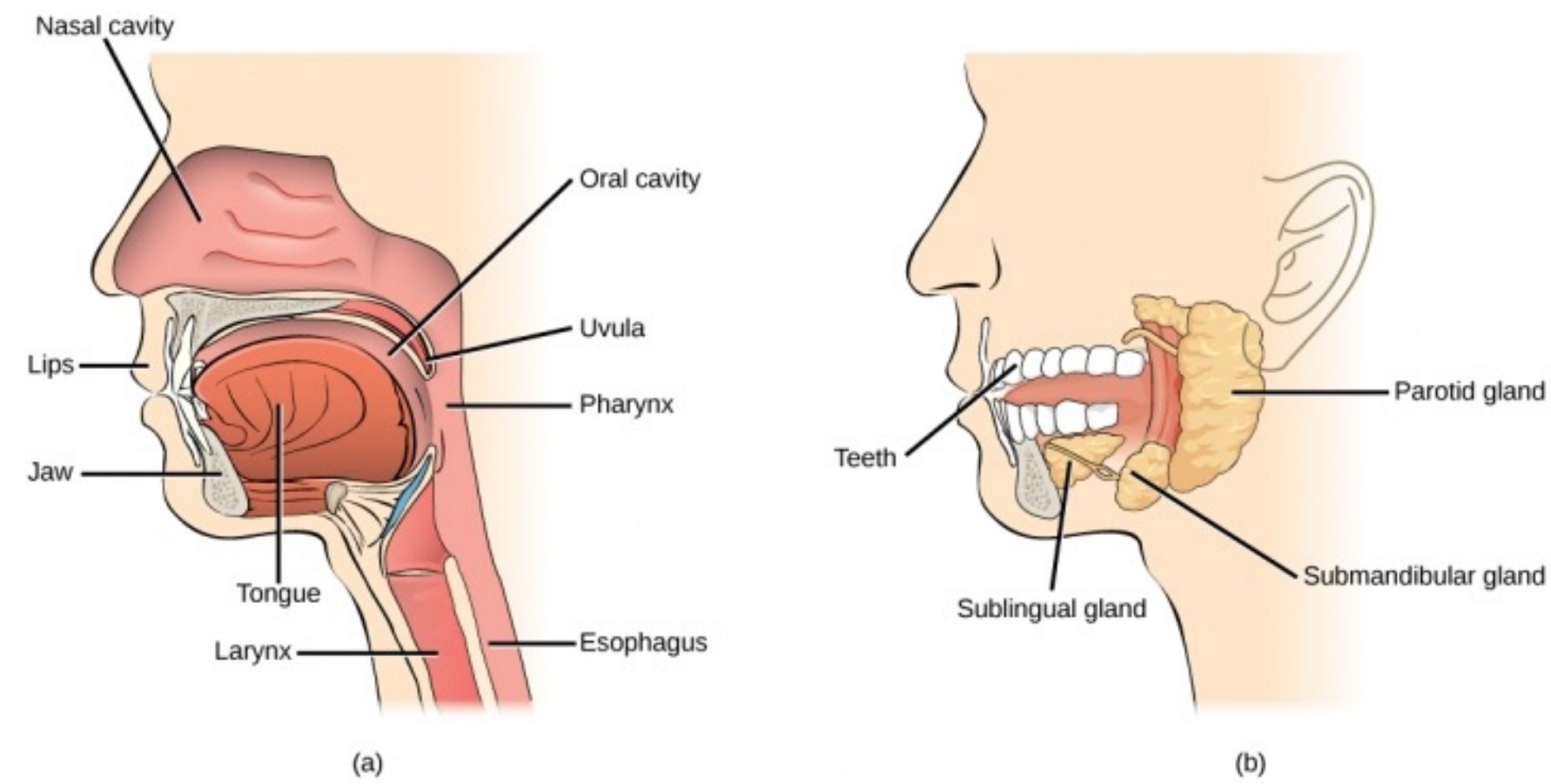


# beta cell of pancreas





VF

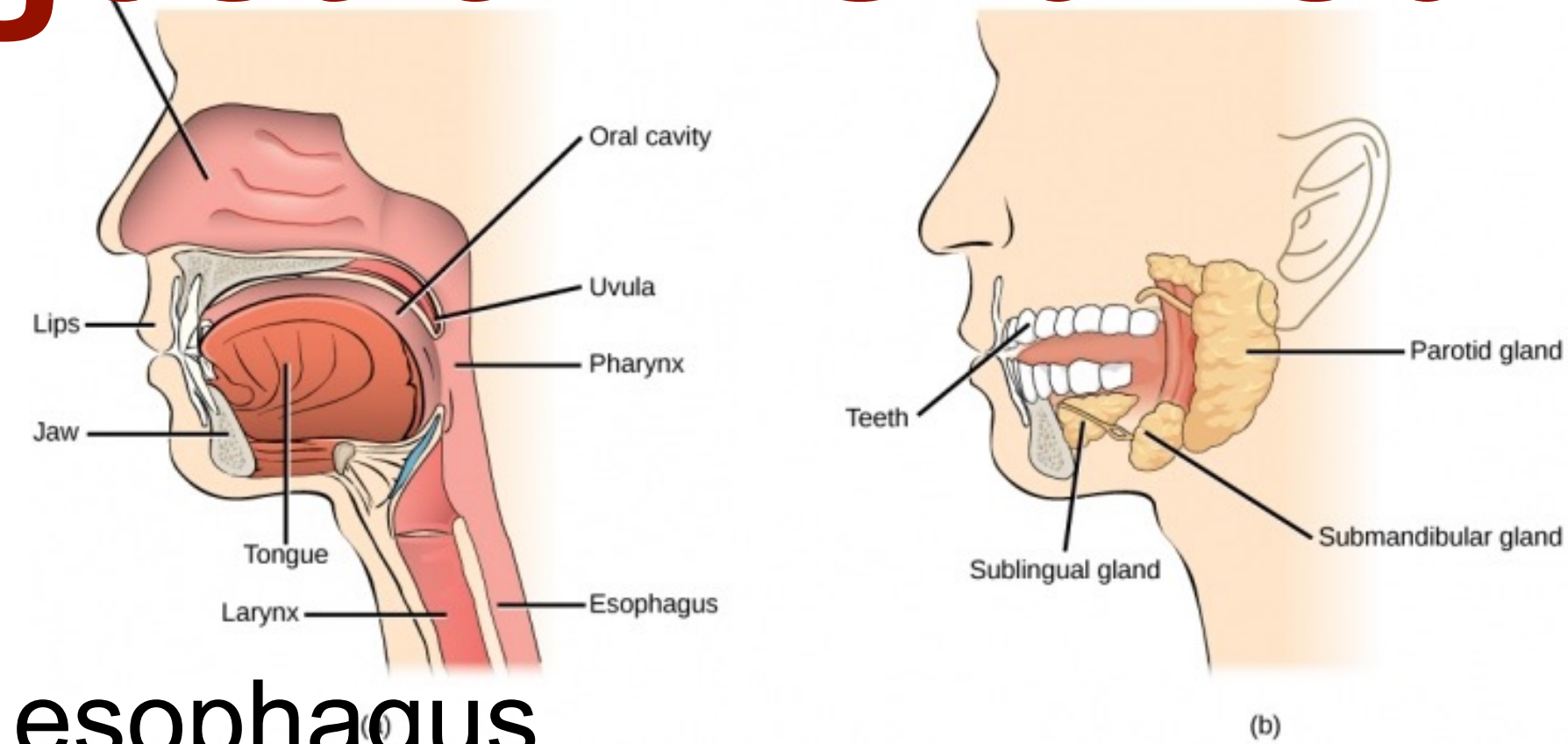


## Digestion: Oral Cavity

When you are eating a Krispy Kreme donut, describe the process of digestion in the Oral Cavity (mouth).

What **hormones** -> stimulate which **cells** -> to secrete what **enzymes** (or perform what **mechanical** actions) -> to digest what **food** molecules?

# Digestion: Oral Cavity



## ? The mouth and esophagus

- Salivary amylase begins the process of carbohydrate digestion (starch i.e. amylose).
- Lingual lipase initiates fat (i.e. lipid) digestion.
- Hormones: (kinda) neurotransmitter via nerves from brain
- other? Buffers, mucous, mechanical, antibacterial compounds
- A combination of smooth and skeletal muscle moves food down the esophagus by peristalsis.

# Stomach

**End of esophagus**

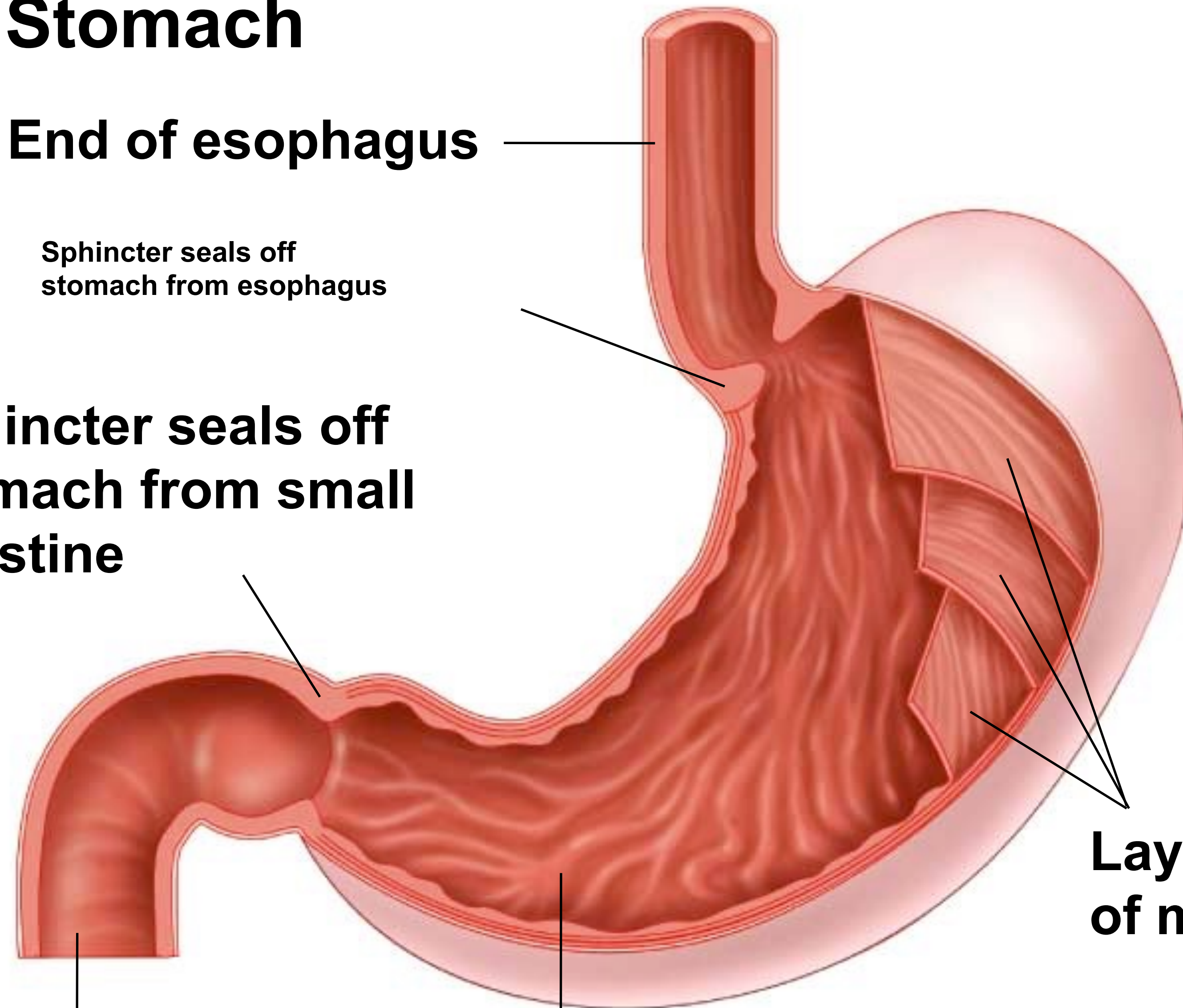
Sphincter seals off  
stomach from esophagus

