Nutrition and Human Metabolism Q&A

1. What major digestive enzyme is secreted in the saliva?
   The main enzyme in saliva is salivary amylase, which hydrolyzes α 1-4 bonds in starch. Salivary amylase has some but not much effect because of the short time of food in the mouth; lingual lipase (infants digest buttermilk).

2. What cells secrete pepsinogen and where are these cells located?
   Chief (peptic or zymogenic) cells, located in the oxyntic glands found in the body of the stomach.

3. What cells secrete HCl and where are these cells located?
   Parietal (oxyntic) cells, located in the oxyntic glands found in the body of the stomach.

4. What stimulates the release of gastrin?
   Gastrin release occurs in response to vagal stimulation, ingestion of specific substances or nutrients, gastric distention, hydrochloric acid in contact with gastric mucosa, as well as local and circulating hormones (i.e., ingested foods, hormones, and neurotransmitters). Foods such as coffee and alcohol, as well as nutrients such as calcium, amino acids, and peptides, present in the GI tract lumen stimulate gastrin release. Epinephrine in the blood and gastrin-releasing peptide, released by some nerves, also stimulate gastrin release.

5. What are the SPECIFIC functions of gastrin?
   Gastrin stimulates the release of hydrochloric acid, but it also stimulates gastric and intestinal motility and pepsinogen release. Gastrin stimulates the cellular growth of (has trophic action on) the stomach, and both small and large intestine.

6. Is there some sort of feedback mechanism that controls how much gastrin is secreted?
   Yes, when the lumen pH gets too acidic, a feedback mechanism reduces acid secretion by inhibiting gastrin release. Somatostatin inhibits gastrin release from the G-cells (as well as inhibiting HCL secretion
   at the parietal cell.)

7. Name an enzyme that digests protein in the stomach.
   Pepsin is the principal proteolytic enzyme in the stomach.

8. Name an enzyme that digests lipids in the stomach.
   Lingual lipase, produced by lingual serous glands in the mouth, hydrolyzes dietary triacylglycerols in the stomach and small intestine.

9. What word ending is associated with enzymes?
   -ase

10. Is there major digestion of carbohydrate in the stomach?
    No. In the mouth, the enzyme salivary amylase (ptylin), which operates at a neutral or slightly alkaline pH, starts the digestive action on starch, hydrolyzing it into smaller molecules. The activity of amylase is halted by contact with

hydrochloric acid. If the digestible carbohydrate were to remain in the stomach long enough, the acid hydrolysis would eventually reduce much of it to the monosaccharides. However, the stomach usually empties itself before significant digestion can take place, and carbohydrate digestion occurs almost entirely in the proximal small intestine.

11. What regulates how much "food" passes into the small intestine?

    Approximately 1 to 5 ml (< 1 tsp.) of chyme enters the duodenum about twice per minute. Contraction of the pylorus and proximal duodenum is thought to be coordinated with contraction of the antrum. Gastric emptying is also partially affected by the macronutrient composition of the food. Carbohydrate and protein appear to empty at approximately the same rate from the stomach; fat, however, slows gastric emptying into the duodenum. Salts and monosaccharides inhibit gastric emptying, as do many free amino acids like tryptophan and phenylalanine. Complex carbohydrates, especially soluble fiber, decrease (slow down) the rate of gastric emptying. Neural gastrointestinal reflexes, along with the release of regulatory peptides such as secretin by the duodenal bulb, also influence gastric emptying, which following a meal usually takes between 2 and 6 hours.

12. What causes the release of cholecystokinin (CCK)?

    CCK is released in response to the presence of lipids (fat) in chyme.

13. What does CCK do?

    CCK stimulates secretion of pancreatic juices and enzymes in response to fat. It causes contraction of the gallbladder (i.e., causes the gallbladder to squirt bile into the small intestine) and slows stomach emptying.

14. What causes the release of secretin?

    Secretin is secreted into the blood by S-cells of the proximal small intestine in response to the release of acid chyme into the duodenum. (Secretin's major action is to increase the pH of the small intestine by stimulating secretion of water and bicarbonate (pancreatic juice) by the pancreas. It also inhibits gastric acid secretion and gastric emptying.)

15. Where do pancreatic secretions enter the intestine?

    Pancreatic secretions (fluid, electrolytes, bicarbonate, and enzymes) are released into the duodenum.

16. Pancreatic secretions contain two distinctly different types of material. What are they?

    1. Enzymes: are responsible for the digestion of approximately half of all ingested carbohydrates, half of all proteins, and almost all of ingested fat.
    2. Bicarbonate: in pancreatic juice released into the duodenum is important for neutralizing the acid chyme passing into the duodenum from the stomach and for maximizing enzyme activity within the duodenum.

17. Where does bile enter the intestine?

    Bile flows into the duodenum from the gallbladder.

18. Describe the pH differences as "food" passes from the mouth to the stomach to

the small intestine.

The pH of saliva in the mouth is about 7. Gastric juices lower the pH to 2 in the stomach. Secretin increases intestinal pH by releasing bicarbonate. Intestinal juice, pancreatic juice, and bile are pH 8.

19. Give an example of a "brush border" enzyme.

Isomaltase (active against α 1-6 bonds).
Aminopeptidases, tripeptidases, dipeptidases.

20. How does surface area affect digestion? Think of a food example that illustrates your point.

The anatomic advantage of the villi-microvilli structure is that it presents an enormous surface area to the intestinal contents, thereby facilitating absorption. It has been estimated that the absorptive capacity of the human intestine amounts to about 5,400 g/day for glucose and 4,800 g/day for fructose -- a capability that would never be challenged in a normal diet.

21. Give an example of how a neural stimulus can affect digestion.

The nervous system of the gastrointestinal tract, the enteric system, provides neural regulation of the gastrointestinal tract by a combination of neural plexuses and reflexes. The myenteric plexus controls peristaltic activity and/or gastrointestinal motility. It is innervated by parasympathetic and sympathetic nervous systems, and it greatly influences gastrointestinal motility. The submucosal plexus controls mainly gastrointestinal secretions and local blood flow. Gastrin release is stimulated, in part, by vagal stimulation (neurotransmitters). Epinephrine in the blood also stimulates gastrin release. Also, simply the thought, sight, or smell of food can make the mouth "water", or release saliva, in anticipation of food.

22. What nutrients is an infant well prepared to digest?

Lingual lipase, which hydrolyzes dietary triacylglycerols in the stomach and small intestine, is mostly of importance to infants. They are well prepared to digest milk, especially breast milk.

23. Why is salivary amylase relatively inactive in the stomach?

The high concentration of hydrochloric acid in the gastric juice results in its low pH, about 2, which inactivates salivary amylase.

24. What is another source of amylase?

The pancreas secretes pancreatic α amylase.

25. What effect does physical processing have on digestion? Why?

The pacemaker, located between the fundus and body of the stomach, determines the frequency of the contractions that occur. As the food moves into the antrum, the rate of contractions increases so that in the distal portion of the stomach, food is liquefied into chyme. The migrating motility complex functions to sweep gastrointestinal contents and prevent bacterial overgrowth in the intestine. Contractions within the stomach promote physical disintegration of solid foods into a liquid form. Chyme, in the small intestine, is mixed and moved through the small intestine by various contractions under nervous system influence. Sleeve

contractions (longitudinal) mix the intestinal contents with the digestive juices. Standing contractions (segmentation) of circular muscles, produces bidirectional flow of the intestinal contents, and serves to mix and churn the chyme with digestive secretions in the small intestine. Peristaltic waves, or progressive contractions, move the chyme distally along the intestinal mucosa toward the ileocecal valve.

26. Where does digestion of protein begin? What are the sources of enzymes that digest protein?

    Digestion of protein begins in the stomach, where pepsin functions as a protease -- that is, an enzyme that hydrolyzes proteins. Hydrochloric acid converts or activates the zymogen pepsinogen to form pepsin. Most protein digestion takes place in the deuodenum, however. The pancreatic proteolytic enzymes pancreatic trypsin, chymotrypsin, and carboxypolypeptidase break down intact protein and continue the breakdown started in the stomach until small polypeptides and amino acids are formed. Proteolytic peptidases located on the brush border also act on polypeptides, changing them to amino acids, dipeptides, and tripeptides. The final phase of protein digestion takes place in the brush border, where dipeptides and tripeptides are hydrolyzed to their constituent amino acids by peptide hydrolases.

27. How is the acid chyme neutralized in the small intestine? What are the effects if the chyme is not effectively neutralized?

    Chyme, moving from the stomach into the duodenum, initially has a pH of about 2 because of its gastric acid content. Chyme is neutralized in the duodenum by secretions from the pancreas and Brunner's glands. If the chyme is not effectively neutralized, the duodenum is not protected from the gastric acidity.

28. Where does digestion of most lipid begin? What enzyme is responsible?

    Enzymes necessary for lipid digestion are produced by the pancreas and secreted into the small intestine. Pancreatic lipase, the major fat-digesting enzyme, hydrolyzes triacylglycerols.

29. Name two substances absorbed from the stomach.

    Water, some fat-soluble drugs (aspirin), and alcohol.

30. Where are enterocytes found?

    The villi of the small intestine are fingerlike projections lined by hundreds of cells (enterocytes, also called absorptive epithelial cells).

31. How frequently are cells in the small intestine renewed (replaced)?

    Intestinal cell turnover is rapid, approximately every 3 to 5 days.

32. Where in the gastrointestinal tract are most nutrients absorbed?

    Most in duodenum and jejunum.

33. If disease or drugs increase intestinal motility, what is the potential effect on absorption?

    Digestion and absorption of nutrients within the small intestine are rapid, with most of the carbohydrate, protein, and fat being absorbed within 30 minutes after chyme has reached the small intestine. About 90-95% of the water and sodium

entering the colon each day is absorbed. Increased intestinal motility could adversely impact the ability of the intestinal tract to adequately perform its job of absorbing nutrients and water.

34. What is recirculation of compounds such as bile salts between the small intestine and the liver called?

The circulation of bile is termed entero-hepatic circulation. The pool of bile is thought to recycle at least twice per meal.

35. Where are bile salts secreted into the intestine? Where are they reabsorbed? Where are they excreted?

Bile flow into the duodenum is regulated by the intraduodenal segment of the common hepatic bile duct and the sphincter of Oddi, located at the junction of the common hepatic bile duct and the duodenum. More than 90% ofthe bile acids and salts secreted into the duodenum are reabsorbed by active transport in the ileum. Small amounts of the bile may be passively reabsorbed in the jejunum and the colon. Bile that is absorbed in the ileum enters the portal vein and is transported attached to plasma protein albumin in the blood back to the liver. New bile acids are typically synthesized in amounts about equal to those that are lost (excreted) in the feces.

36. What type of nutrients pass into the portal blood?

Carbohydrates (the monosaccharides: glucose, galactose, and fructose) pass through the mucosal cell and, via the capillary of the villus, into the bloodstream, where they are carried by the portal vein to the liver. Protein (peptides and amino acids) are transported to the liver via the portal vein for release into the general circulation.

37. What type of nutrients pass into lacteals for transport by the lymphatic system?

Lacteals are intestinal lymph carrying vessels, arising from the villi, that convey chyle (lymph and emulsified fat or free fatty acids) to the thoracic duct.

