Section 2

LECTURE

Overview of Physiology

Overview of Gastrointestinal Physiology

The gastrointestinal tract is a specialized unidirectional conduit for digestion and absorption of dietary nutrients. In order to achieve its goals, the structural design of the gastrointestinal tract must satisfy a number of requirements. First, the gastrointestinal tract must include a propulsion mechanism for the flow of food from the mouth to the anus, and to prevent its accidental back-flow. Second, the gastrointestinal tract must be able to mechanically disrupt large particles of food into progressively smaller particles to facilitate efficient enzymatic breakdown of the nutrients and enable their specific transport across the epithelial barrier. Fourth, the epithelial lining of the gastrointestinal tract must be able to absorb the dietary nutrients and reabsorb the water and other valuable chemical resources used to accomplish the first three requirements. This lecture will provide you with an overview of the structural and functional elements involved in each of the above processes. In the remainder of the course, you will have an opportunity to study each of these processes in more detail, and to learn the clinical and pathological implications of the breakdowns in structure or function.

Structure of the Gastrointestinal Tract

Although there are many site-specific exceptions to the rule, the wall of the gastrointestinal tract is composed of four basic layers: mucosa, submucosa, muscularis propria, and serosa. The mucosa is in turn divided into the epithelium, the basement membrane, the lamina propria, and the muscularis mucosae. The detailed microscopic anatomy of the gastrointestinal tract varies from site to site, and the above simple scheme can become highly complex by the addition of the supportive structures such as nerves, vessels, submucosal glands, and the mucosa-associated lymphoid tissue (Figure 1). You will be introduced to the basic histology of the major sites in the subsequent pathology lectures and laboratory sessions.

Figure 1. Schematic drawing of the general organization of the gastrointestinal tract (from Bloom and Fawecett, Histology, Chapman & Hall, 1994).

Gastrointestinal Motility

Motility refers to the active processes by which a bolus of food is mechanically manipulated in the gastrointestinal tract. Motility propels the food forward, grinds the food into smaller pieces, and mixes the food and other luminal contents for more efficient processing. The effector tissue for almost all of the motility functions is the muscularis propria, which is primarily composed of unitary smooth muscle. Contraction of the inner circular muscular layer results in narrowing of the lumen, while contraction of the outer longitudinal muscular layer results in local shortening of a longitudinal segment. Through coordinated ***periodic phasic contractions*** of the inner and outer muscular layers, gastrointestinal contents are propelled forward, ground, and mixed. At the same time, ***local tonic contractions*** maintain a constant tone (or pressure) at the specific ***sphincter*** zones, thus providing check-points for controlled flow of the luminal contents.

Table 2. Gastrointestinal Neurocrine Peptides

Peptide	Actions
Acetylcholine (ACh)	• Smooth muscle contraction • Sphincter relaxation • Increased salivary, gastric, and pancreatic secretions
Norepinephrine (NE)	• Smooth muscle relaxation • Sphincter contraction • Increased salivary secretion
Vasoactive Intestinal Peptide (VIP)	• Smooth muscle relaxation • Increased intestinal and pancreatic secretions
Gastrin-Releasing Peptide (GRP, Bombesin)	• Increased gastrin secretion
Enkephalins	• Smooth muscle contraction • Decreased intestinal secretions
Substance P	• Smooth muscle contraction • Increased salivary secretions
Neuropeptide Y	• Smooth muscle relaxation • Decreased intestinal secretions

Secretion

Throughout the gastrointestinal tract, fluids, proteins, mucus and mucopolysacchardies are ***secreted*** into the lumen. The major organs of secretion are the salivary glands, stomach, pancreas, and the liver.

Saliva is secreted by the salivary glands at a rate of approximately 1-1.5 liter/day, and its primary role is dilution and lubrication of the food particles, as well as the initial digestion of lipids and carbohydrates. Saliva is produced by the three major salivary glands (parotids, submaxillary, and sublingual), as well as numerous minor salivary glands. The parotid glands are compose entirely of serous cells, while the other two major salivary glands are composed of a mixture of serous and mucous cells. Saliva contains water, electrolytes, proteins, and mucus, and is produced by a two-step process in the salivary acinar units. The ***acinar*** cells secrete an isotonic solution which is similar to plasma in its electrolyte composition. The ***ductal*** cells modify this solution by actively reabsorbing sodium and chloride in exchange for potassium and bicarbonate. Because of the relative water impermeability of the ductal epithelium, the net result of this two-step process is the production of a hypotonic solution rich is potassium and bicarbonate. The acinar cells also secrete the organic components of the saliva: ***lingual lipase*** and ***α-amylase*** are involved in the initial digestions of lipids and carbohydrates, respectively; ***kallikrein*** is an enzyme involved in the production of bradykinin; ***mucus*** acts as a lubricant; and ***secretory IgA*** is a component of the mucosal immune system. Salivary secretions are stimulated by parasympathetic stimuli which interact with muscurinic receptors and lead to the production of IP_3, and to a lesser extent by sympathetic stimuli which interact with the adrenergic receptors and lead to the activation of the adenylyl cyclase.