**Sphincter seals off  
stomach from small  
intestine**

**Beginning of  
small intestine**

**Lumen  
(interior)**

**Layers  
of muscle**

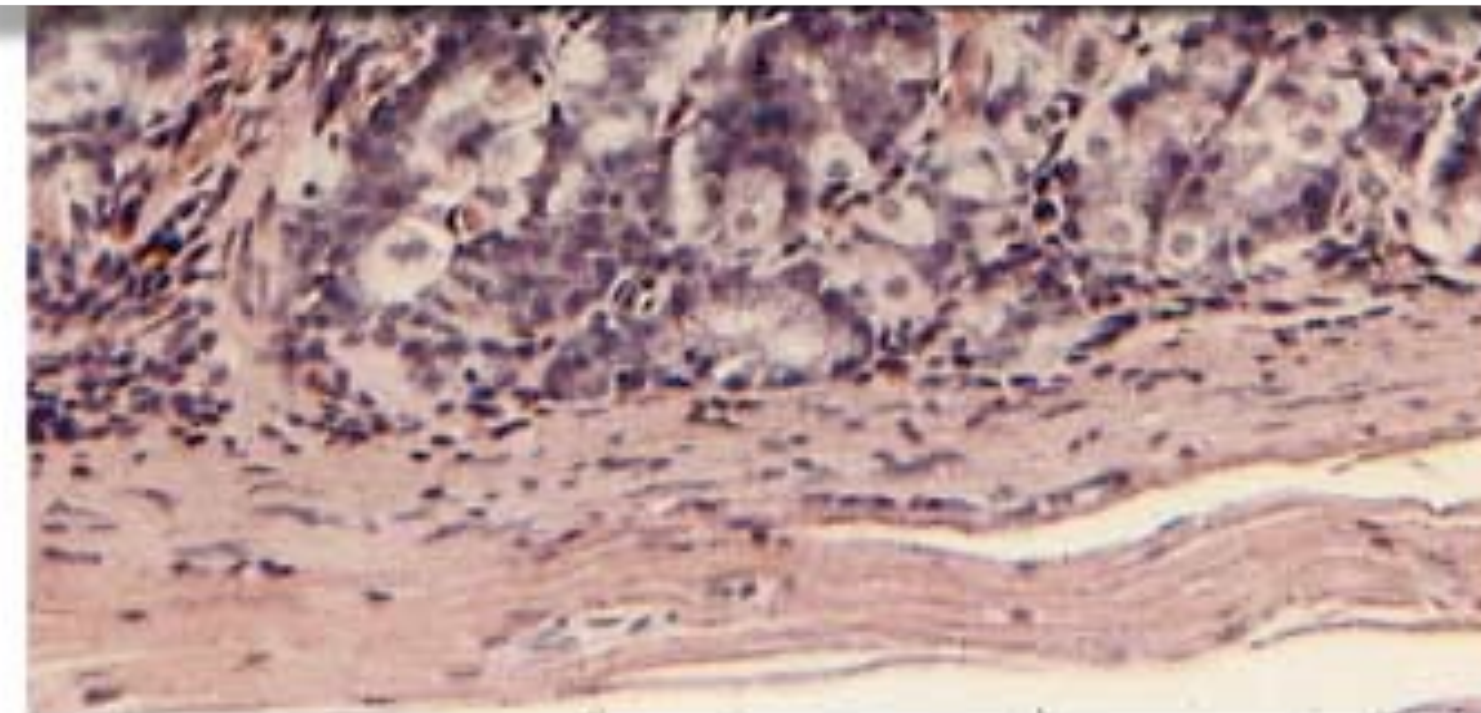
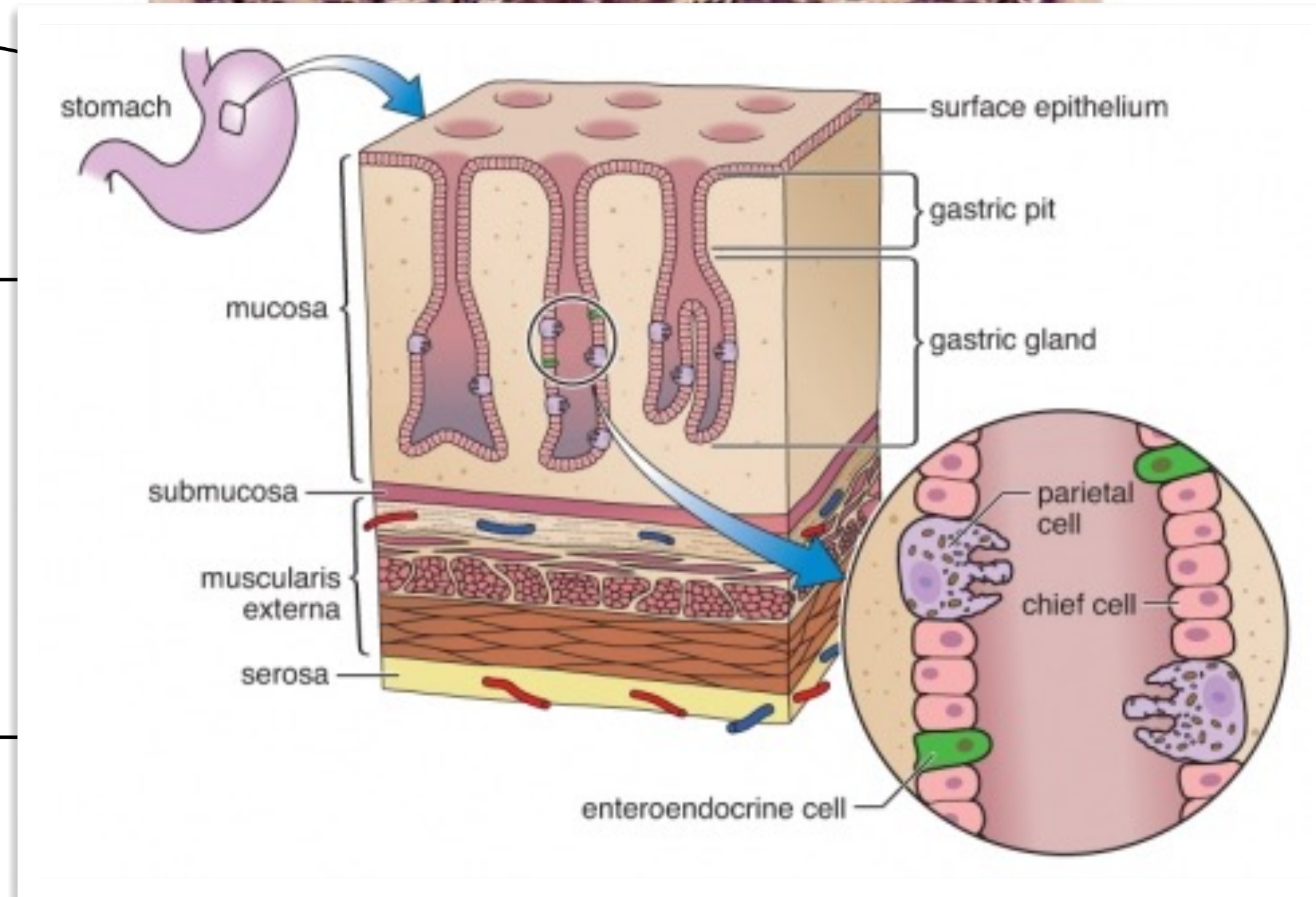