38. What difference does the route of absorption make in the destination of nutrients or drugs?

Fat soluble vitamins (A, D, E, K), fat, and cholesterol are carried by lacteals in the lymphatic system and enter the bloodstream at a slow rate. Entry of chylomicrons into the blood from the lymph continues for up to 14 hours after consumption of a meal rich in fat.

39. What are the principle nutrients absorbed in the large intestine?

The proximal colonic epithelia absorb sodium, chloride, and water.

40. What effect does fiber in the ileum have on enterohepatic recirculation?

Bile acids bound to fiber cannot be reabsorbed and recirculated. Fiber-bound bile acids are typically sent into the large intestine for either fecal excretion or colonic microflora degradation.

41. The immediate risk of severe diarrhea is loss of which nutrients?

Excessive loss of fluid and electrolytes, especially sodium and potassium.

42. How much energy is provided by a gram of carbohydrate?
    4 kcal/g.

43. What % of energy is provided by carbohydrate in the usual American diet?
    48%

44. Is free glucose commonly found in food?
    No. There's almost no free glucose. There is some free glucose and fructose in honey, certain fruits, and the carbohydrates added to processed foods.

45. What tissues depend on glucose for fuel?
    The brain and other tissues of the Central Nervous System, and Red Blood Cells are particularly dependent on glucose as a nutrient.

46. What word ending designates a carbohydrate?
    -ose,

47. What is the storage form of carbohydrate in plants?
    Starch, the energy storage product of the cell, is found within the cell walls.

48. What is the storage form of carbohydrate in animals?
    The major form of stored carbohydrate in animal tissues is glycogen, which is localized primarily in liver and skeletal muscle.

49. Is meat a good source of glycogen? Why or why not?
    No. Slaughtered animals have no glycogen by the time the meat is packaged.

50. What are the components of each of the common dietary disaccharides?
    Sucrose: glucose + fructose
    Lactose: glucose + galactose
    Maltose: glucose + glucose

51. Into what compound in the body is 2-deoxy-D-ribose incorporated?
    Deoxyribonucleic acid (DNA).

52. Where is lactose synthesized? Where is it digested?
    Lactose is made almost exclusively in the mammary glands. The β linkage in lactose is hydrolyzed by lactase in the intestinal cell.

53. What are the public health implications of an inability to digest lactose?
    Lactose intolerance eliminates the whole dairy food group as a possible nutrient source. Lactose intolerance increases with age and its distribution varies with ethnic background. It is low in Caucasions and high in Native Americans, Asians, and Black populations.

54. How are the symptoms of lactase deficiency related to osmotic pressure and to the actions of colonic bacteria?
    Lactose that is not hydrolyzed into galactose and glucose remains in the gut and acts osmotically to draw water into the intestines. Colonic bacteria ferment the undigested lactose, generating short-chain fatty acids, carbon dioxide, and

hydrogen gas. Consumption of quantities greater than 12 g (the amount typically found in 240 mL of milk) may result in bloating, flatulence, cramps, and diarrhea.

55. In the "usual U.S. diet", how much of the digestible carbohydrate is starch and how much is sucrose?

Roughly half of dietary carbohydrate is in the form of polysaccharides such as starches and dextrins, derived largely from cereal grains and vegetables. The remaining half is supplied as simple sugars, the most important of which include sucrose, lactose, and, to a lesser extent, maltose, glucose, and fructose. Sucrose, consisting of a glucose and a fructose residue, furnishes approximately one-third of total dietary carbohydrate in an average diet.

56. How many grams of carbohydrate in the "usual U.S. diet"?

48% of 2000 kcal = 960 kcal from carbohydrate.
960 kcal / 4 kcal/g = 240 g. of carbohydrate in the "usual U.S. diet".

57. Which carbohydrate is sweeter? Sucrose or fructose?

Fructose is the sweetest of the sugars.

58. Are amino acids transported via the portal blood or the lymphatic system?

Amino acids are transported across the cell membrane into the surrounding fluid where they enter the capillaries on their way to the liver.

59. What lipids make up the cell membrane?

Membrane lipids consist primarily of phospholipids. Phosphoglycerides and phosphingolipids (phosphate-containing sphingolipids) comprise most of the membrane phospholipids. Of the phosphoglycerides, phosphatidylcholine and phosphatidylethanolamine are particularly abundant in higher animals. Another important membrane lipid is cholesterol.

60. What effects does lack of bile acids have on lipid digestion and absorption?

Bile salts are necessary to decrease the surface tension of the fat, thus permitting emulsification of the fat and enabling digestion (hydrolysis) of the triacylglycerol molecules to occur by pancreatic and intestinal lipases. Once hydrolyzed, bile acids and salts help in the absorption of these end products of lipid digestion. Bile acids and salts, along with phospholipids, help in the absorption of lipids by forming small, spherical, cylindrical, or disklike shaped complexes called micelles that permit solubility in the watery digestive fluids and transportation to the intestinal brush border for absorption. Without bile acids, digestion and absorption of lipids (fat) would not be possible.

61. Are bile acids still secreted if the gall bladder is removed?

Bile acids are still secreted, but cannot be stored and released in response to the presence of fat. Rather, the bile drips continuously into the duodenum.

62. What is a micelle?

A micelle is a small (<10 mm) spherical, cylindrical, or disklike shaped complex that can contain as many as 40 bile salt molecules. The hydrophobic steroid portion of bile salts and acids, which is mostly fat soluble, position themselves together and surround the monoacylglycerols and fatty acids that formed

following the action of lipases. Polar portions of the bile salts, bile acids, and phospholipids project outward from the lipid core of the micelle, thus permitting solubility in the watery digestive fluids and transportation to the intestinal brush border for absorption.

63. What effect does chain length of a fatty acid have on the route of absorption?
Some substances such as water and small lipid molecules cross membranes freely by diffusion. Other compounds cannot cross cell membranes without a specific carrier, such as in facilitated diffusion and active transport. Some large molecules are moved into the cell via pinocytosis, engulfment by the cell membrane.

64. What are the principle components of the plasma membrane?
Membrane lipids
- phospholipids
- cholesterol
- hydrophobic)
Membrane proteins -- pumps, receptors and enzymes
Protects cellular components
Allows exposure to the environment
Contains some carbohydrate

Membranes are sheetlike structures composed primarily of lipids and proteins held together by noncovalent interactions. Membrane lipids consist primarily of phospholipids, which have both a hydrophobic and hydrophilic moiety. In water, they form lipid bilayers which retard the passage of many water-soluble compounds into and out of the cell. Membrane proteins serve as pumps, gates, receptors, energy transducers, and enzymes. The plasma membrane has a greater carbohydrate content owing to the presence of glycolipids and glycoproteins. The plasma membrane has a higher content of cholesterol which enhances the mechanical stability of the membrane and regulates its fluidity.

65. What are the key metabolic pathways in the cytoplasmic matrix?
Glycolysis
Pentose phosphate pathway
Glycogenesis
Glycogenolysis
Fatty acid synthesis
Production of nonessential, unsaturated fatty acids

66. What are the key metabolic reactions that occur in mitochondria?
Oxidative phosphorylation - production of most of ATP (via electron transport chain).
Electron transport chain is exothermic.
Release energy from food/couple to form ATP.
Includes Krebs cycle and fatty acid oxidation.
All cells except RBC have mitochondria.

67. What organ secretes the majority of the digestive enzymes?
The pancreas is the major source of most digestive enzymes. Enzymes from the pancreas digest 50% of all carbohydrates - alpha-amylase, 50% of all proteins -

proteases, and 90% of all fat - pancreatic lipase. Endocrine secretions include insulin and glucagon. It also secretes bicarbonate.

68. Where is the pyloric sphincter and what is its role?

The pyloric sphincter at the distal end of the stomach controls the release of chyme (partially digested food existing as a thick semiliquid mucky mass) from the stomach into the duodenum.

69. Is the net energy transformation for the Kreb's cycle endothermic or exothermic? What does this mean?

The net energy transformation for the Kreb's cycle is exothermic. That means it is energy releasing. The high energy output of the Krebs cycle is attributed to mitochondrial electron transport, with oxidative phosphorylation being the source of ATP formation.

70. What is oxidative phosphorylation? What is produced?

A process by which a molecule of inorganic phosphate is condensed with ADP to form ATP.
Oxidation of fuel molecules utilizes O_2.
Energy yield can be measured by oxygen consumption.

71. Approximately what % of energy from food is trapped as ATP?

We're about 40% efficient in converting food to ATP. The other 60% goes to maintaining body heat.

72. What hormones regulate the circulating level of carbohydrate in the blood? What is the name of the primary circulating carbohydrate?

Insulin and glucagon. Glucose.

73. When in relation to meals does glycogenesis occur?

When you just ate. An increase in glucose leads to the synthesis of glycogen (glycogenesis) for storage of the extra glucose.

74. When would glycogenolysis occur?

When you haven't just eaten. A decrease in blood glucose is a stimulus to glycogenolysis.

75. Where in the cell is most of the energy produced?

The mitochondria are responsible for most of the metabolic energy produced in cells.

76. What are the end products of the Kreb's cycle and how are they utilized/removed by the body?

Over 90% of energy released from food occurs here.
Oxidative phosphorylation.
Pyruvate transferred to mitochondria -- yields acetyl CoA and Co2 (released by Exhalation).
Acetyl CoA - from fatty acids, glucose, amino acids.

The oxidation of 1 mol of acetyl CoA in the Krebs cycle yields a total of 12 ATPs. 12 ATPs x 2 mol of acetyl CoA per mole of glucose = 24 ATPs. Plus 6 ATPs from intramitochondrial ppyruvate dehydrogenase reaction = 38 ATPs..

77. What does gluconeogenesis mean?

Glucose synthesis from noncarbohydrate sources. (i.e., generation of new glucose.)

78. What is a normal fasting serum glucose level?

70-105 mg/dL fasting..

79. What is glycogen loading?

Consuming carbohydrates over a period of several days prior to an athletic event in an attempt to store up glycogen which is a limiting factor for exercise at intensities requiring 70-85% VO_{2max}.

80. What effect does dietary fiber have on water in the stool? What effect does this have on constipation?

The gastrointestinal effects of the ingestion of fibers that can hold water and create viscous solutions within the GI tract include:

delayed (slowed) emptying of food from the stomach,
reduced mixing of gastrointestinal contents with digestive enzymes,
reduced enzyme function,
ecreased nutrient diffusion rate and thus delayed nutrient absorption, and
altered small intestine transit time.

Fibers that are nonfermentable, especially cellulose and lignin, and fibers that are more slowly fermentable, such as some hemicelluloses, have been shown to be helpful in overcoming constipation, particularly constipation associated with symptomatic diverticular disease and/or irritable bowel syndrome.

81. What effect do free sugars have on stool water?

Free sugars would alter osmolarity, leading to a high osmotic pressure and an influx of water into the cells from the surroundings (the stool water).

82. Name some specific chemical compounds produced by carbohydrate fermentation in the colon.

The principal metabolites of fermentable fibers (including any starch that has passed into the cecum and been degraded by bacteria) are lactate and short-chain fatty acids (SCFAs). The short chain fatty acids include primarily acetic, butyric, and propionic acids. Other products of fiber fermentation are hydrogen, carbon dioxide, and methane gases that are excreted as flatus or are expired by the lungs.