Carbohydrates

Dietary carbohydrates consist of both digestible and indigestible components. Indigestible carbohydrates primarily consist of cellulose from vegetable materials, and are the major constituents of dietary fiber. Digestible carbohydrates are the major source of caloric intake, and consist of complex polysaccharides (starch) and simple sugars (sucrose, fructose, and lactose). The enterocytes will only absorb single sugar molecules (such as glucose, fructose, and galactose), and more complex di- and polysaccharides must be *digested* into single sugar molecules before absorption. Digestion of disacchardies (sucrose and lactose) into single sugar molecules is simply mediated by microvillar disaccharidases (sucrase and lactase). Digestion of complex carbohydrates begins with the action of salivary and pancreatic α-amylase, and is completed by the action of microvillar brush border enzymes maltase and α-dextrinase (Figure 2). Mechanisms involved in the active transport of single sugar molecules into the enterocytes are discussed in detail in future lectures.

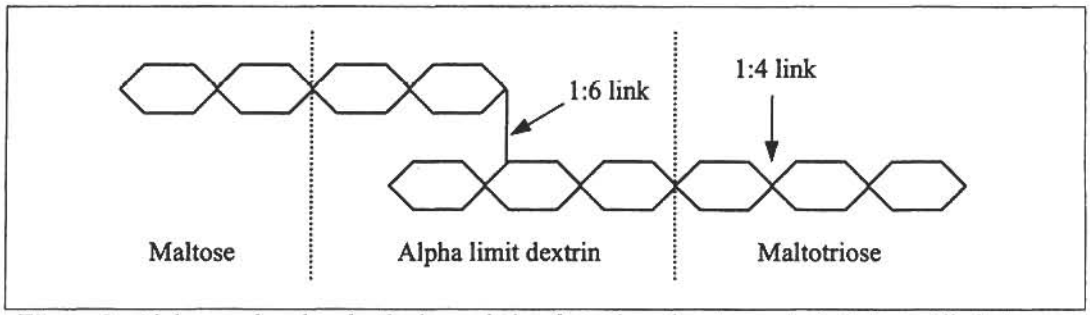

Figure 2. Alpha-amylase breaks the long-chain of starch molecules at the 1:4 glucosidic linkages, except at either end of the chain, thereby digesting starch into maltose and maltotriose molecules. Alpha-amylase cannot break the 1:6 glucosidic linkages either, resulting in the production of alpha-limit dextrins from the side chains (adapted from Jacobson and Levine, Clinical GI Physiology, W.B. Saunders, 1994).

Proteins

Proteins can be a source of caloric intake, but they are essential to compensate for the constant protein breakdown in muscles and for proteins lost in the gastrointestinal tract in the form of sloughed cells and secretory products. Similar to complex carbohydrates, digestion of proteins also occurs in two stages (luminal and microvillar). Luminal endopeptidases in the stomach (pepsin) and small intestine (trypsin) cleave internal peptide bonds, while carboxypeptidases cleave the C-terminal amino acids from polypeptides. Collectively, these enzymes digest the ingested proteins into dipeptides and tripeptides. Some dipeptides and tripeptides are absorbed as such, while most are broken down into single amino acids by the action microvillar dipeptidases. Intestinal absorption of amino acids is discussed in detail in subsequent lectures.

Lipids

Digestion of lipids begins in the stomach with the action of gastric lipases, and is completed in the small intestine by the addition of pancreatic enzymes (pancreatic lipase, cholesterol esterase, and phospholipase A_2). The major obstacle in the digestion of lipids is that while the digestive enzymes are water soluble proteins, the substrate lipids are not soluble in water. Dietary lipids must therefore be emulsified and then solubilized by the biliary detergents before they can be broken down by the lipases. The breakdown products of lipids must also be packaged in mixed micelles for delivery to the microvillar surface of enterocytes. The micelles are decomposed in the unstirred layer adjacent to the apical membrane of the enterocytes. Fatty acids, monoglycerides, cholesterol, and lysolecithin diffuse into the enterocytes, while bile acids are returned to the lumen. (Fat soluble vitamins A, D, E, and K are also delivered to enterocytes by incorporation into these micelles.) Free bile acids are eventually captured by receptors in the distal small intestine, actively