# Stomach lining

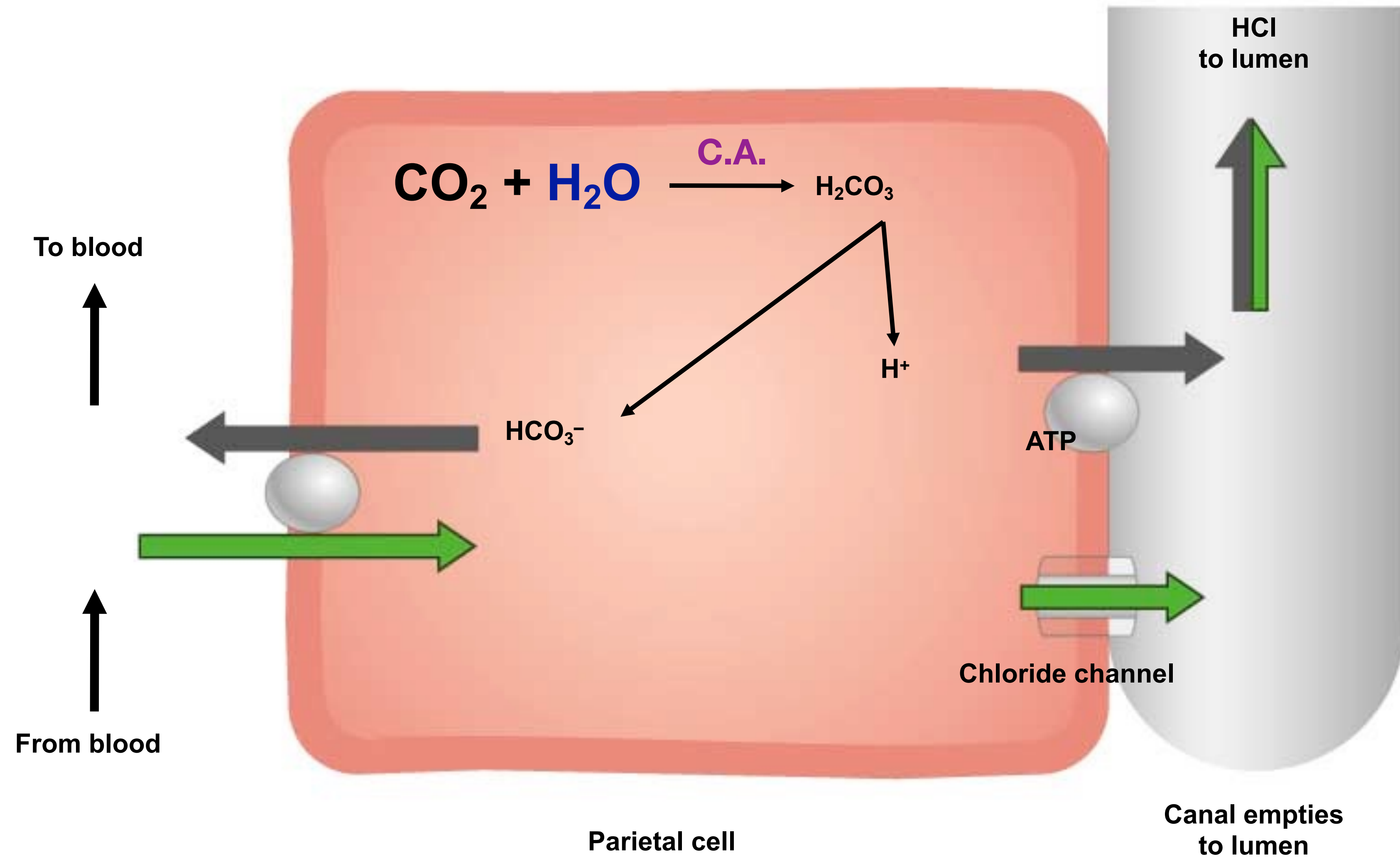
Canal empties to lumen

**Parietal cells  
(secrete HCl)**

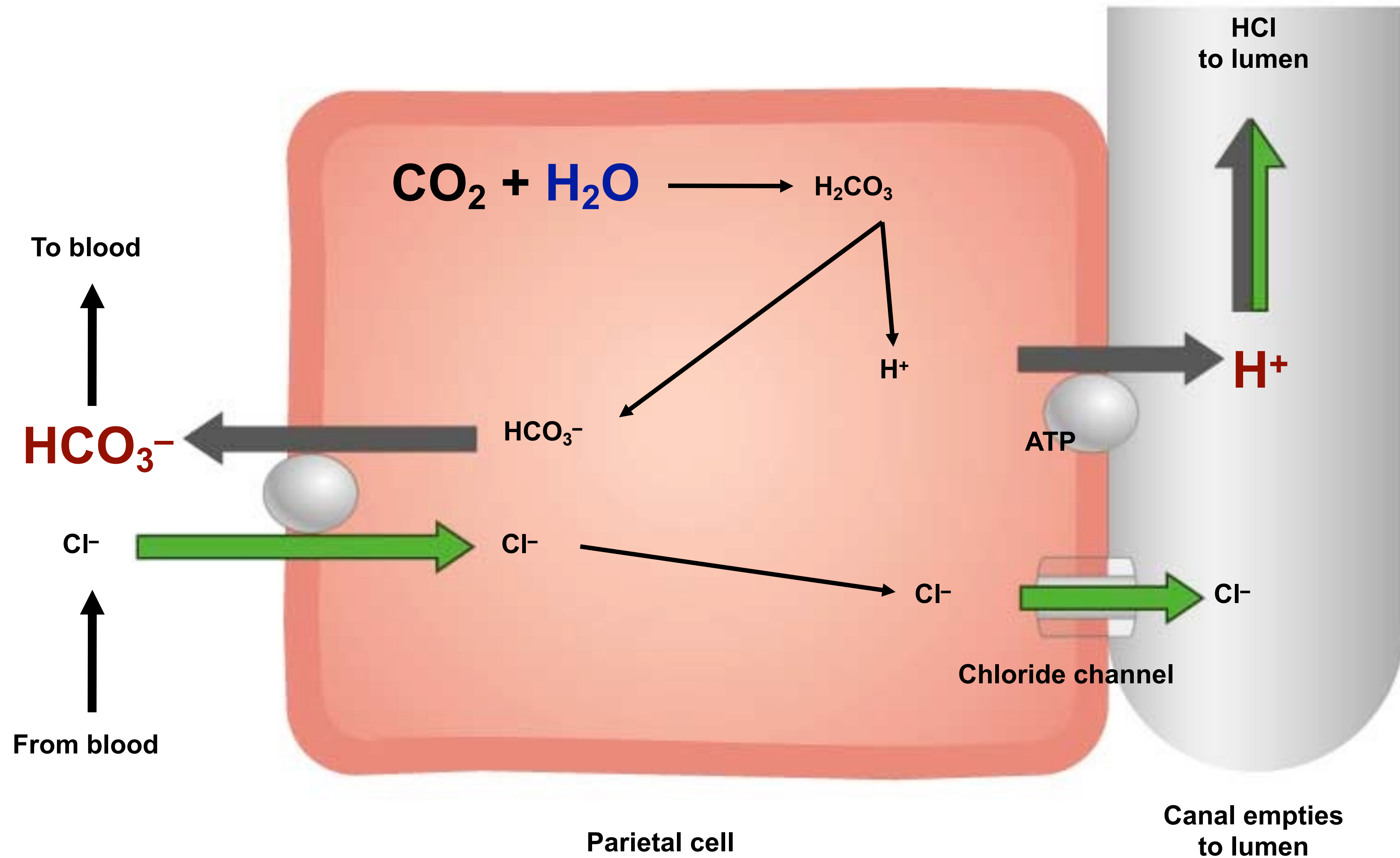
**Chief cells  
(secrete pepsinogen)**



# Secretion of HCl by parietal cells

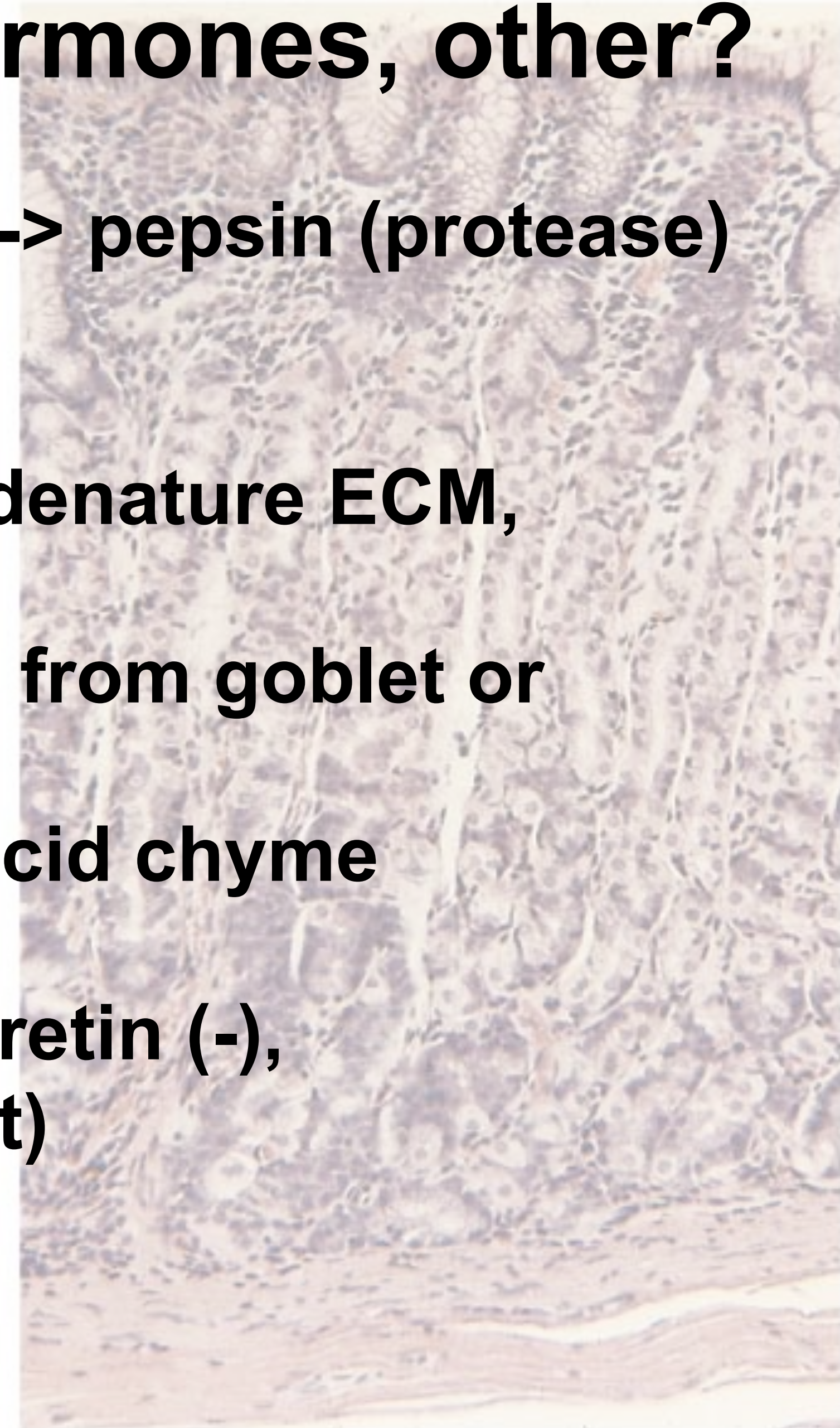


# Secretion of HCl by parietal cells



# Stomach -Enzymes, Hormones, other?

- **Enzymes**: pepsinogen (inactive) → pepsin (protease) from chief cells
- **Other**: HCl from parietal cells → denature ECM, bacteria, activator of pepsin
- **Other**: Mucins/mucus protective from goblet or mucus cells
- **Other**: mechanical churning → acid chyme
- **Hormones**: Gastrin (+), CCK/secretin (-), enterogastrone (-- pyloric sphinct)