83. What difference does it make if glucose is joined by alpha-1-4 linkages or beta-1-4 linkages?

The key enzyme in the digestion of dietary polysaccharides is α-amylase, a glycosidase that specifically hydrolyzes α-1,4 glycosidic linkages. Resistant to the action of the enzyme, therefore, are the β-1,4 bonds of cellulose.

84. Give an example of a digestible polysaccharide and of a non-digestible polysaccharide?

Starch is a digestible polysaccharide.

Cellulose and lignin are indigestible polysaccharides.

85. What causes the sensation of "heartburn"?

On swallowing, the LES pressure drops. This drop in LES pressure relaxes the sphincter so that food may pass from the esophagus into the stomach. Closure of the LES sphincter is important because it prevents gastroesophageal reflux, the movement of chyme from the stomach back into the esophagus. The gastric acid in the chyme when present in the esophagus is an irritant to the esophageal mucosa. The individual experiencing reflux feels a burning sensation in the midchest region, a condition referred to as heartburn.

86. Think about nutrients in a meal. For each of these, where would most digestion and absorption occur?

Nutrient	Digestion	Absorption
Protein	Stomach, Small Intestine	Small Intestine
Carbohydrate	Small Intestine	Small Intestine
Lipid	Small Intestine	Small Intestine

87. What types of foods provide fiber?

Dietary fiber is derived from plant cells. The consumption of plant foods provides fiber in the diet. Cereal bran such as wheat bran provides primarily hemicellulose as well as lignin. Psyllium provides primarily mucilages but also some nonpolysaccharides. Consumption of fruits and vegetables provides almost equal quantities of cellulose and pectin.

88. What makes a carbohydrate "a fiber" for humans?

Probably the most widely accepted definition for dietary fiber is "plant polysaccharides and lignin which are resistant to hydrolysis by the digestive enzymes of man."

89. What are the health benefits of insoluble fiber?

Insoluble fibers decrease (speed up) intestinal transit time and increase fecal bulk. A shortened fecal transit time decreases the time during which toxins can be synthesized and in which they are in contact with the colon. Insoluble fibers such as lignin that resist degradation bind carcinogens, thereby minimizing the chances of interactions with colonic mucosal cells.

90. What are the health benefits of soluble (viscous) fiber?

Generally, soluble fibers delay gastric emptying, increase transit time (slower movement) through the intestine. This effect creates a feeling of postprandial (after eating) satiety (fullness) as well as slows down the digestion process. Wheat bran is one of the most effective fiber laxatives because it can absorb three times its weight of water, thereby producing a bulky stool. Fibers that increase fecal bulk decrease the intraluminal concentrations of carcinogens and thereby reduce the likelihood of interactions with colonic mucosal cells.

91. What are the effects of fiber on stomach emptying? What type of fiber is involved?

When fibers form viscous gels or hydrate within the stomach (i.e. soluble fiber), the release of the chyme from the stomach into the duodenum (proximal small intestine) is delayed (slowed). Thus, nutrients remain in the stomach longer with

these fibers than would occur in the absence of the ingested fiber. This effect creates a feeling of postprandial (after eating) satiety (fullness) as well as slows doen the digestion process, because carbohydrates and lipids that remain in the stomach undergo no digestion in the stomach and must move into the small intestine for further digestion to occur.

92. What are the effects of fiber on fermentation in the colon? What types of products are produced from fermentation in the colon?

Many of the microflora in the large intestine are capable of degrading (fermenting) fiber, especially pectins, gums, mucilages, and algal polysaccharides. The principal metabolites of fermentable fibers are lactate and short-chain fatty acids (SCFAs). The short chain fatty acids include primarily acetic, butyric and propionic acids, as well as hydrogen, carbon dioxide, and methane gases that are excreted as flatus or are expired by the lungs. Some general effects of short-chain fatty acids generated from fiber fermentation by intestinal microbes include increased water and sodium absorption in the colon, mucosal cell proliferation, provision of energy, and acidification of luminal environment.

93. Why does fiber have an effect on satiety?

Nutrients remain in the stomach longer due to delayed gastric emptying; this effect creates a feeling of postprandial satiety.

94. What are fiber effects on absorption of nutrients? Give an example where this is beneficial and an example where it is detrimental.

Generally, soluble fibers delay gastric emptying, increase transit time through the intestine, and decrease nutrient (e.g., glucose) absorption. This could be of benefit to someone with diabetes mellitus. In contrast, insoluble fibers decrease intestinal transit time and increase fecal bulk. Soluble fibers may affect lipid absorption by adsorbing fatty acids, cholesterol, and/or bile acids within the digestive tract. Thus fiber-bound lipids (i.e. cholesterol) are not absorbed in the small intestine and pass into the large intestine where they will be excreted in the feces or degraded by intestinal bacteria. Adsorption of bile acids to fibers prevents the use of the bile acids for micelle formation. Bile acids bound to fiber cannot be reabsorbed and recirculated.

95. What are ways that fiber can have an effect on serum cholesterol?

Soluble fibers may affect lipid absorption by adsorbing fatty acids, cholesterol, and/or bile acids within the digestive tract. Thus fiber-bound lipids (i.e. cholesterol) are not absorbed in the small intestine and pass into the large intestine where they will be excreted in the feces or degraded by intestinal bacteria.

96. What types of fiber are most protective against colon cancer? Why?

Insoluble fibers such as lignin that resist degradation bind carcinogens, thereby minimizing the chances of interactions with colonic mucossl cells.

97. What would be a recommendation for fiber intake for an adult consuming foods providing 2000 kcal/day?

The recommended intake of fiber for the general population ranges from 20 to 40 g/day. Another recommendation is 10 to 13 g dietary fiber intake per 1000 kcal. So, for a 2000 kcal/day diet, that would be 20 to 26 g/day.

98. What are the indispensable (essential) amino acids?

PVT TIM HALL
Phenylananine
Valine
Tryptophan

Threonine
Isoleucine
Methionine

Histidine
(Arginine)
Leucine
Lysine

99. Where does protein digestion begin? What initiates digestion?

Protein digestion begins in the stomach. There is no protein digestion in the mouth and esophagus. Protein digestion is initiated by the release of HCL, stimulated by gastrin, GRP (glucokinase regulatory protein), acetylcholine, and histamine.

100. What are enzymes involved in digestion of protein?

Gastrin, GRP, acetylcholine, and histamine, pepsin, pepsinogen, secretin, CCK, bicarbonate, trypsinogen, chymotripssinogen, collage-nase, proelastase, procarboxypeptiases, trypsin, additional peptidases.

101. What are the sources of the enzymes that digestion protein?

The release of HCL is stimulated by gastrin, GRP, acetylcholine, and histamine, and denatures 4º, 3º, and 2º structure. Pepsin is activated by pepsinogen and yields large polypeptides by breaking long protein chains. Acid chyme in the intestine lowers the pH and stimulates secretin and CCK. The pancreas secretes bicarbonate. Digestive enzymes from the pancreas include trypsinogen, chymotripssinogen, collage-nase, proelastase, procarboxypeptiases. Trypsin is formed and activates others. Additional peptidases in brush border.

102. Where are most amino acids absorbed?

Most a.a. absorption is in the proximal small intestine (first few feet).

103. What is the RDA for protein? Calculate the protein recommendation for someone weighing 154 lbs.

The RDA for protein for adults is 0.8 g/kg of body weight.
154 lbs. / 2.2 kg/lb = 70 kg. 70 kg x 0.8 g/kg = 56 g. protein required/day.

104. When amino acids are degraded, what compound is formed in the largest amounts from the amino group?

Ammonia is formed in the body from chemical reactions such as deamination.

The urea cycle, in the liver, is the body's way of removing ammonia.

105. What are four possible fates of the carbon skeleton from amino acids?

Once an amino group has been removed from an amino acid, the remaining molecule is referred to as a carbon skeleton or α-keto acid. Carbon skeletons of amino acids can be further metabolized with the potential for multiple uses in the cell. An amino acid's carbon skeleton, for example, can be used for the production of

1. Energy — Energy, CO_2, NH_4^+ and H_2O
2. Glucose — Conversion of a.a. to glucose increased by high glucagon: insulin & cortisol
3. Ketone bodies
4. Cholesterol — Leucine generates HMG CoA; others generate acetyl CoA
5. Fatty acids

106. What is 3-methylhistidine? Why would it be measured?

3-Methlyhistidine is an index of protein degradation for tissues in the body. It's an indicator of muscle mass/catabolism.

107. What does a "post-translational" modification mean?

Translation is the process by which genetic information in an mRNA molecule specifies the sequence of amino acids in the protein product. The completed protein dissociates from the mRNA in active form, although some post-translational, chemical modification of the protein is often necessary.

108. Approximately what % of basal energy need is associated with protein turnover?

Protein turnover accounts for 10-25% of resting energy expenditure.

Amino Acid Metabolism?

~ 20% for protein/N compound synthesis (14% remains in liver for protein synthesis, 6% plasma proteins - synthesized in liver and secreted into bloodstream)

~ 57% catabolized in liver (assuming adequate a.a. intake).

~ 23% released to systemic circulation -- primarily branched a.a.

109. What are two tissues that have a very high protein turnover rate? What are two tissues that have low turnover rates?

Rapid turnover: plasma protein, visceral protein

Low turnover: muscle protein, bone? nerves?

110. How can a habitually high intake of amino acids affect the mRNA for enzymes that catabolize amino acids?

Protein synthesis is affected by the amount of mRNA, ribosomes, availability of a.a for tRNA and hormonal environment. Amino acid oxidation increases if a.a are in surplus or if an essential a.a is missing. Therefore, a habitually high intake of a.a would induce the production of more enzymes to catabolize a.a.

111. What are some conditions that increase proteolysis of muscle tissue? Why does each cause these increases?

- • Counterregulatory hormones, glucagon, catecholamines, and glucocorticoids promote protein degradation and a negative nitrogen balance.
- • Prostaglandins and thyroid hormones can also promote changes in protein turnover.
- • Nitric oxide has been shown to inhibit hepatic protein synthesis.
- • Amino acid oxidation.
- • The molecular form of the consumed nitrogen also appears to affect protein turnover.

112. Is insulin anabolic or catabolic?

Protein digestion by the lysosomal proteases (macroautophagy) is enhanced by glucagon and suppressed by insulin as well as amino acids. i.e., insulin is anabolic. Insulin is anabolic. (So is growth hormone, although it is counterregulatory).

113. If you fast for a day, are you likely to degrade muscle? Why or why not?

No. When gluconeogenesis begins depends on energy needs. Breaking down LBM to use C-skeleton from a.a pool may begin in the postabsorptive state (~3 to 12-16 hours), but muscle protein breakdown is the chief gluconeogenesis substrate in the fasting state (after ~48 hrs with no food intake).

114. How does fasting affect circulating insulin and glucagon levels?

Gluconeogenesis occurs in the wake of glycogen depletion to help maintain blood glucose levels. The shift to gluconeogenesis during prolonged fasting is signaled by the secretion of the hormone glucagon and the glucocorticosteroid hormones in response to low levels of blood glucose.

115. How does fasting affect the activity of hormone-sensitive lipase in the adipose tissue?

In the starvation state, the protein-sparing shift is from gluconeogenesis to lipolysis, as the fat stores become the major supplier of energy. The blood level of fatty acids increases sharply, and these replace glucose as the preferred fuel of heart, liver, and skeletal muscle tissue that oxidize them for energy. Therefore, fasting would increase the activity of hormone-sensitive lipase in the adipose tissue.

116. Name a transport protein in serum that is reduced in malnutrition. Would this be the only protein that is reduced?

Albumin which transports a variety of nutrients such as calcium, zinc, and vitamin B_6 is reduced in malnutrition. Transthyretin (formerly called prealbumin), which complexes with another protein, retinol-binding protein, for the transport of retinol (vitamin A) is also reduced in malnutrition.

117. Give examples of what would cause muscle hypertrophy or muscle atrophy.

There is a threshold for protein intake -- up to this level, secretion of hormones such as growth hormone increase with intake. Above the threshold-- there is little or no effect of increased intake. The threshold is approximately the dietary protein requirement. Insulin promotes protein synthesis. It is affected by the amount of mRNA, ribosomes, availability of amino acids for tRNA and hormonal environment. Insufficient intake causes oxidation of protein for energy needs.

During illness, starvation, malnutrition, protein synthesis and degradation are not in balance. In malnutrition, protein synthesis decreases. In starvation, protein catabolism is decreaseed (begin to use ketones). In sepsis, ketone formation is reduced so the body has to degrade body protein for glucose synthesis.

118. What determines if an amino acid is indispensable or dispensable?

Essential or indispensable a.a's must be provided in the diet. We can't make them at all or in enough quantity. The structure of the carbon chain makes a.a. essential or indispensable, i.e., we can't make a ring structure or branch chains; we have no enzymes to do that. Newer categories added to the essential/indispensable and nonessential/dispensable categories include conditionally or acquired indispensable a.a.'s. A dispensable amino acid may become indispensable should an organ fail to function properly as in the case of infants born prematurely or in the case of disease associated organ malfunction. For example, neonates born prematurely often have immature organ function and are unable to synthesize many nonessential amino acids such as cysteine and proline. Immature liver function or liver malfunction due to cirrhosis, for example, impairs phenylalanine and methionine metabolism, which occurs primarily in the liver. Consequently, the a.a's tyrosine and cysteine normally synthesized from phenylalanine and methionine catabolism, respectively become indispensable until normal organ function is established. In some kidney diseases, serine becomes indispensable because it cannot be synthesized in sufficient quantity by the diseased kidneys. Inborn errors of amino acid metabolism resulting from genetic disorders in which key enzymes in amino acid metabolism lack sufficient enzymatic activity also illustrate a situation in which dispensable amino acids become indispensable. Individuals with classical phenylketonuria (PKU) exhibit little to no phenylalanine hydroxylase activity. This enzyme converts phenylalanine to tyrosine. Without hydroxylase activity, tyrosine is not synthesized in the body and must be provided completely by diet; it is indispensable. In other inborn errors of metabolism, amino acids such as cysteine become indispensable. Thus, a.a's that are normally dispensable may become indispensable under certain physiological conditions.

119. How does the usual amount of dietary protein compare with the amount of protein that is turned over in the body?

RDA for protein is calculated on the basis of 0.8 g protein per kg body weight.
The average American eats 80-100 g protein per day.
Protein turnover is about 4.6 g/kg body weight. (For a 180 lb. person, it's 376 g.)
(e.g., for a 70 kg male, protein turnover would be approx. 320 g daily.)

120. Do amino acids compete with each other for transport? Explain.

Competition between a.a for transport by a common carrier has been documented. Multiple energy-dependent transport systems with overlapping specificity for a.a. have been demonstrated in the intestinal brush border. Both sodium dependent and sodium-independent transport systems exist. Amino acids using the same carrier system compete with each other for absorption.

121. What is transamination?

Transamination reactions involve the transfer of an amino group from one amino acid to an amino acid carbon skeleton of α-keto acid (an amino acid without an

amino group). The carbon skeleton/α-keto acid that gains the amino group becomes an amino acid, and the amino acid that loses its amino group becomes an α-keto acid.

122. Does catabolism of amino acids increase or decrease after a meal?

Amino acids not used by the intestinal cell are transported across the basolateral membrane of the enterocyte into interstitial fluid, where they enter the capillaries of the villi and eventually the portal vein for transport to the liver. The liver is the primary site for the uptake of most of the amino acids following ingestion of a meal. The liver is thought to monitor the absorbed amino acids and to adjust the rate of their metabolism according to the needs of the body. Approximately 57% of amino acids taken up by the liver are typically catabolized in the liver. "That percentage goes way up if intake is a very big protein meal. Extra a.a are destroyed really rapidly." Therefore, catabolism of amino acids would increase after a meal.

123. If energy is inadequate, are more or less amino acids catabolized than normal?

Amino acids are used for energy in the body when diets are inadequate in energy (measured in kilocalories). Therefore, less amino acids would be catabolized than normal.

124. What is elevated during stress that increases protein breakdown?

With stress, including sepsis, trauma, surgery, and burns, glucocorticoids (primarily cortisol), catacholamines (e.g. epinephrine), insulin, and glucagon release increase. However, the glucagon:insulin ratio favors glucagon. Consequently, tissues become resistant to insulin action, and hyperglycemia (high blood glucose concentrations) persists. In addition, cortisol concentrations may remain elevated in the blood for prolonged periods following severe trauma or stress events. High blood cortisol promotes proteolysis and hyperglycemia.

The principal mechanism of adjustment to starvation is a change in hormone balance. In particular, there is a sharp decrease in insulin production. Decreased insulin activity, coupled with increased synthesis of counterregulatory hormones such as glucagon, promotes fatty acid mobilization from adipose tissue, production of ketones, and the availability of amino acids for gluconeogenesis.

125. What does the half-life of serum or plasma proteins have to do with their effectiveness for measuring nutritional status?

Because of albumin's relatively long half-life (~14-18 days), it is not as good or as sensitive an indicator of visceral protein status as some of the other plasma proteins. The half-life is the time that it takes for 50% of the amount of a protein such as albumin to be degraded. Transthyretin (pre-albumin) and retinol-binding proteins are used as indicators of visceral protein status. However, because these two proteins have relatively shorter half-lives (~2 days and 12 hours, respectively) than albumin, they are more sensitive indicators of changes in visceral protein status than albumin. Pre-albumin is a better indicator for short-term changes than is albumin because of the half-lives of the proteins.

126. Presence of what enzymes is serum is taken as a measure of tissue damage?

Alanine in serum means heart attack (leakage of alanine from damaged tissue to

blood).

Aspartate aminotransferase (AST) is highest in heart; serum indicates damage.

127. Are amino acids "stored" in the body like glycogen is?

"You don't store a.a except as in an a.a.-chain (growth hormone, testosterone, synthesize new tissue).

128. What impact does an MAO inhibitor have on metabolism of amino acids or their derivatives?

Monoamine oxidase inhibitors usually inactivates tyramine from food. It is found in red wines, aged cheeses, fermented foods etc. It slows the breakdown of MAO's. An MAO inhibitor may prevent MAO from catabolizing amines in the diet. It may yield vasoconstriction. Increases blood pressure -- precipitously high.

129. What are special roles for glutamine?

- excitatory
- synthesis of GABA (γ-amino butyric acid) -- an inhibitory neurotransmitter
- removal of ammonia as glutamine

130. Elevated levels of what derivative of methionine are considered to be a risk factor for coronary heart disease?

Homocysteine. Elevated levels of homocysteine in the blood have been found as a risk factor for heart disease.

131. Taurine is a derivative of what compound? What is one of the uses of taurine?

Taurine, a β-amino sulfonic acid, is concentrated in muscle and the CNS. While taurine is not involved in protein synthesis, it is important

- in the retina for vision
- in membrane stability where it is a scavenger of peroxidative (e.g. oxychloride) products
- as a bile salt taurocholate
- as an inhibitory neurotransmitter

132. What is phenylketonuria?

A genetic absence or deficient activity of phenylalanine hydroxylase results in the genetic disorder phenylketonuria (PKU) and necessitates a phenylalanine restricted diet.

133. What are neurotransmitters/catecholamines produced from metabolism of tyrosine?

Tyrosine hydroxylase, an iron-dependent enzyme, catalyzes the first step in tyrosine metabolism to generate 3,4-dihydroxyphenylalanine (L-dopa). Subsequent reactions with L-dopa yield the catecholamines (dopamine, norepinephrine, and epinephrine). In the thyroid gland, tyrosine is taken up and used with iodine to synthesize thyroid hormones.

134. What is melanin? What is its source?

Tyrosine hydroxylase, catalysis of tyrosine metabolism also yields in other cells, such as the skin, eye and hair cells, and melanin (a pigment that gives color to skin, eyes, and hair).

135. What neurotransmitter is synthesized from tryptophan? What neurotransmitter?
Tryptophan is partially glucogenic as it is metabolized to form pyruvate; it is also partially ketogenic and forms acetyl CoA. It can be metabolized to produce nicotinamide, serotonin, and melatonin.

136. What is melatonin?
The hormone melatonin is derived in the brain from the a.a. tryptophan. Use of tryptophan supplements to promote sleep has been promoted, as has supplements of melatonin, which is also made from tryptophan in the pineal gland, which lies about in the center of the brain. Melatonin plays a role in the regulation of sleep. Yet, melatonin supplements of 2-500 mg for use as a sleep aid have yielded variable results. The LT use of melatonin and a.a, as well as effective dosing and administration, remain unknown.

137. What is the metabolic role of carnitine?
The oxidation of fatty acids is compartmentalized within the mitochondrion. Fatty acids and their CoA derivatives, however, are incapable of crossing the inner mitochondrial membrane, necessitating a membrane transport system. The carrier molecule for this system is carnitine which can be synthesized in humans from lysine and methionine, and which is found in high concentration in muscle. Carnitine is needed for the transport of long-chain fatty acids across the inenr mitochondrial membrane for oxidation. In muscle, carnitine also may serve as a buffer for free coenzyme (Co)A and may be involved in branched-chain amino acid metabolism. Carnitine is also thought to be involved with immune system function.

138. In what tissues are branched chain amino acids metabolized?
Muscle, as well as the heart, kidney, diaphragm, and other organs, possess BCAA transferases, located in both the cytosol and mitochondria. The enzyme complex needed for the next step is found in the mitochondria of many tissues, including liver, muscle, heart, kidney, intestine, and the brain.

130. What are the products of complete catabolism of a simple amino acid?
Energy, CO_2, NH_4^+ and H_2O.

140. Which tissue has the complete urea cycle? Are these enzymes sensitive to the amount of substrate?
The urea cycle occurs in the liver. Activities of urea cycle enzymes fluctuate with diet and hormone concentrations. For example, with low-protein diets or acidosis, urea synthesis (the amount of mRNA for each of the enzymes) diminishes and urinary urea nitrogen excretion decreases significantly. In the healthy individual with a normal protein intake, blood urea nitrogen (BUN) concentrations range from 8 to 20 mg/dL, and urinary urea nitrogen represents about 80% of total urinary nitrogen. Glucocorticoids and glucagon typically increase mRNA for the urea cycle enzymes.

141. How is urea removed from the body?

Through the urinary system. With normal protein intakes, urea may be 80% of total urinary nitrogen.