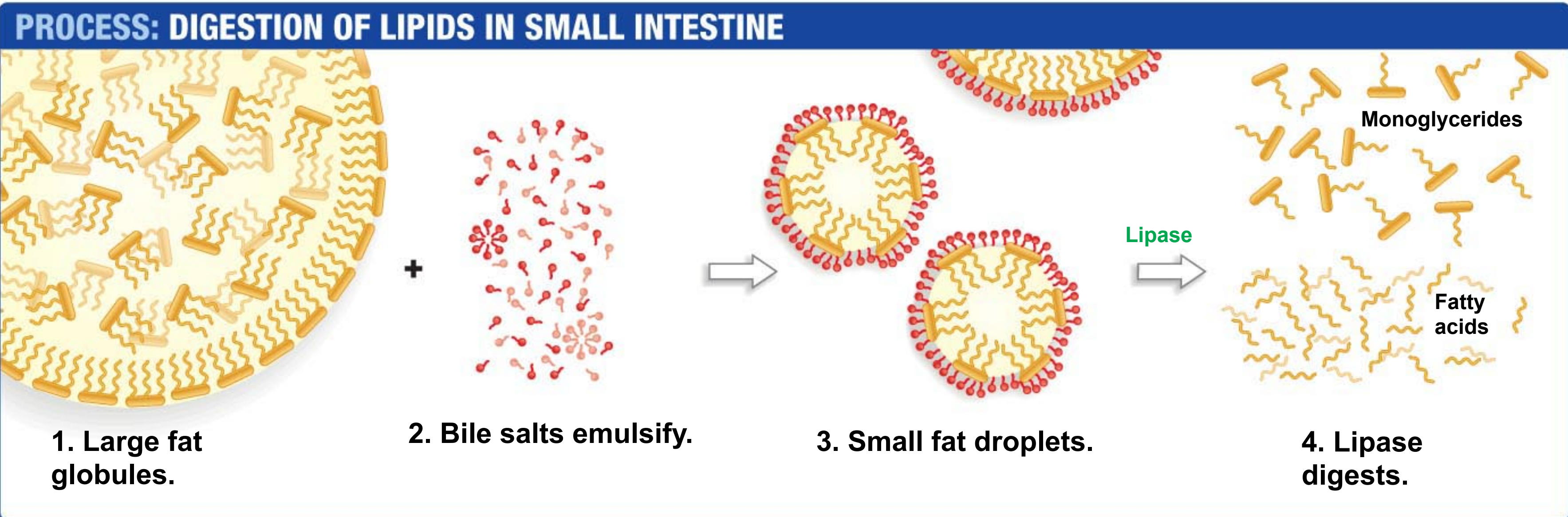


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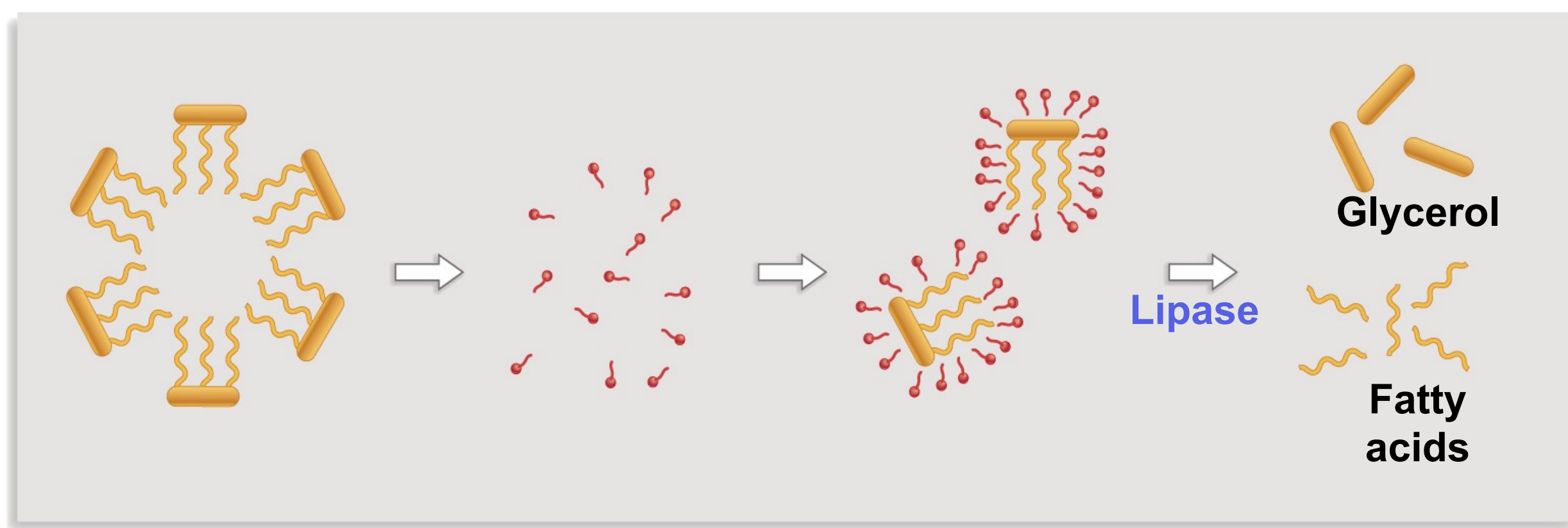
# Digestion

## ☐ The small intestine

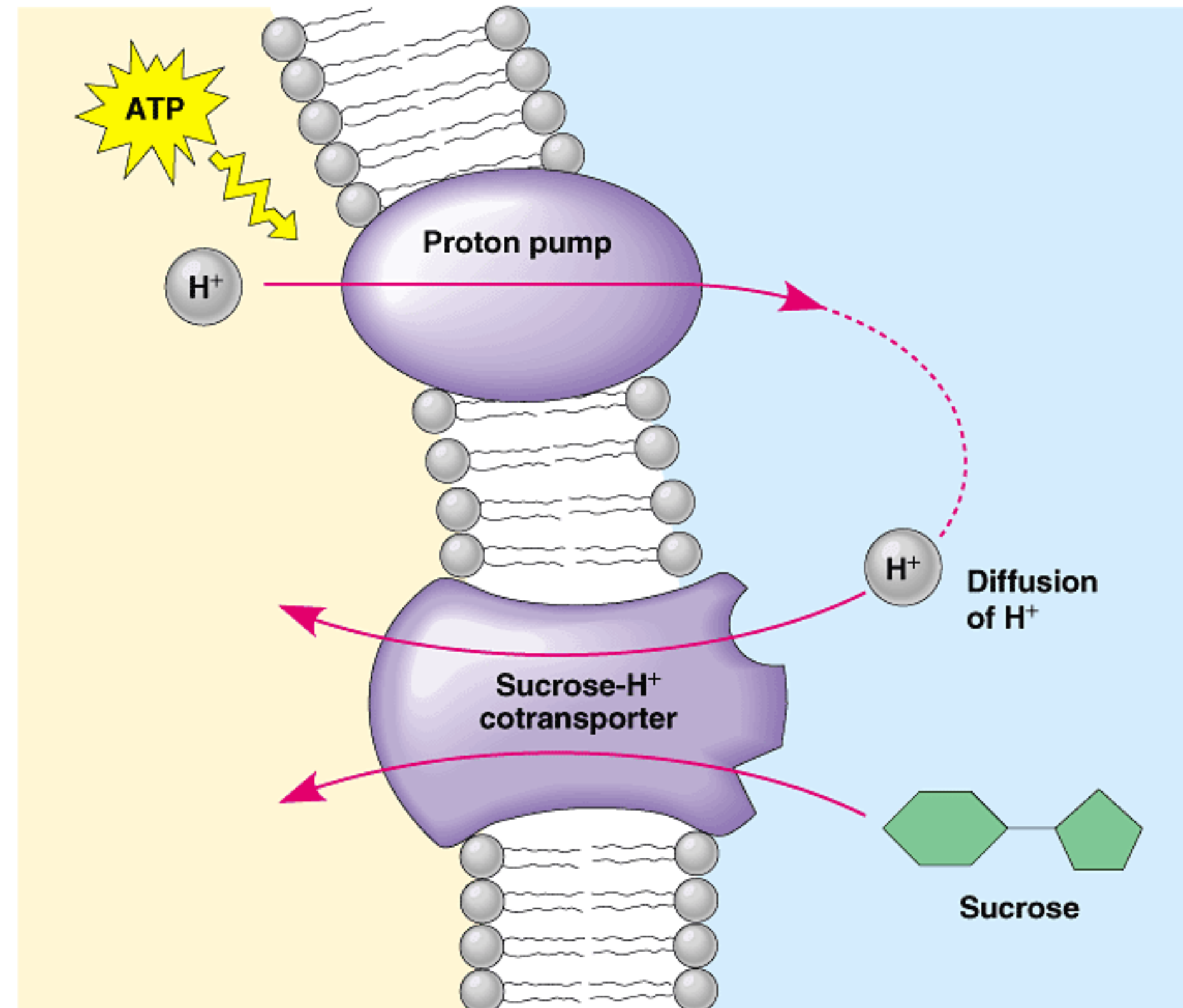
- The hormone *cholecystinin (CCK)* released from the duodenum into the bloodstream soon stimulates the secretion of enzymes from the pancreas and bile salts from the gall bladder, into the small intestine.
- Bile salts emulsify fats (lipids) so they can be digested by the enzyme lipase secreted by the pancreas.
- The epithelium of the small intestine is highly folded, and have fingerlike projections called microvilli which provide a large surface area for absorption of food into the body and bloodstream.



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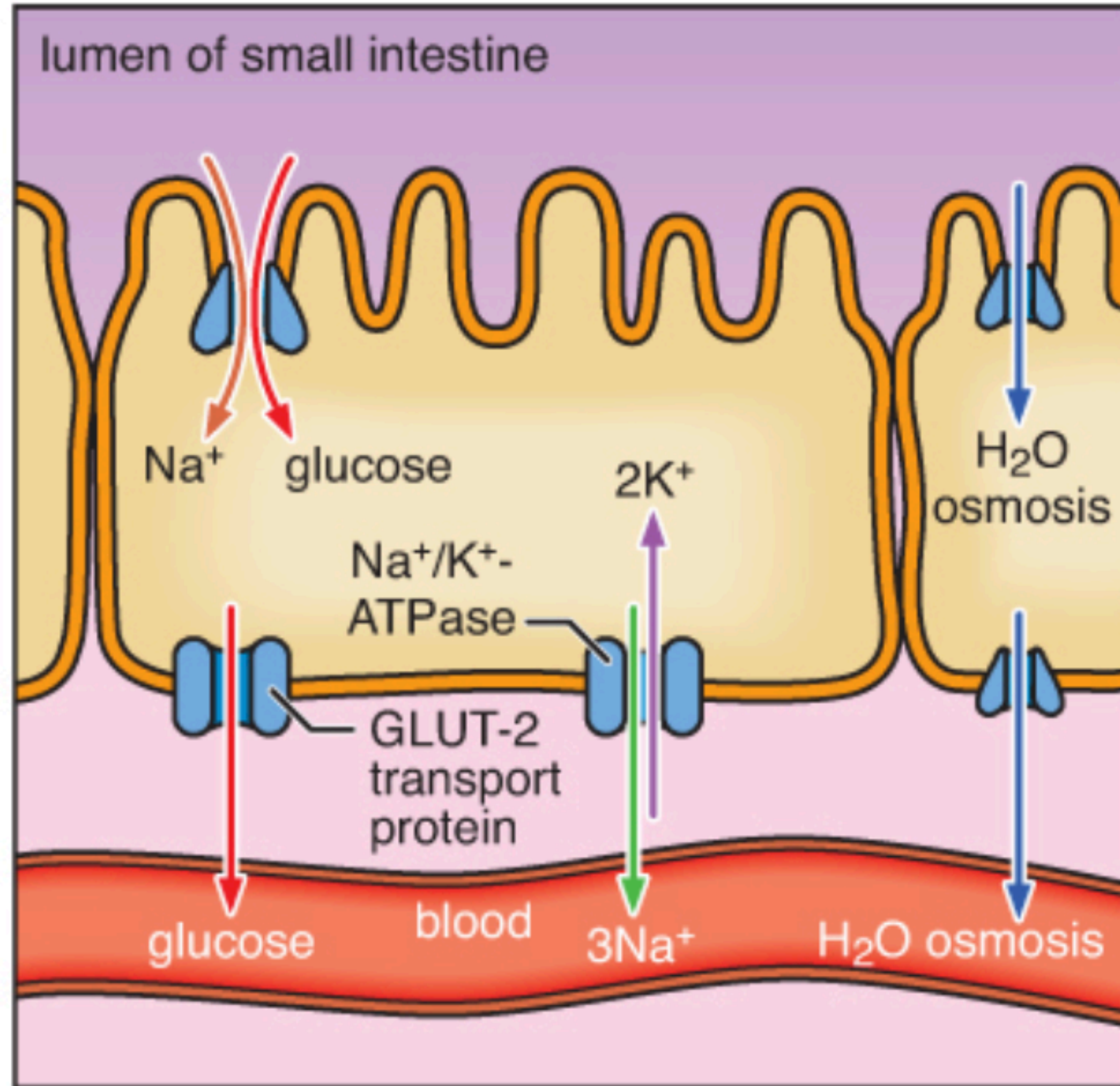