142. How is creatinine related to muscle mass?

Urinary excretion of creatinine and 3-methylhistidine are used as indicators of the amount of existing muscle mass and the rate of muscle degradation, respectively. Urinary creatine excretion is considered to be a reflection of muscle mass because it is the degradation product of creatine, which makes up approximately 0.3% to 0.5% of muscle mass by weight. The creatinine excreted in the urine reflects about 1.7% of the total creatine pool per day. However, urinary creatinine excretion is not considered to be a completely accurate indicator of muscle mass because of the variation that occurs in muscle creatine content.

143. What are key metabolic reactions that occur in the mitochondria?

The mitochondria are the primary sites of oxygen use in the cell and are responsible for most of the metabolic energy (adenosine triphosphate, or ATP) produced in cells. The electron transport chain couples the energy released by nutrient oxidation to the formation of ATP. Among the metabolic enzyme systems functioning in the mitochondrial matrix are those catalyzing reactions of the Krebs cycle and fatty acid oxidation. Other enzymes are involved in the oxidative decarboxylation and carboxylation of ppyruvate and in certain reactions of amino acid metabolism. Mitochondrial genes (inherited only from the mother) code for proteins vital to the production of ATP.

144. Can amino acids from muscle be metabolized for energy?

Yes. BCAA + aspartate, asparagine, glutamate are catabolized in skeletal muscle. When insulin increases, BCAA move in. α-keto acids may be oxidized in muscle (mitochondria) or transported to other tissues. Creatine and CP cyclize to creatinine which is an indicator of the amount of existing muscle mass.

145. When is a person in positive N balance?

During growth, protein synthesis exceeds degradation, and nitrogen intake exceeds excretion, resulting in a positive nitrogen balance. Positive nitrogen balance means there is more coming in than going out. Growth, pregnancy. Excess energy intake fosters nitrogen retention.

146. Describe a situation in which a person would be in negative nitrogen balance.

Protein synthesis and protein degradation are under independent controls. Rates of synthesis can be quite high as with protein accretion during growth. Alternately, protein degradation can be quite high, as during fever. Negative balance means more is going out than coming in. Loss of LBM. Insufficient calories from carbohydrate and/or fat mandate the oxidation of some protein to supply energy needs.

147. Give some examples of transport proteins.

Albumin - transports a variety of nutrients such as calcium, zinc, and vitamin B_6.
Transthyretin (formerly called prealbumin) - complexes with retinol-binding protein, for the transport of
retinol (vitamin A).

Hemeproteins, iron-containing proteins - bind and/or transport oxygen.
Transferrin - an iron transport protein
Ceruloplasmin - a copper transport protein

148. What is a protein of the immune system?

Immunoproteins may also be referred to as immunoglobulins (Ig) or antibodies (Ab). Immunoglobulins, of which there are five major classes -- IgG, IgA, IgM, IgE, and IgD -- are Y-shaped proteins made of four polypeptide chains. Immunoglogulins function by binding to antigens and inactivating them. Antigens typically consist of foreign substances such as bacteria or viruses that have entered the body. By complexing with antigens, immunoglobulin-antigen complexes can be recognized and destroyed through reactions with either complement proteins or cytokines. In addition, white blood cells such as macrophages and neutrophils also destroy foreign antigens through the process of phagocytosis.

149. Why is a protein able to serve as a buffer?

Proteins, because of their constituent amino acids, can serve as a buffer in the body. A buffer is a compound that ameliorates a change in pH that would otherwise occur in response to the addition of alkali or acid to a solution. The pH of the blood and other body tissues must be maintained within an appropriate range. Blood pH ranges from about 7.35 to 7.45, whereas cellular pH levels are often more acidic. The H+ concentration within cells is buffered by both the phosphate system and proteins. For example, the protein hemoglobin functions as a buffer in red blood cells. In the plasma and extracellular fluid, proteins and the bicarbonate system serve as buffers. Amino acids act as acids or bases in aqueous solutions such as in the body by releasing and accepting hydrogen ions, and they thereby contribute to the buffering capacity of proteins in the body. The buffering ability of proteins can be illustrated by the reaction: H+ + protein <----> Hprotein

150. What are two examples of conjugated proteins?

Conjugated proteins also play important and diverse roles in the body. Conjugated proteins are proteins that are conjugated (joined) to nonprotein components. Examples of some conjugated proteins include glycoproteins, proteoglycans, lipoproteins, flavoproteins, and metalloproteins.

151. Approximately how much protein does the body process per day?

Exogenous sources: Dietary animal and plants products: The average American eats 80-100 g/d.
Endogenous sources: Mucosal cells: ~ 50 g/d from shedding of cells in intestines. Re-used protein.
Digestive enzymes & glycoproteins: ~ 17 g

152. What factors affect protein quality?

Several methodologies are available to determine the protein quality of foods containing protein.

- Chemical Score (Amino Acid Score) - involves determination of the amino acid composition of a test protein. Only the indispensible amino acid content of

the test protein is determined, and then compared with that of egg protein or with an ideal reference pattern of a.a's.

- Protein Efficiency Ratio - represents body weight gained on a test protein divided by the grams of protein consumed. PER allows determination of which proteins promote weight gain (per gram of protein ingested).
- Biological Value - a measure of how much nitrogen is retained in the body for maintenance and/or growth versus the amount of nitrogen absorbed. Foods with a high BV are those that provide the amino acids in amounts that are consistent with body amino acid needs. The body will retain much of the absorbed nitrogen, if the protein is of high BV.
- Net Protein Utilization - measures retention of food nitrogen consumed rather than retention of food nitrogen absorbed. Proteins of higher quality typically cause a greater retention of nitrogen in the carcass than poor-quality proteins and would have a higher NPU.

153. Explain specifically what the term "limiting amino acid" means.

The term limiting amino acid is used to describe the indispensable amino acid that is present in the lowest quantity in the food.

154. What is the major limiting amino acid in grains? In legumes?

In wheat, rice, corn, other grains and grain products, the limiting a.a.'s are lysine, threonine (sometimes), and tryptophan (sometimes). In legumes, the limiting a.a is methionine.

155. What does a bioassay for protein quality tell you that a chemical score does not?

- Chemical Score (Amino Acid Score) - involves determination of the amino acid composition of a test protein. Only the indispensible amino acid content of the test protein is determined, and then compared with that of egg protein or with an ideal reference pattern of a.a's.
- Biological Value - a measure of how much nitrogen is retained in the body for maintenance and/or growth versus the amount of nitrogen absorbed. Foods with a high BV are those that provide the amino acids in amounts that are consistent with body amino acid needs. The body will retain much of the absorbed nitrogen, if the protein is of high BV.

The bioassay (biological value) tells you how much nitrogen was retained versus the amount absorbed, whereas the chemical score only tells you the indispensible amino acid composition of the test protein.

156. What does complementation mean when referring to amino acids?

To ensure that the body receives all the indispensible amino acids, certain proteins can be ingested together or combined so that their amino acid patterns become complementary. For example, legumes, with their high content of lysine but low content of sulfur-containing amino acids, complement the grains, which are more than adequate in methionine and cysteine but limited in lysine.

157. What does a sudden increase in oxidation of an amino acid mean about the adequacy of the diet?

Amino acid oxidation increases if a.a are in surplus. Amino acid oxidation increases if an essential a.a is missing.

158. How does total energy value of the diet affect protein utilization?

If energy intake is too low, protein will be used for energy, not growth. Energy needs must be met first. This is a big factor in developing countries. Insufficient energy intake causes oxidation of protein for energy needs.

159. Is conversion of carbohydrate and protein to triacylglycerols higher in the fed state or in the fasted state? Why?

The fed state favors synthesis of adipose tissue from free fatty acids. In fasting, blood glucose & insulin decrease, allowing lipolytic activity in adipose. FFa oxidized for energy, and some formation of ketone bodies. Excess glucose that cannot be oxidized or stored as glycogen is converted into triacylglycerols for storage. Glucose-rich cells (as in the fed state) do not actively oxidize fatty acids for energy. Instead, a switch to lipogenesis is stimulated, accomplished in part by inhibition of the entry of fatty acids into the mitochondrion. In the fasted state, there is a shift to ketones to support the CNS. Gluconeogenesis is going on in the liver. Muscle protein breakdown is the chief gluconeogenesis substrate. In this circumstance, carbohydrate and protein are not being converted to triacylglycerols. If they were present, they would be used for energy becauseenergy in being used for energy out is more efficient than storing energy and then using it. It requires energy to store it.

160. What are the essential fatty acids?

- Linoleic (18:2 n-6)
    - Arachidonic (20:4 n-6)
- Alpha-linolenic (18:3 n-3)

161. In what form is most of the lipid in food?

Fatty acids are of vital importance as an energy nutrient, furnishing most of the calories from dietary fat. Most stored body fat is in the form of triacylglycerols, which represent a highly concentrated form of energy. They account for nearly 95% of dietary fat. Structurally they are composed of trihydroxy alcohol, glycerol, to which are attached three fatty acids by ester bonds.

162. Do plants have cholesterol?

Cholesterol comes from animal tissue. Found in the cell membrane, particularly nerve tissue, it is the precursor for bile acids, estrogens, androgens, corticosteroids, & vitamin D.

163. How is the absorption of short-chain fatty acids different from the absorption of long-chain fatty acids. Explain in detail.

The process of absorption of free fatty acids is a function of the chain length of the fatty acids involved. Fatty acids having more than 10 to 12 carbon atoms are first activated by being coupled to coenzyme A by the enzyme acyl CoA synthetase. They are they reesterified into triacylglycerols, phosphatidylcholine, and cholesteryl esters. Short-chain fatty acids, those containing fewer than 10 to 12 carbon atoms, in contrast, pass from the cell directly into the portal blood. In the blood, short-chain fatty acids attach to albumin for transport to other tissues for processing. The different fate of the long- and short-chain

fatty acids is due to the specificity of the acyl CoA synthetase enzyme for long-chain fatty acids only.

164. Where is bile synthesized?

Bile is synthesized in the liver, in the hepatocytes. Bile is composed of mainly bile acids (and/or salts) but also cholesterol, phospholipids, and bile pigments (bilirubin and biliverdin) dissolved in an alkaline solution. Hepatic synthesis of the bile salts, indispensable for the digesting and absorbing dietary lipids, is one of its functions.

165. What are chylomicrons?

Chylomicrons are the primary form of lipoprotein formed from exogenous (dietary) lipids. Chylomicrons belong to a family of compounds called lipoproteins. Lipids resynthesized in the enterocytes, together with fat-soluble vitamins, are collected in the cell's endoplasmic reticulum as large fat particles. While still in the endoplasmic reticulum, the particles receive a layer of protein on their surface, which tends to stabilize the particles in the aqueous environment of the circulation, which they eventually enter. The particles are pinched off as lipid vesicles that then fuse with the Golgi apparatus. There, carbohydrate is attached to the protein coat, and the completed particles, called chylomicrons, are transported to the cell membrane and exocytosed into the lymphatic circulation.

166. What role do lipids have in membrane structure?

Meats, egg yolk, and dairy products contain fairly large amounts of cholesterol, and the sterol is an essential component of cell membranes, particularly those comprising nerve tissue. Cholesterol enhances the mechanical stability of the membrane and regulates its fluidity. Cholesterol helps to form the lipid bilayer. By regulating fluidity of the membrane, cholesterol regulates membrane permeability, thereby exercising some control over what may pass into and out of the cell. Fluidity of the membrane also appears to affect the structure and function of the proteins embedded in the lipid membrane.

167. Where are long-chain fatty acids oxidized?

Many tissues are capable of oxidizing fatty acids by way of a mechanism called β-oxidation. The oxidation of fatty acids is compartmentalized within the mitochondrion. The activated fatty acid is joined covalently to carnitine at the cytoplasmic side of the mitochondrial membrane by a transferase enzyme. The oxidation of the activated fatty acid in the mitochondrion occurs via a cyclic degradative pathway, by which two-carbon units in the form of acetyl CoA are cleaved one by one from the carboxyl end.

168. Fatty acids are elongated or oxidized from which end of the chain?

The carboxyl end.

169. What is the role of lipoprotein lipase?

Lipid undergoes hydrolysis by LPL. Chylomicrons and VLDL, which is formed endogenously in the liver, are transported by the blood throughout all tissues in the body while undergoing intravascular hydrolysis at certain tissue sites. This hydrolysis occurs through the action of the enzyme lipoprotein lipase, associated with the endothelial cell surface of the small blood vessels and capillaries within

adipose and muscle tissue. Its extracellular action on the circulating particles releases free fatty acids and diacylglycerols, which are quickly absorbed by the tissue cells. In this manner, chylomicrons and VLDL are cleared rapidly from the plasma in a matter of minutes and a few hours, respectively, from the time they enter the bloodstream. It is the large, triacylglycerol-laden chylomicrons that account for the turbidity of postprandial plasma. Because lipoprotein lipase is the enzyme that solubilizes these particles by its lipolytic action, it is sometimes referred to as "clearing factor." That which is left of the chylomicron following this lipolytic action is called a chylomicron remnant -- a smaller particle relatively less rich in triacylglycerol but richer in cholesterol. These are removed from the bloodstream by liver cell endocytosis. Nascent VLDL of liver origin also undergoes triacylglycerol stripping by lipoprotein lipase at extracellular sites, resulting in the formation of a transient IDL particle, and finally, a cholesterol-rich LDL. ApoC-II is an activator of lipoprotein lipase and a component of both chylomicrons and VLDL.

170. What is the role of hormone-sensitive lipase?

The key enzyme for the mobilization of fat is hormone-sensitive triacylglycerol lipase, found in adipose tissue cells. Lipolysis is stimulated by such hormones as epinephrine and norepinephrine, adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), glucagon, growth hormone, and thyroxine. Insulin antagonizes the effects of these hormones by inhibiting the enzymatic activity.

171. What typically happens to free fatty acids if they are taken up by muscle? By adipose tissue?

In muscle, FFA is used for energy. In adipose tissue, FFA is used for synthesis. LPL removes FFA leaving more cholesterol -- remnants removed in liver.

172. Triacylglycerol from liver is secreted into the blood as part of which lipoprotein?

Chylomicrons.

173. Why is there increased delivery of fatty acids to the muscle during exercise?

Plasma free fatty acids are mobilized from adipose tissue -- their importance increases with duration of exercise. In the fasted state, at 25-30% VO_2 max, most energy is from plasma fatty acids. As intensity increases to 65-85%, f.a. are not replaced in plasma fast enough and more glycogen is used. At VO_2 max, carbohydrate becomes ~sole energy source.

174. What are ketone bodies?

In addition to its direct oxidation via the Krebs cycle, acetyl CoA may follow other catabolic routes in the liver, one of which is the pathway by which the ketone bodies (acetoacetate, β-hydroxybutrate, and acetone) are formed.

175. What is the substrate for the synthesis of ketone bodies? Are ketone bodies produced during normal metabolism?

Ketone body formation is actually an "overflow" pathway for acetyl CoA use (i.e., the substrate), providing another way for the liver to distribute fuel to peripheral cells. Normally, the concentration of the ketone bodies is very low in the blood, but it may reach very high levels in situations of accelerated fatty acid oxidation combined with low carbohydrate intake or impaired carbohydrate use.

Such a situation would occur in diabetes mellitus, starvation, or simply a very low-carbohydrate diet.

176. What is ketosis? In what type of patient is ketosis particularly a problem?

The shift to fat catabolism, coupled with reduced oxaloacetate availability, results in an accumulation of acetyl CoA. A sharp increase in ketone body formation follows as would be expected, resulting in the condition known as ketosis. Ketosis can be dangerous in that it can disturb the body's acid-base balance (two of the ketone bodies are organic acids). However, the liver's ability to deliver ketone bodies to peripheral tissues such as the brain and muscle is an important mechanism for providing fuel in periods of starvation. It is the lesser of two evils. Ketone bodies can fuel muscle & brain during fasting & starvation. Ketosis is particularly a problem in diabetes mellitis. Ketosis changes the binding capacity of hemoglobin for O_2 (ability to bind O_2 decreases). Therefore, hemoglobin carries less O_2.

177. What is an average daily dietary cholesterol intake? How much cholesterol is synthesized in the body per day?

The average intake is about 600 mg/day -- but only half is absorbed. Endogenous cholesterol production is ~ 1 gram/day. Therefore, there is not much response from dietary change. Endogenous cholesterol accounts for greater than two-thirds of the total cholesterol store.

178. Cholesterol synthesis begins with what compound?

Nearly all the tissues in the body are capable of synthesizing cholesterol from acetyl CoA.

179. Why is HMG CoA reductase important in cholesterol synthesis?

The conversion of HMG-CoA to squalene includes the important rate-limiting step of cholesterol synthesis in which HMG-CoA is reduced to mevalonic acid by HMG-CoA reductase. This rate-limiting step is targeted by statin drugs which attempt to lower serum cholesterol levels.

180. Explain the pattern of double bonds in an omega-3 and an omega-6 fatty acid.

In an omega-3 fatty acid, the first double bond will be between the third and fourth carbon from the omega (methyl) end. In an omega-6 fatty acid, the first double bond will be between the sixth and seventh carbon from the omega (methyl) end.

181. What are some health advantages of omega-3 fatty acids?

- hypolipidemic
- antithrombotic (reduce blood clotting)

Good sources are soy, canola, linseed, fish & shellfish (EPA), human milk, fish (DHA)

182. What is a good source of EPA? Of DHA?

Eicosapentaenoic acid (EPA) - good source is cold water fish. Fish oils are particularly rich in EPA. DHA is a longer chain with 6 double bonds. It is high in breast milk and in fish.

183. Give an example of competing effects of eicosanoids.

- Prostacyclin (PGI_2) - platelet anti-aggregating - stimulates adenylate cyclase (produces cAMP).
- Thromboxane A_2 - inhibits adenylate cyclase & is pro-aggregating

- PGE_2 - causes vasodilation of blood vessels
- vasoconstriction by PGF_2.

184. What besides enzymes is required for the digestion of lipid?

Emulsification by bile makes enzyme action possible.

185. Are most naturally occurring double bonds “cis” or “trans”?

Cis is the natural form. Trans is a result of hydrogenation for stability. Trans fits into the membrane differently.

186. What fatty acid is the substrate for prostaglandin synthesis?

The most important fatty acid serving as precursor for eicosanoid synthesis is arachidonate. Its oxygenation follows either of two major pathways:

- the "cyclic" pathway, which results in the formation of prostaglandins and thromboxanes
- the "linear" pathway, which produces leukotrienes.

187. Identify a fat or oil that has a large amount (>10%) of omega-3 fatty acids.

Soy.

188. How important a component of cell membranes are the PUFA?

Membranes are sheetlike structures composed primarily of lipids and proteins held together by noncovalent interactions.

189. How/why does fatty acid composition affect membrane fluidity?

Cholesterol enhances the mechanical stability of the membrane and regulates its fluidity. Cholesterol helps to form the lipid bilayer. By regulating fluidity of the membrane, cholesterol regulates membrane permeability, thereby exercising some control over what may pass into and out of the cell. Fluidity of the membrane also appears to affect the structure and function of the proteins embedded in the lipid membrane.

190. Why are PUFA susceptible to lipid peroxidation?

Carbon to carbon double bonds are much more easily attacked by free radicals than are single bonds. The more double bonds in a PUFA, the more vulnerable it is to peroxidation. Normal protection against peroxidation is provided for by anti-oxidant enzymes in the membrane and cytosol and by anti-oxidant vitamins A, E, and C and b-carotene.

191. What are some fatty acids that increase plasma cholesterol concentrations?

Saturated fatty acids (lauric, myristic, palmitic acids).

192. What is the major carrier of cholesterol in the blood?

The LDL fraction is the major carrier of cholesterol, binding about 60% of the total serum cholesterol. Its function is to transport the sterol to tissues, where it may be used for membrane construction or for conversion into other metabolites such as the steroid hormones.

193. What are the results of lack of the LDL receptor?

Mutant cells unable to bind and/or internalize LDL efficiently and thereby deprived of the cholesterol needed for membrane synthesis must obtain the needed sterol via de novo synthesis. In these cells HNG CoA reductase is activated while ACAT is depressed.

194. If cholesterol is taken up by the liver, what is the potential effect on cholesterol synthesis?

The enterohepatic circulation can return absorbed bile salts to the liver. Bile salts returning to the liver from the intestine repress the formation of an enzyme catalyzing the rate-limiting step in the conversion of cholesterol into bile acids. If the bile salts are prevented from returning to the liver, the activity of this enzyme increases, thus stimulating the conversion of cholesterol and therefore its excretion. This effect is exploited therapeutically in the treatment of hypercholesterolemia by the use of unabsorbable, cationic resins that bind bile salts in the intestinal lumen and prevent their return to the liver. As total body cholesterol increases, the rate of synthesis tends to decrease, and this is known to be due to a negative feedback regulation of the HMG-CoA reductase reaction. This suppression of cholesterol synthesis by dietary cholesterol seems to be unique to the liver and is not evident inother tissues to a great extent. The effect of feedback control of biosynthesis depends to a great extent on the amount of cholesterol absorbed. The suppression is not sufficient to prevent an increase in the total body pool of cholesterol when dietary intake is high.

195. Do you want HDL-cholesterol or LDL cholesterol to be higher?

HDL is "helper" cholesterol; LDL is "laying it down" cholesterol. You would want HDL-cholesterol to be higher.

196. What is the usual composition of plaque in the arteries?

Lipid material in the form of foam cells (phagocytic cells that become engorged with lipid) infiltrates the endothelium, and as lipid accumulates, the lumen of the blood vessel involved is progressively occluded. The deposited lipid, known to derive from blood-borne lipids, is called fatty plaque.

197. What are major sources of trans fatty acids in the U.S. diet?

Most natural fats and oils contain only cis double bonds. The much smaller amount of naturally occurring trans fats are found mostly in the fats of ruminants, for example in milk fat, which contains 4% to 8% trans fatty acids. Much larger amounts are found in certain margarines and margarine-based products, shortenings, and frying fats as a product of the partial hydrogenation of PUFA. Trans fatty acids are also high in processed, fried, and frozen foods.

198. Are there health implications for diets high in trans fatty acids?

Still contradictory reports. If at high risk of atherosclerosis, it seems beneficial to avoid a high intake of trans fatty acids. More well-designed research is needed.