# Absorption

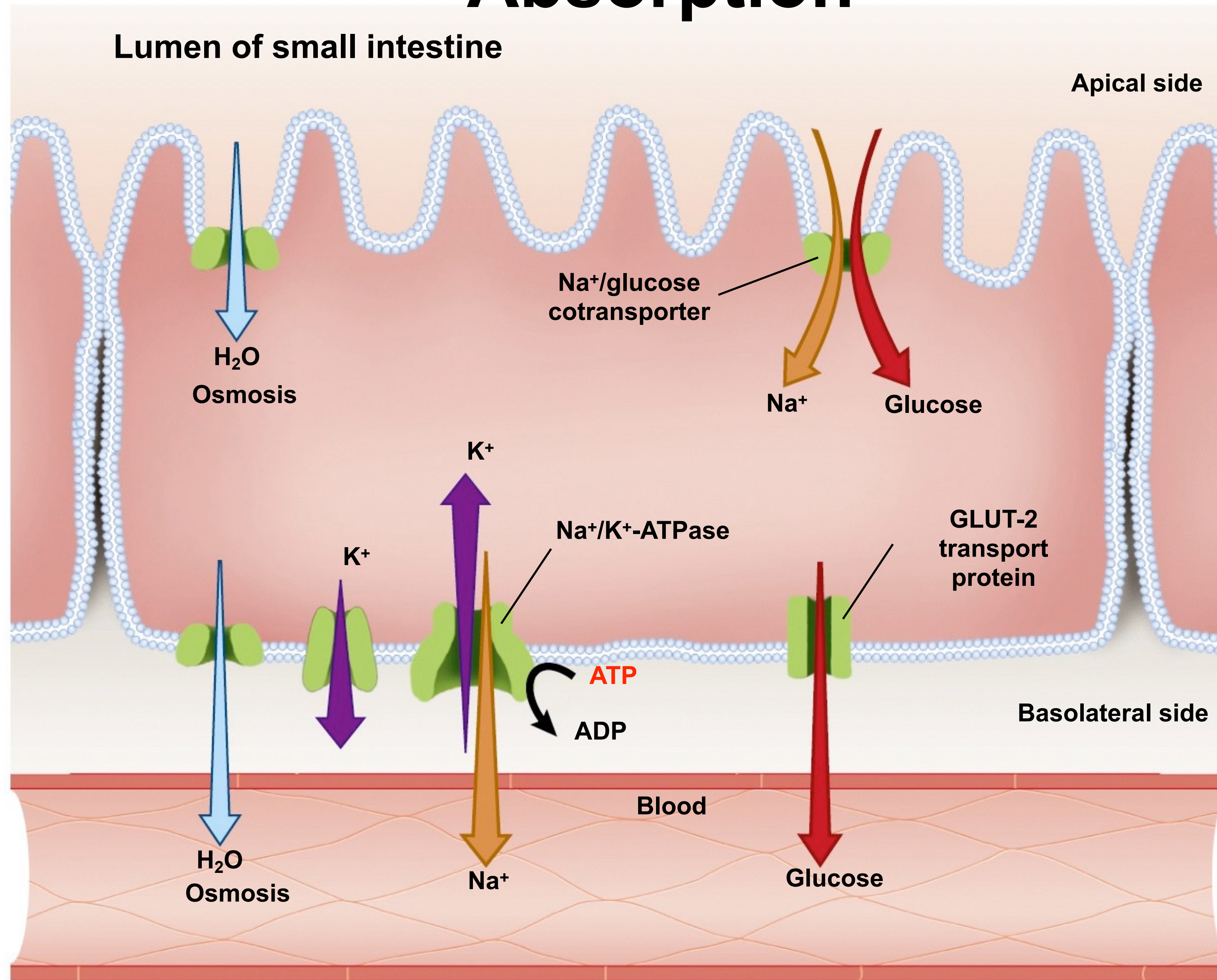


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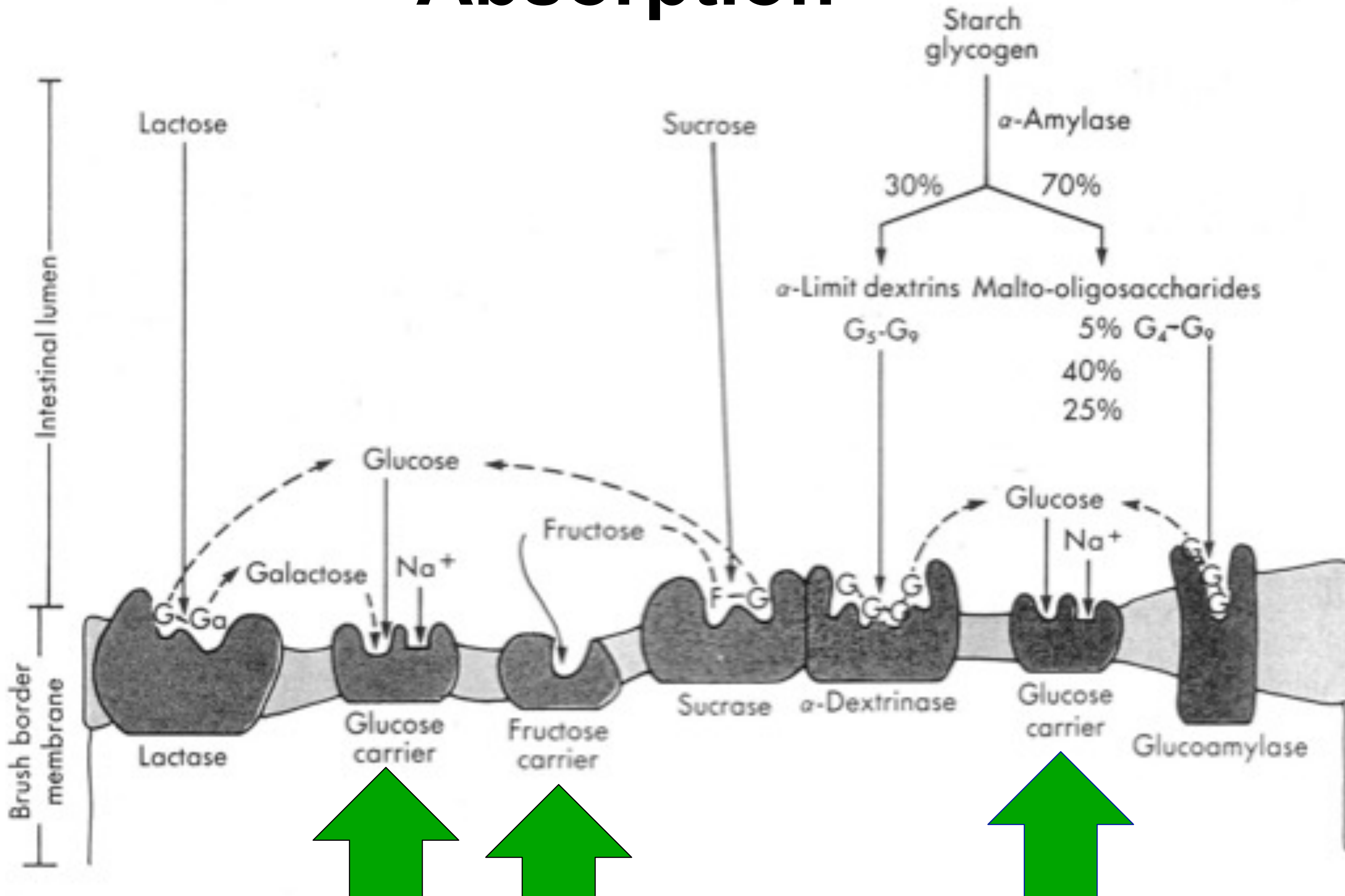
# Absorption