199. What is the role of carnitine in lipid metabolism?

The oxidation of fatty acids is compartmentalized within the mitochondrion. Fatty acids and their CoA derivatives, however, are incapable of crossing the inner mitochondrial membrane, necessitating a membrane transport system. The carrier molecule for this system is carnitine, which can be synthesized in humans from lysine and methionine, and which is found in high concentration in muscle. The activated fatty acid is joined covalently to carnitine at the cytoplasmic side of the mitochondrial membrane by the transferase enzyme carnitine acyltransferase I (CAT I). A second transferase, acyltransferase II (CAT II), located on the inner face of the inner membrane, releases the fatty acyl CoA and carnitine into the matrix. The oxidation of the activated fatty acid in the mitochondrion occurs via a cyclic degradative pathway, by which two-carbon units in the form of acetyl CoA are cleaved one by one from the carboxyl end.

200. What is enterohepatic circulation? Explain why it is an important pathway.

The circulation of bile is termed enterohepatic circulation. New bile acids are typically synthesized in amounts about equal to those that are lost in the feces (about 0.5 g daily). New bile mixed with recirculated bile is sent via the cystic duct for storage in the gallbladder. The presence of certain dietary fibers in the gastrointestinal tract, however, may bind to the bile salts and acids and prevent bacterial de-conjugation and conversion to secondary bile acids. The pool of bile is thought to recycle at least twice per meal.

201. Why is olestra "low-calorie"?

Olestra cannot be broken down by pancreatic lipases and thus has no caloric value. It is a non-absorbable lipid in the GI tract.

202. What is respiratory quotient?

The respiratory quotient is the ratio of the volume of CO_2 expired to the volume of O_2 consumed. It has served for nearly a century as the basis for determining the relative participation of carbohydrates and fats in exercise. $RQ = CO_2 / O_2$

For carbohydrate catabolism, the RQ is 1.
$C_6H_{12}O_6$ (glucose) + 6 CO_2 ---> 6 CO_2 + 6 H_2O

For fat catabolism, the RQ is approximately 0.7:
$C_{16}H_{32}O_2$ (palmitic acid) + 23O_2 ---> 16 CO_2 + 16 H_2O

The RQ for protein is about 0.8

203. Would the R.Q. be higher or lower than normal in starvation?

Should the principal fuel source shift from mainly fat to carbohydrate, the RQ correspondingly increases, while a shift from carbohydrate to fat lowers the RQ.

In the starvation state, in an effort to spare body protein, there is a shift from gluconeogenesis to lipolysis -- fat stores become the major supplier of energy. So, in starvation, the RQ would be lower than normal.

204. Why does VO_{2Max} have an effect on the ability of an athlete to continue exercise for long periods of time?

VO_{2Max} is the workload that places the highest possible demand on the working muscle of that subject, and it is generally used to monitor intensity of exercise, An athlete who can continue exercise for long periods of time will have a high VO_{2Max}, because as VO_{2Max} increases, your indurance increases. Maximum oxygen uptake (VO_{2Max}) refers to the highest rate at which oxygen can be taken up and consumed by the body during intense exercise (Bassett & Howley 2000). Traditionally, the magnitude of an individual's VO_{2Max} has been viewed as one of the most important predictors of endurance performance. A classic study, conducted in the 1970's at Ball State University, confirmed the importance of VO_{2Max} to endurance performance with findings indicating a strong correlation between VO_{2Max} and 10-mile run times (Costill 1970).

Prolonged exercise requires sustained energy provision to maintain muscle contraction and is accomplished through the continual production of ATP. The production of ATP is accomplished through three metabolic pathways (breakdown of a fuel to release energy), which include the phosphagen system (the production of ATP from creatine phosphate), glycolysis (glucose breakdown), and mitochondrial respiration (aerobic metabolism within the mitochondrion of the cell). The first two pathways are only capable of energy production for short durations; consequently, ATP regeneration for extended exercise is accomplished predominantly through mitochondrial respiration.

205. What enzyme removes free fatty acids from circulating triacylglycerols?

The complete hydrolysis of triacylglycerols yields glycerol and three fatty acids. In the body, this occurs largely through the activity of <u>lipoprotein lipase</u> of vascular endothelium and through an intracellular lipase that is active in the liver and particularly active in adipose tissue.

206. What enzyme breaks down triacylglycerols in the tissue to release free fatty acids?

<u>Hormone sensitive lipase</u> hydrolyzes f.a from intramuscular triacylglycerols.

207. What effect does insulin have on hormone-sensitive lipase?

Insulin inhibits the activity of hormone-sensitive triacylglycerol lipase.

208. Is breakdown of triacylglyerols in adipose tissue enhanced or reduced by eating?

Reduced. The fed state favors synthesis. Insulin inhibits adipose tissue lipase.

209. When do you get free fatty acids from adipose tissue?

In fasting, decreased insulin allows lipolytic activity in adipose to become more active. FFA are oxidized for energy. Start releasing FA for energy. Travel to muscle.

210. In what tissue does most of the glycogen accumulate after eating if the body is at rest?

The greatest concentration of glycogen is in the liver, although there is more actual volume of glycogen in the muscle. In the fed state, glucose is sent to muscle for energy and for storage of excess as glycogen.

211. Why is utilization of fatty acids (as percentage of fuel) decreased at very high work intensity?

At very high work intensity, utilization of FFA is reduced because you can't get enough oxygen to utilize it. VO_{2Max} becomes the limiting factor.

212. What duration of energy expenditure does the ATP/creatine phosphate system support?

Creatine phosphate lasts about 10 seconds.

213. What duration of energy expenditure does the lactic acid system support?

High intensity events of 20 seconds to a few minutes.

214. Why is aerobic energy metabolism classed as “more efficient”?

It is efficient in terms of ATP generation. This system involves the Krebs cycle, through which carbohydrates, fats, and proteins are completely oxidized to CO_2 and H_2O. The system, which requires oxygen, is highly efficient from the standpoint of the quantity of ATP produced. Since oxygen is necessary for the system to function, an individual's VO_{2Max} becomes an important factor in his or her performance capacity.

215. What is a mineral that can be limiting for full efficiency of aerobic energy metabolism?

Iron is a vital component of hemoglobin and affects the oxygen-carrying capacity of blood. Also, the transfer of electrons along the electron transport chain is made possible by the change in the oxidation state of iron.

216. What are ways that training enhances aerobic energy metabolism?

Some effect on cardiovascular function such as increased exchange in lungs and increased cardiac output. The main adaptation may be an increase in the number of nitochondria in skeletal muscle. This is very inportand and very fast (1-2 weeks). Elite runers can run much farther on the same amount of glycogen (not "hitting the wall").

217. What is the primary fuel for low intensity exercise (25-30% VO_{2max})

In the fasted state, at 25-30% VO_{2Max} , most energy is from plasma fatty acids. As intensity increases to 65-85%, f.a. are not replaced in plasma fast enough and more glycogen is used. At VO_{2Max}, carbohydrate becomes ~sole energy source. Marathon runner uses f.a.'s.

218. What is the purpose of carbohydrate loading?

Because muscle glycogen was identified as the limiting factor for the capacity to exercise at intensities requiring 70% to 85% VO_{2Max} , dietary manipulation to maximize glycogen stores is called carbohydrate loading.

219. Why does carbohydrate loading frequently produce muscle stiffness?

Your body has to store 4g water per 1g glycogen. This results in stiffness.

220. What nutrient is MOST important for athletes?

Water is the most important nutrient for athletes because of the need for hydration and lowering temperature.

221. Why are glycogen stores very important as exercise intensity approaches VO_{2max}

High muscle glycogen levels allow exercise to continue longer at a submaximal workload. Even in the absence of carbohydrate loading, a strong positive correlation exists between initial glycogen level and time to exhaustion and/or performance during exercise periods lasting at least 1 hour. Glycogen depletion is a limiting factor under these conditions.

222. What are products of aerobic metabolism? How are they removed?

In the Krebs cycle, carbohydrates, fats, and proteins are completely oxidized to CO_2 and H_2O.

223. What are products of anerobic metabolism? How are they removed?

Glycolysis is the initial way of utilizing glucose in all cells, and is used exclusively by certain cells to provide ATP when insufficient oxygen is available for aerobic metabolism. Glycolysis doesn't produce much ATP in comparison to aerobic metabolism, but it has the advantage that it doesn't require oxygen. In addition, glycolysis occurs in the cytoplasm, not the mitochondria. So it is used by cells which are responsible for quick bursts of speed or strength. Like most chemical reactions, glycolysis slows down as its product, pyruvic acid, builds up. In order to extend glycolysis the pyruvic acid is converted to lactic acid in a process known as fermentation. Lactic acid itself eventually builds up, slowing metabolism and contributing to muscle fatigue.

Ultimately the lactic acid must be reconverted to pyruvic acid and metabolized aerobically, either in the muscle cell itself, or in the liver. The oxygen which is "borrowed" by anaerobic glycolysis is called oxygen debt and must be paid back. Oxygen debt is partly oxygen reserves in the lungs, tissues, and myoglobin in the lungs (alactacid oxygen debt). But mostly it is the amount of oxygen which will be required to metabolize the lactic acid produced.

Strength training increases the myofilaments in muscle cells and therefore the number of crossbridge attachments which can form. Training does not increase the number of muscle cells in any real way. (Sometimes a cell will tear and split resulting in two cells when healed). Lactic acid removal by the cardiovascular system improves with training which increases the anaerobic capacity. Even so, the glycolysis-lactic acid system can produce ATP for active muscle cells for only about a minute and a half.

224. What is a tissue that predominately uses fatty acids for fuel? What is a tissue that cannot use fatty acids for fuel?

Fatty acids are the preferred fuel for most tissues. Red blood cells cannot use fatty acids for fuel because they have no mitachondria. The brain and neurons cannot use fatty acids because they cannot pass the blood-brain barrier.

225. Can the body synthesize glucose from fatty acids?

No. Fatty acids can never form glucose.

226. What is the primary source of blood glucose after 24 hrs of fasting?

The post-absorptive state or "early fasting state" is ~3 to 12-16 hrs. Gluconeogenesis begins. Breakdown of LBM to use C-skeleton from a.a. pool.

227. Which yields more energy----complete oxidation of 1 gram of glucose or complete oxidation of 1 gram of fatty acids? How much? Why?

CHO yields 4 kcal/g and fat yields 9 kcal/g.

Fatty acids are a very rich source of energy, and on an equal-weight basis they surpass carbohydrates in this property. This is because fatty acids exist in a more reduced state than that of carbohydrate and therefore undergo a greater extent of oxidation en route to CO_2 and H_2O.

228. Why is pyruvate dehydrogenase such an important enzyme in metabolism of energy nutrients? Is it reversible?

The ppyruvate dehydrogenase reaction is a complex one requiring a multienzyme system and various cofactors. The cofactors include coenzyme A (CoA), thiamine pyrophosphate (TPP), Mg^{+2}, NAD^+, FAD, and lipoic acid. Four vitamins are therefore necessary for the activity of the comple: pantothenic acid (a component of CoA), thiamine, niacin, and riboflavin. The net effect of the complex results in decarboxylation and dehydrogenation of pyruvate, with NAD^+ serving as the terminal hydrogen acceptor. This reaction therefore yields energy, because the reoxidation by electron transport of the NADH produces 3 mol of ATP by oxidative phosphorylation. The reaction is regulated negatively by acetyl CoA and by NADH, and positively by ADP and CA^{+2}.

The pyruvate dehydrogenase reaction is shown below. It is not reversible.