# Absorption

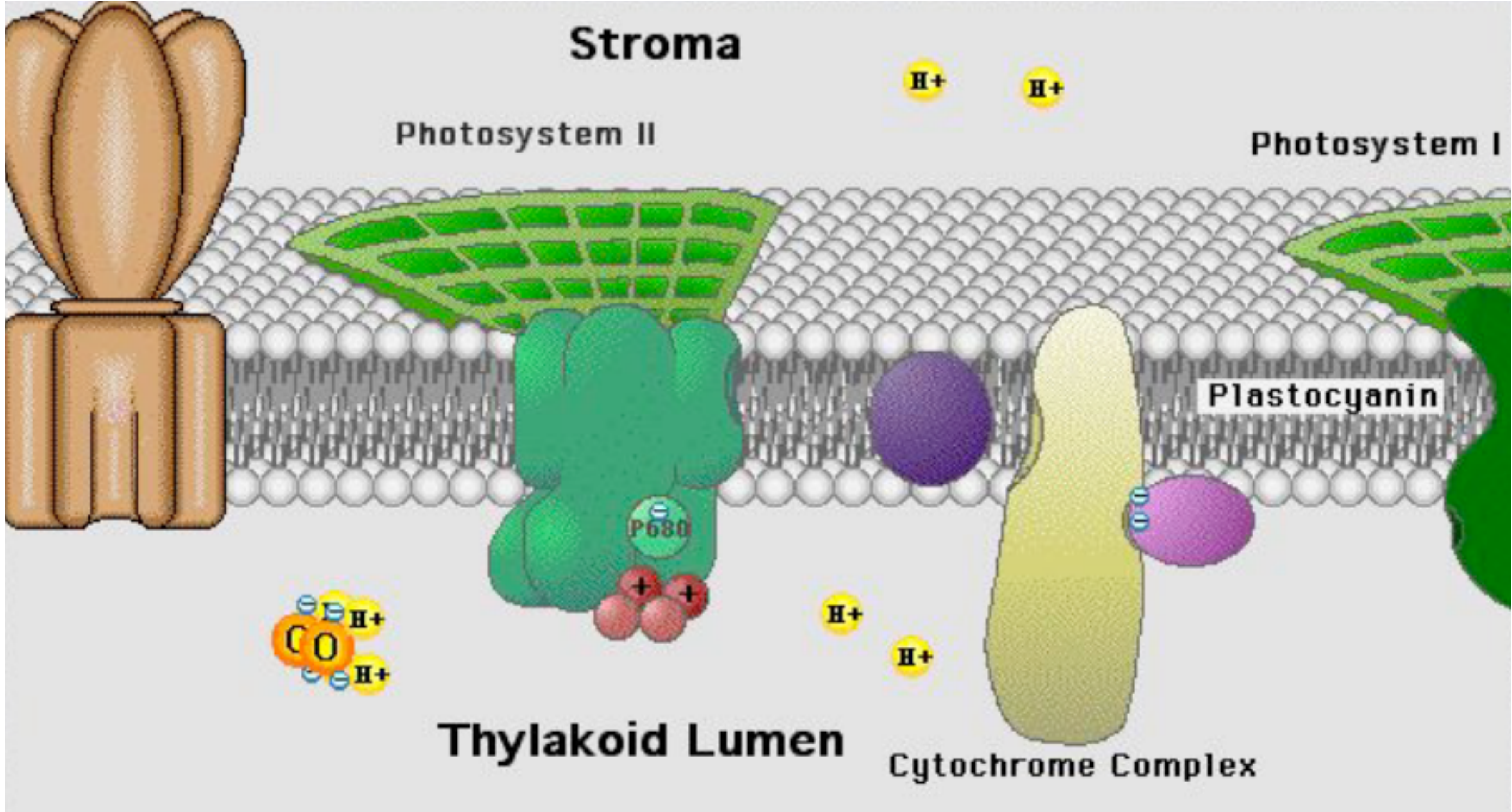


# Absorption +

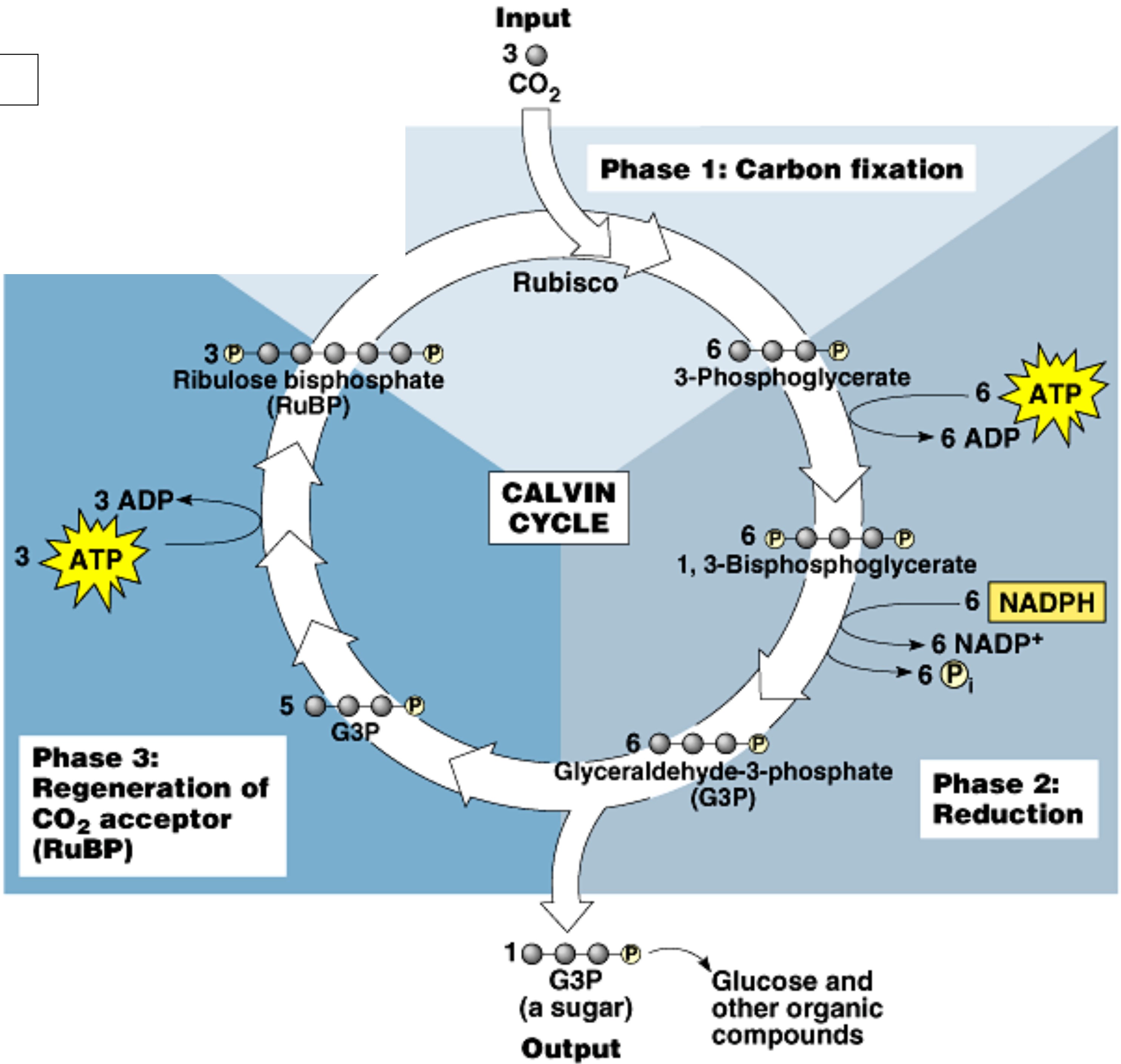


■ Fig. 44-2. Functions of the major brush border oligosaccharidases. The glucose, galactose, and fructose molecules released by enzymatic hydrolysis are then transported into the epithelial cell by specific transport carrier proteins. G, Glucose; Ga, galactose; F, fructose. (From Gray, G.M.: N. Engl. J. Med. 292:1225, 1975. Reprinted by permission of *The New England Journal of Medicine*.)

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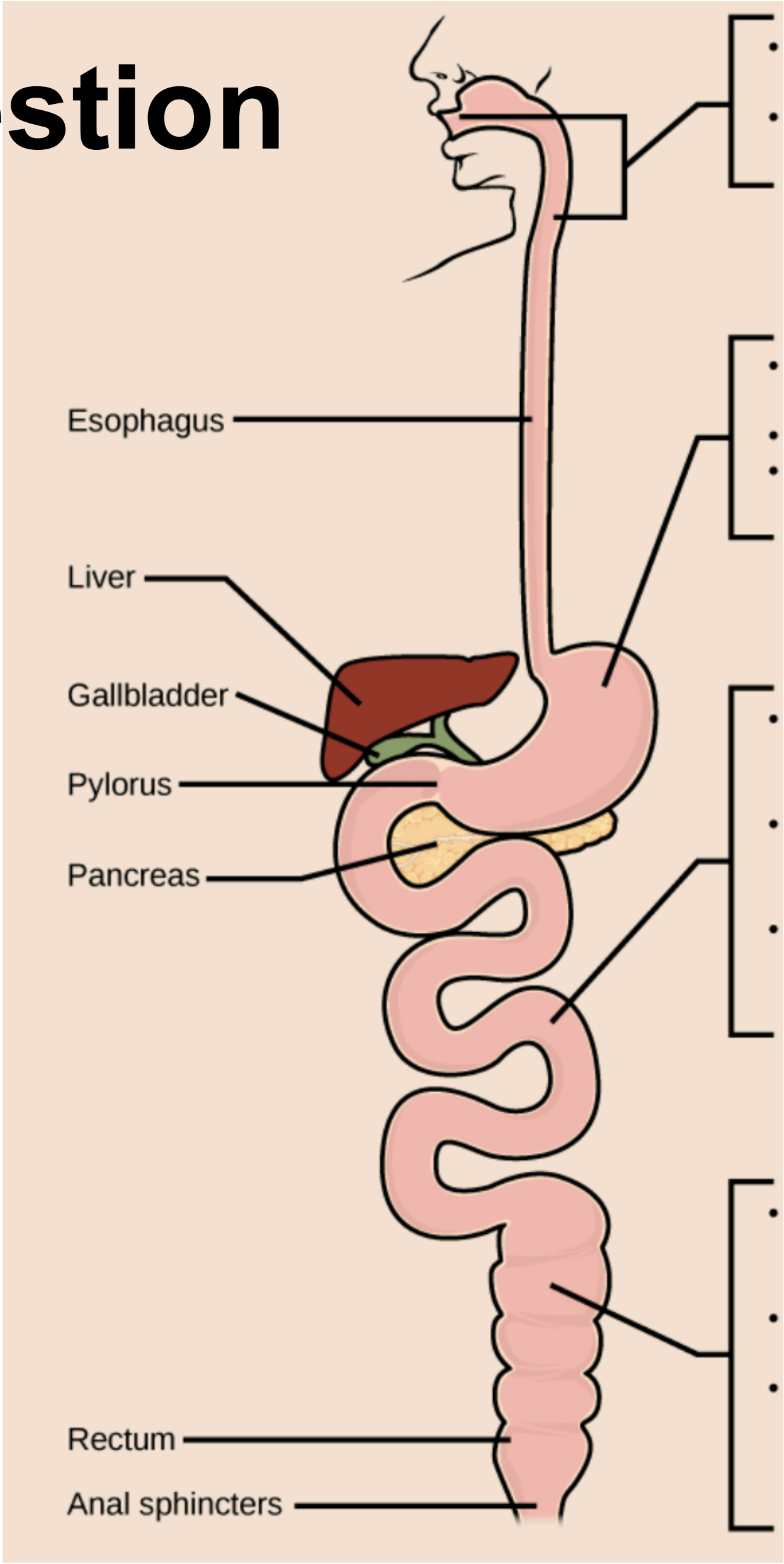


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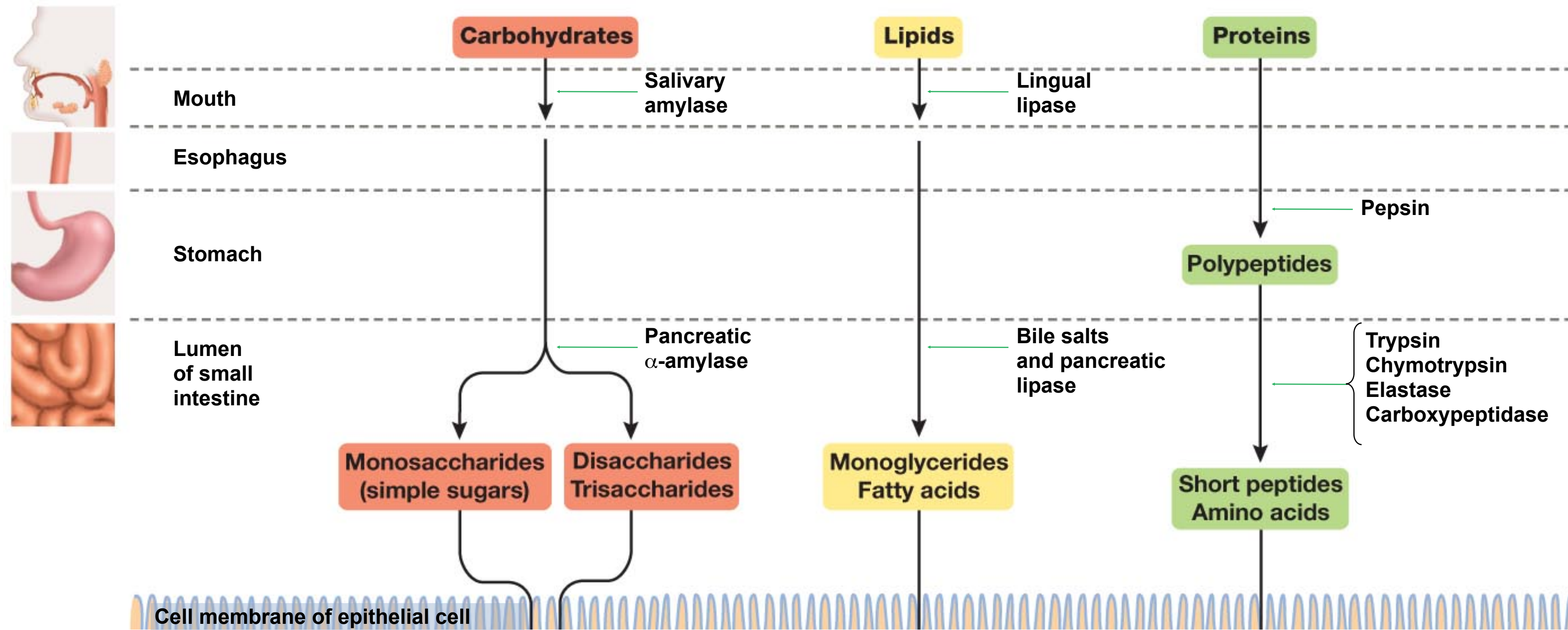
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# Digestion

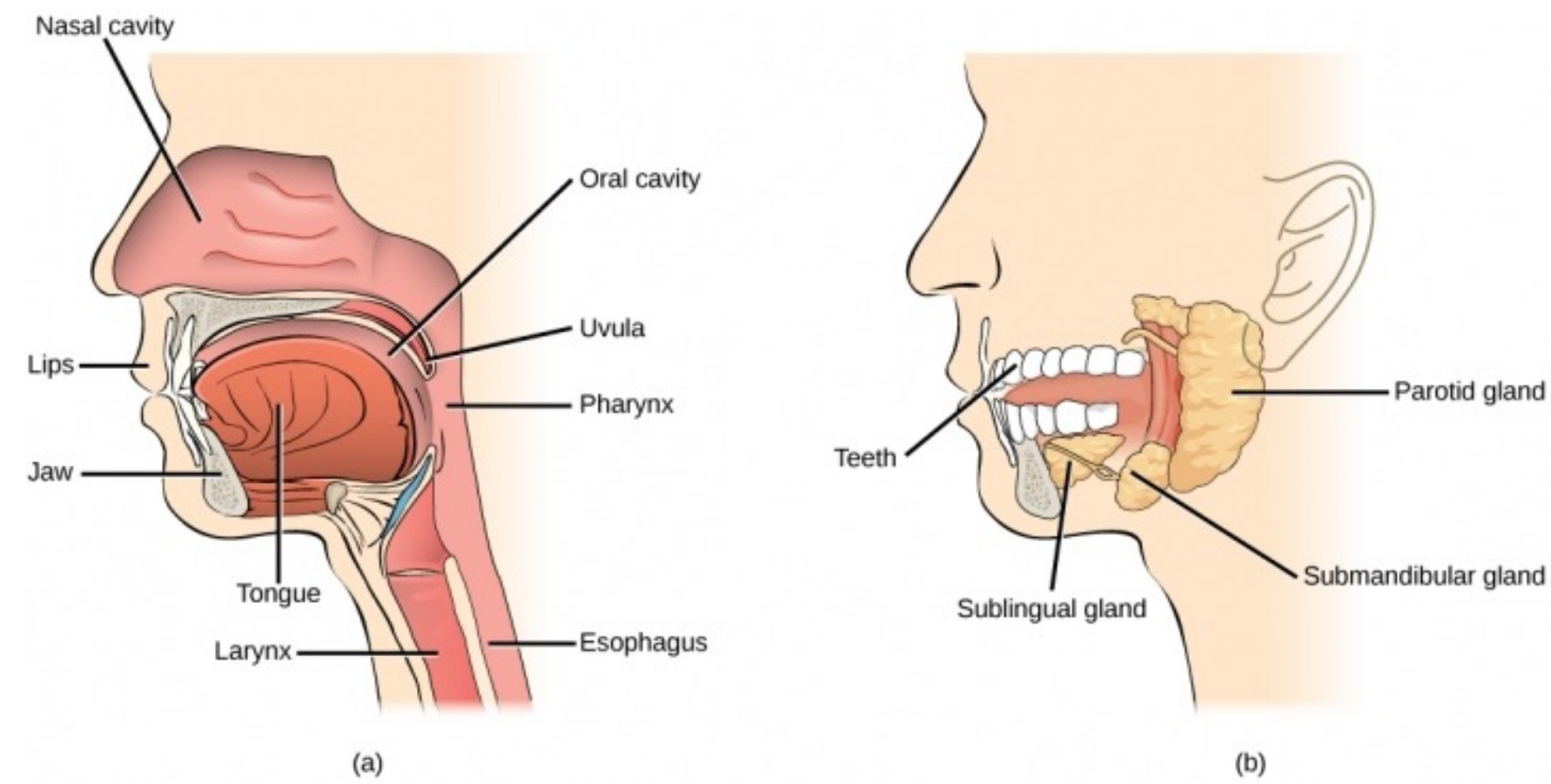


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# Digestion



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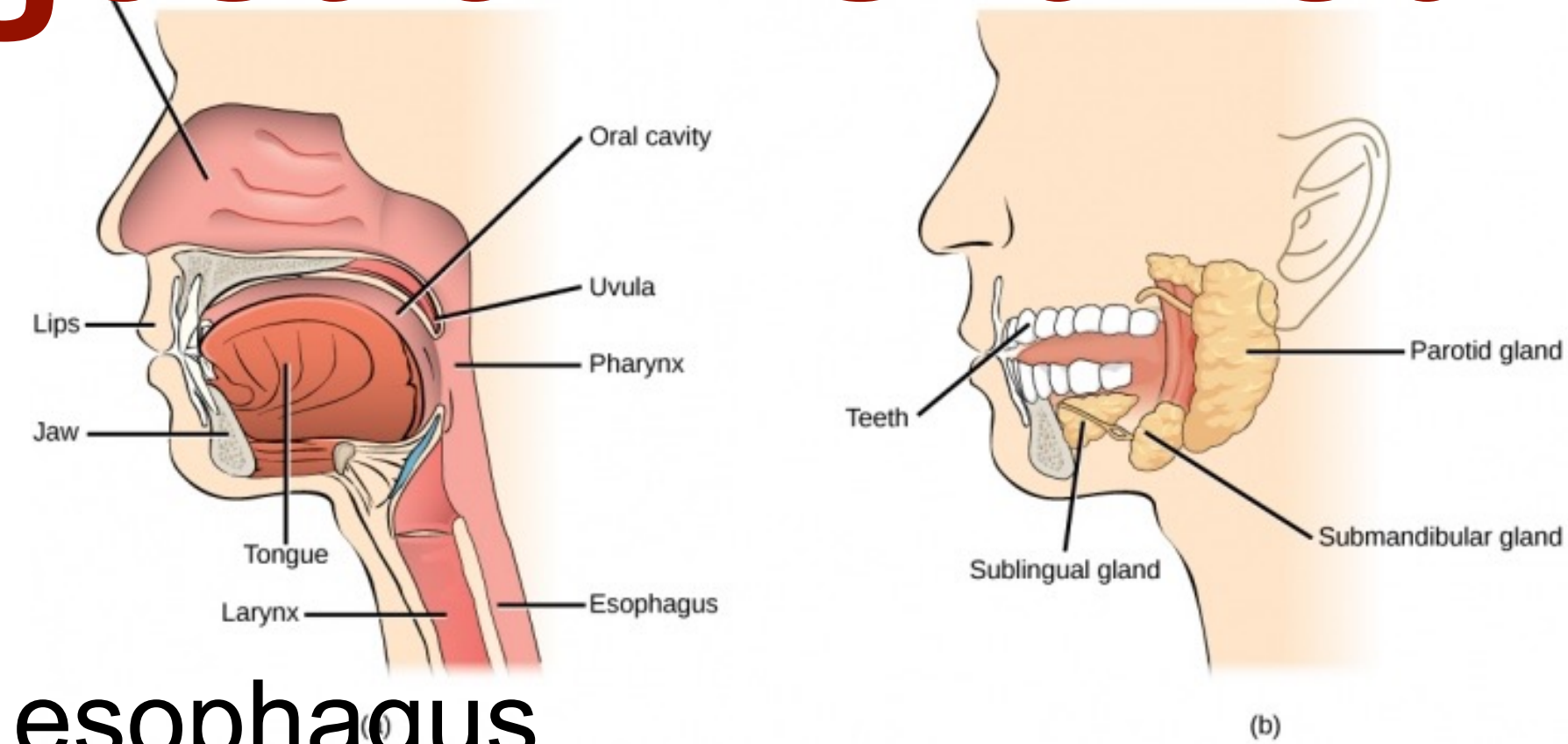


## Digestion: Oral Cavity

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# Digestion: Oral Cavity

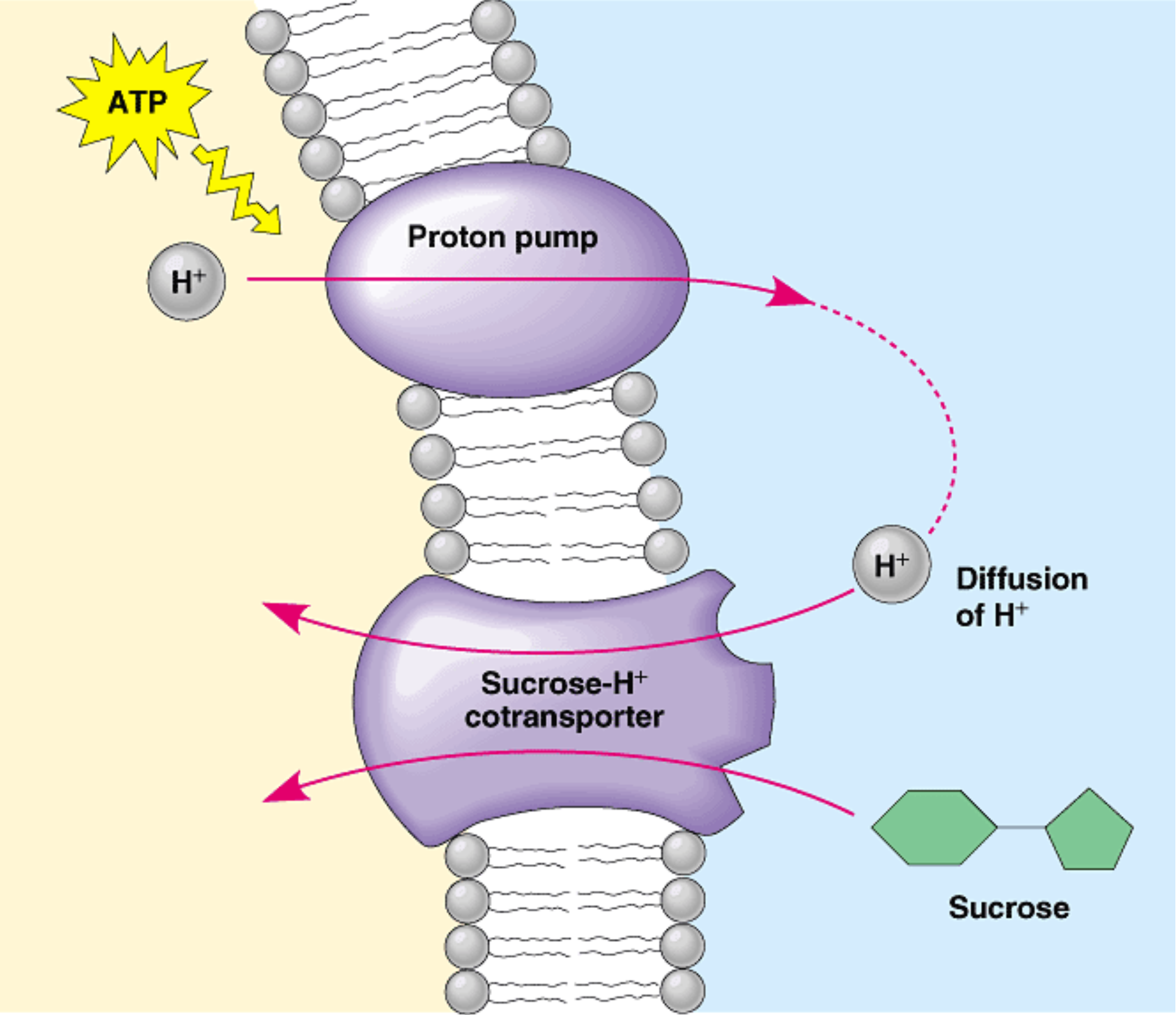


## ? The mouth and esophagus

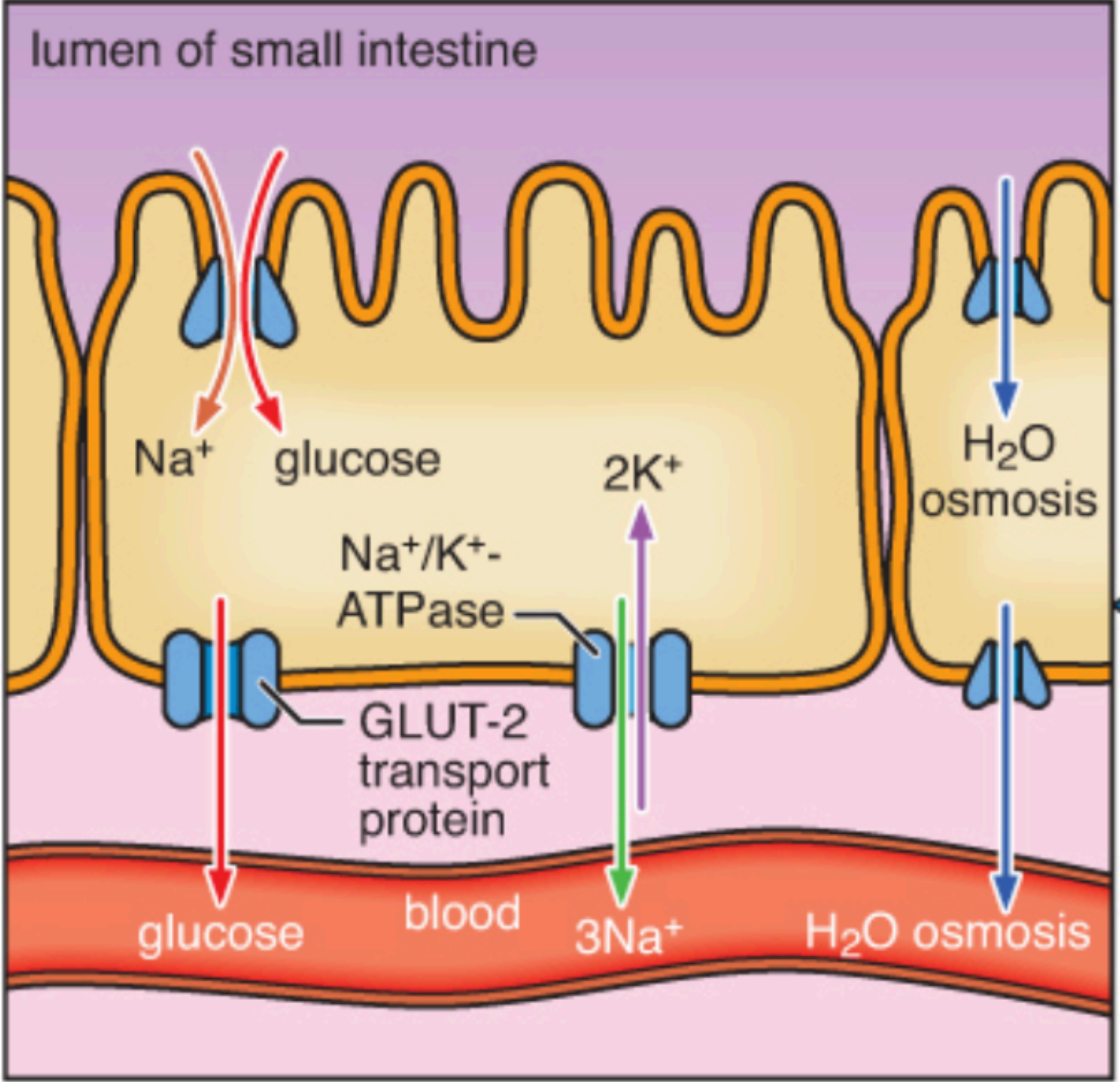
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VF

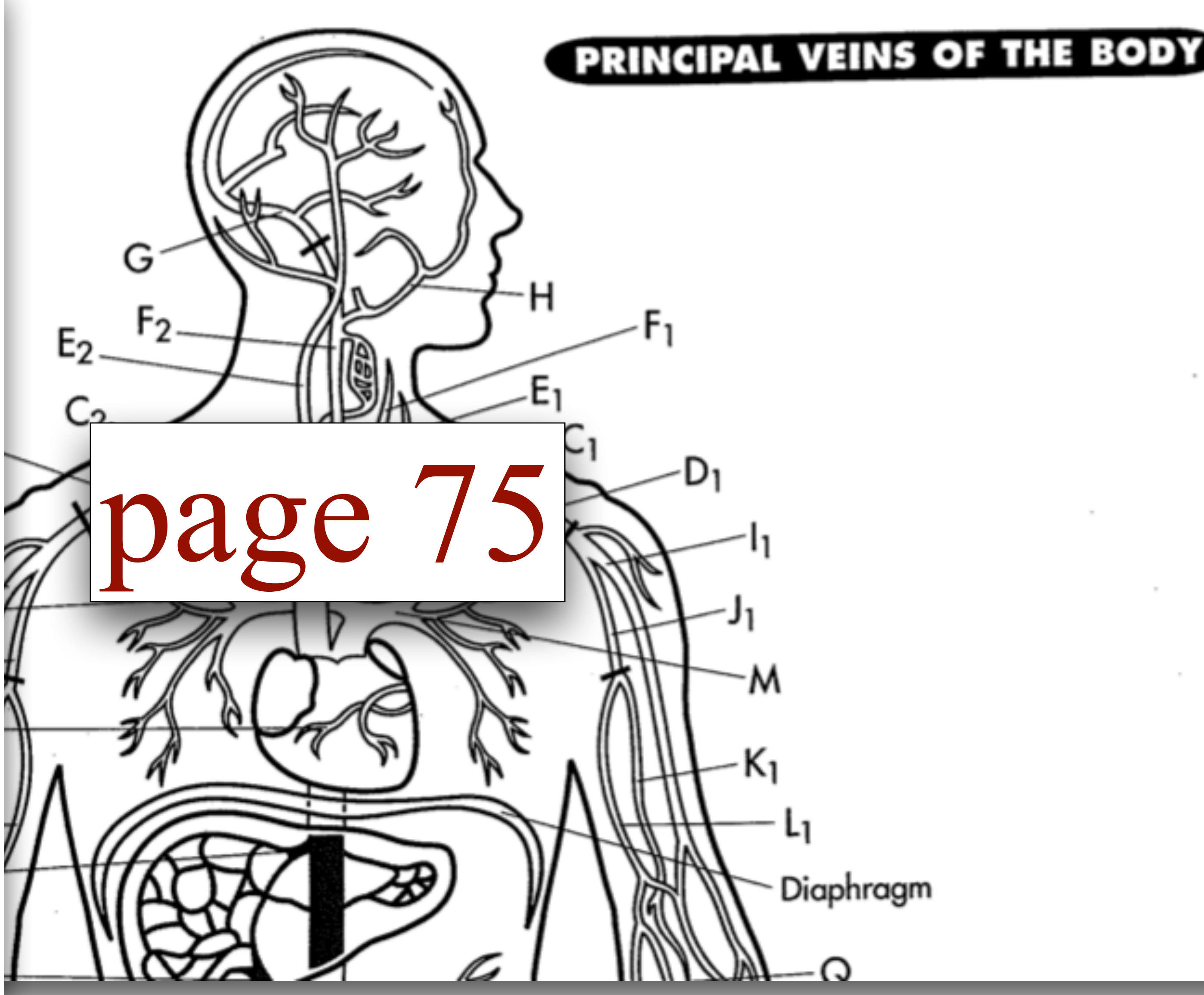
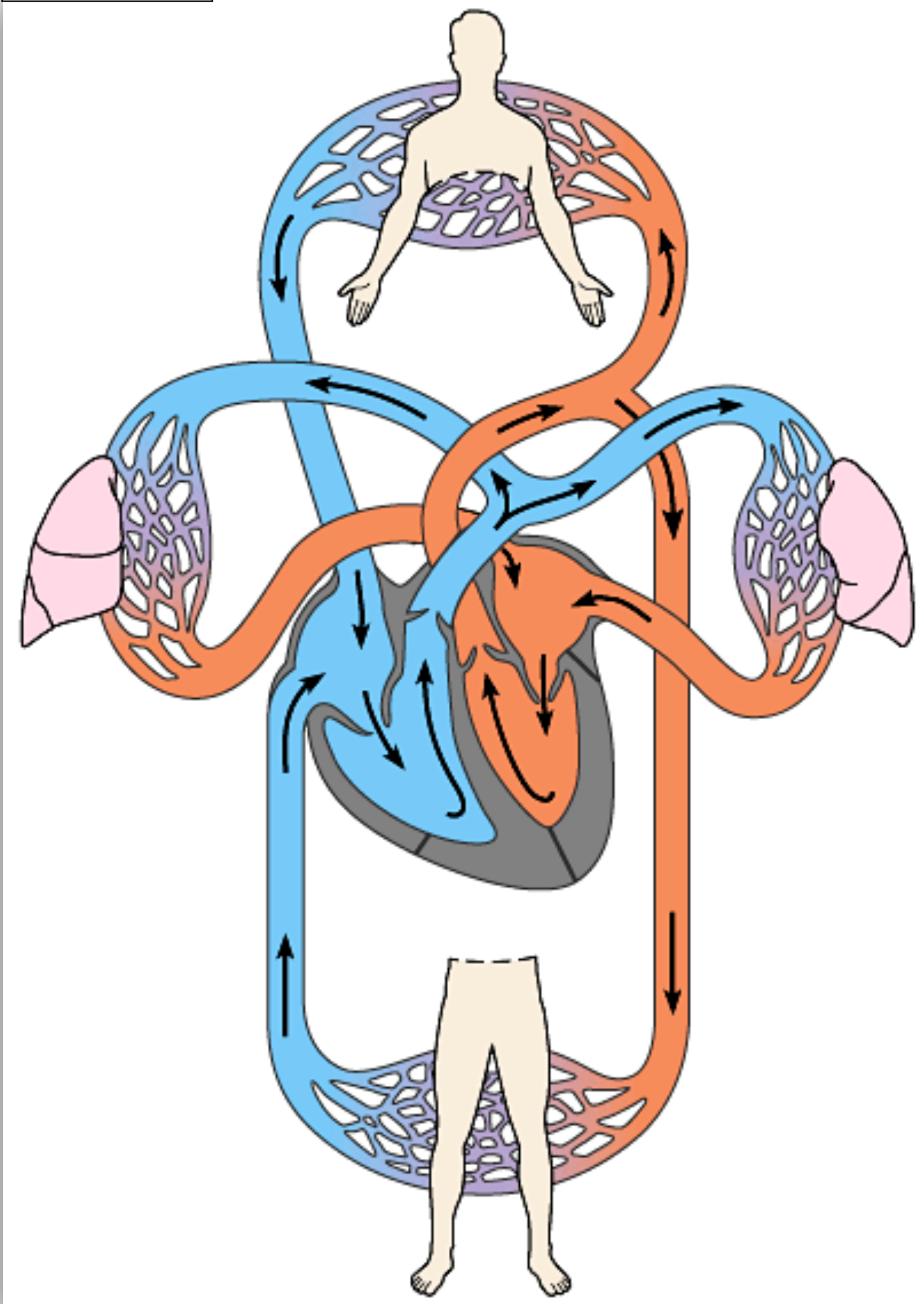
# Absorption



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page 75

VF

# Beta cell of pancreas