Pyruvate

Pyruvate Dehydrogenase Acetyl CoA

Complex

229. Can cholesterol be formed from acetyl CoA? Does this mean that cholesterol can ultimately be derived from carbohydrate or protein?

Nearly all the tissues in the body are capable of synthesizing cholesterol from acetyl CoA. Yes. Acetyl CoA is the starting point. At least 26 steps are known to be involved in the formation of cholesterol from acetyl CoA.

230. What are ketone bodies?

In addition to its direct oxidation via the Krebs cycle, acetyl CoA may follow other catabolic routes in the liver, one of which is the pathway by which the socalled ketone bodies (acetoacetate, β-hydroxybutrate, and acetone) are formed. Ketone body formation is actually an "overflow" pathway for acetyl CoA use, providing another way for the liver to distribute fuel to peripheral cells. Normally, the concentration of the ketone bodies is very low in the blood, but it may reach very high levels in situations of accelerated fatty acid oxidation combined with low carbohydrate intake or impaired carbohydrate use. Such a situation would occur in diabtes mellitus, starvation, or simply a very low-carbohydrate diet.

231. Where is urea formed?

The urea cycle, which is found in the liver, is important for the removal of ammonia from the body.

232. What organ is responsible for synthesis of most of the plasma proteins?

Albumin, the most abundant of the plasma proteins, is synthesized by the liver. Other proteins synthesized by the liver and released into the plasma include transthyretin (formerly called pre-albumin), retinol-binding protein (complexed together and involved with retinaol and thyroid hormone transport), blood-clotting proteins, and globulins.

233. What enzyme (specific) releases free fatty acids from chylomicrons?

Chylomicrons and VLDL, which is formed endogenously in the liver, are transported by the blood throughout all tissues in the body while undergoing intravascular hydrolysis at certain tissue sites. This hydrolysis occurs through the action of the enzyme lipoprotein lipase, associated with the endothelial cell surface of the small blood vessels and capillaries within adipose and muscle tissue. Its extracellular action on the circulating particles releases free fatty acids and diacylglycerols, which are quickly absorbed by the tissue cells.

234. Why is glucose metabolized to lactate in the red blood cell?

The erythrocyte, in the process of maturing, disposes of its mitochondria and must depend solely on the energy produced through anaerobic mechanisms, primarily glycolysis. Glycolysis is the pathway by which glucose is degraded into two units of pyruvate, a triose. Under anaerobic conditions-- that is, in a situation of oxygen debt -- pyruvate is converted to lactate. In cells that lack mitochondria, such as the erythrocyte, the pathway of glycolysis is the sole provider of ATP by the mechanism of substrate-level phosphorylation of ADP.

235. What compound is depleted first to maintain blood glucose levels?

In the course of an overnight fast, nearly all reserves of liver glycogen and most of the muscle glycogen have been depleted.

236. What are three very different compounds that can be synthesized from acetyl CoA?

Acetyl CoA produced from whatever source must be used for energy, lipogenesis, cholesterogenesis, or ketogenesis, i.e.., lipid, cholesterol, ketones. A most significant reaction linking glucose metabolism to fatty acid synthesis is the reaction of the pyruvate dehydrogenase complex, which converts pyruvate to acetyl CoA by dehydrogenation and decarboxylation. Acetyl CoA is the starting material for the synthesis of long-chain fatty acids as well as a variety of other lipids.

237. If you fast for a day and a half, are you likely to degrade muscle? Why or why not?

Yes. Gluconeogenesis begins in the postabsorptive state of early fasting -- ~3 to 12-16 hours. After 48 hours with no food intake, the fasting state is in progress with gluconeogenesis in the liver using muscle protein breakdown as the chief gluconeogenesis substrate. When gluconeogenesis begins depends on energy needs; it involves breaking down lean body mass to use the C-skeleton from a.a pool. A day and a half (36 hours) is well within the time in which this process would begin occurring, and by 48 hours, it would be well underway with a shift to ketones to support the CNS..

238. How does fasting affect circulating insulin and glucagon levels?

During fasting, low blood glucose causes glucagon and glucocortico-steroid hormones to rise. Insulin is low because of the low blood glucose.

239. Name a transport protein in serum that is reduced in malnutrition. Would this be the only protein that is reduced?

Albumin is reduced in malnutrition; it is used quite extensively as an indicator of visceral protein status. Albumin functions in the plasma to maintain oncotic pressure as well as to transport nutrients such as vitamin B6, minerals including zinc, calcium, and small amounts of copper, nutrients such as fatty acids; and the amino acid tryptophan. Some drugs and hormones such as the thyroid hormones are also transported by albumin. Transthyretin (pre-albumin) is also reduced in malnutrition, as is retinol-binding protein.

240. For vitamins A, D, E, and K, and for calcium, phosphorus, magnesium, sodium, potassium, sulfur, chloride, iron, zinc, copper, selenium, chromium, iodine, manganese, molybedenum, and fluoride identify functions, percent absorption, name of the deficiency disease (if any), deficiency symptoms, groups (or conditions) at risk for deficiency, good food sources, recommended intakes and upper levels, enzyme or hormone with which the nutrient is associated (if any) and key nutrient interactions.

	Vitamin A (retinol, retinal, retinoic acid) Provitamins (carotenoids, particularly β-carotene)
Function	Synthesis of rhodopsin and other light receptor pigments; metabolites involved in growth failure, growth and differentiation of epithelia, nervous, bone tissue and immune function. • Vision • Cellular differentiation • Growth • Reproductive • Bone development • Immune System
% Absorption.	Retinol: 70-90% β-carotene: 20-50%; can be as low as 5%
Deficiency Disease	
Deficiency Symptoms	Children: poor dark adaptation, xerosis, keratomalacia Adults: night blindness, xeroderma • Night-blindness • Retarded growth/anorexia • Increased susceptability to infection • xerothalmia
Groups at Risk	• Malabsorption • Intestinal parasites • Measles • Malnourished preschool children • In the US, alcoholics
Food Sources	Good sources in rank order: Beef liver, sweet potato, carrots, spinach, butternut squash, dandelion greens Retinal palmitate: Egg yolks, butter, milk, liver, fish liver oil Carotenoids: red, orange, yellow pigments. Sweet potato, carrots, spinach, butternut squash, dandelion greens
Recommended Intake	700 μg, women 900 μg, men 1 μg all-trans retinol = 1 RAE 2 μg supplemental all-trans β-carotene = 1 RAE 12 μg all-trans β-carotene = 1 RAE 24 μg other pro vitamin A carotenoids
UL	3000 μg/d preformed vit A Equivalent to 10,000 IU/d
Enzymes/ Hormone Associated	
Key Nutrient Interactions	• Vit E & K • Protein - critical for RBP • ZN - synthesis of RBP & mobilization of A from storage • Fe - Vit A deficiency may result in microcytic anemia

	Vitamin D Provitamins: Ergosterol, 7-dehydrocholesterol, Vitamin D_2 (ergocalciferol), Vitamin D_3 (cholecalciferol)
Function	Regulator of bone mineral metabolism, primarily calcium • Active form – 1,25-$(OH)_2$ D_3 (functions like a steroid hormone) • Receptors in intestine, kidney, bone; also receptors in other tissues • Controls blood Ca concentrations (w/parathyroid hormone or PTH)
% Absorption.	• Dietary vit D is absorbed from a micelle – bile needed. • 50% absorbed – incorporated into chylomicrons. • Chylomicron remnants deliver to liver. • Hypocalcemia causes PTH secretion.
Deficiency Disease	Children: Rickets Adults: Osteomalacia
Deficiency Symptoms	Rickets: failure of bone to mineralize in infants and children; Weight bearing activity causes deformity. Osteomalacia: impaired Ca (&P) absorption; Bone matrix not remineralized.
Groups at Risk	• Insufficient sunlight exposure • Agine reduces D synthesis in skin • Fat malabsorption • Anti-convulsant drug therapy • Breast-fed infants • Renal disease
Food Sources	Good sources in rank order: Synthesized in skin exposed to ultraviolet light; fortified milk is a reliable good source • Liver, eggs, dairy products, beef, veal, herring, salmon, tuna, sardines. • Synthesis in skin from exposure to UV light. • Irradiation of ergosterol -→ergocalciferol (D_2)
Recommended Intake	AI Infants -→ age 50 5 μg or 200 IU 1 IU = 0.025 μg Adults 51-70 10 μg or 400 IU Adults >70 15 μg or 600 IU
UL	> 1 yr. 50 μg (2000 IU)/d Infants < 1 yr. 25 μg (1000 IU)/d
Enzymes/ Hormone Associated	PTH (Parathyroid hormone)
Key Nutrient Interactions	Ca P Vit K

	Vitamin E Tocopherols, Tocotrienols
Function	Antioxidant • Maintain membrane integrity • Antioxidant – prevents oxidation of PUFA in phospholipids & hemolysis of RBC • Cell membrane particularly susceptible ○ Lungs, brain, and erythrocytes ○ removal of peroxides & superoxide radicals
% Absorption.	20-50% or 80% <10% from 200 mg dose
Deficiency Disease	
Deficiency Symptoms	Infants: anemia Children and adults: neuropathy and myopathy • Degeneration of the retina • Hemolytic anemia • Muscle weakness, neuromuscular degeneration
Groups at Risk	Premature infants & persons with malabsorption syndromes. • Digestive system is immature; may not digest. • Lungs not developed. Put in higher O2 environment, so need more protection from oxidizing O2. • Fe tends to be an oxidant. Give more Fe, but tend to be susceptible to oxidation. • DHA 6 double bonds.
Food Sources	Good sources in rank order: vegetable seed oil are major source; widely distributed in foods. • Widely distributed, especially oils from plants • Vitamin E correlates with level of PUFA • Wheat bran & germ – tocotrienols • Animal products are low in vitamin E • Limiting fat may limit vitamin E
Recommended Intake	• RDA for adults – 15 mg/d of α-tocopherol (tend to get in US diet) • Smokers have increased free-radical burden but not known if vit E requirements need adjustment.
UL	UL for adults – 1000 mg/d of any form of supplementary α-tocopherol.
Enzymes/ Hormone Associated	
Key Nutrient Interactions	• Selenium (for glutathione peroxidase) • Superoxide dismutase removes free radicals & requires Zn, Mn,

	Cu • High intakes of E antabonize vitamin K (excessive bleeding) • Antagonizes absorption & conversion of beta-carotene Increased PUFA increases need for E

	Vitamin K Phylloquinones (from plants), Menaquinones (from bacteria), Menadione (synthetic)
Function	Activates blood-clotting factors II, VII, IX, X by γ-carboxylating glutamic acid residues; carboxylates bone and kidney proteins • Posttranslational carboxylation of glutamate to form γ-carboxyglutamate ○ 4 of 13 factors for blood coagulation ○ Binds Calcium • Prothrombin binds Ca and forms thrombin • Thrombin catalyzes the proteolysis of fibrinogen to yield fibrin • Anticoagulants like coumarin and warfarin interfere with synthesis of K-dependent blood-clotting factors • Two vitamin K-dependent proteins identified in skeletal tissues ○ Bone Gla protein (BGP or osteocalcin) ○ Matrix Gla protein (MGP) ○ Also kidney Gla protein (KGP)
% Absorption.	• Enhanced by bile salts and pancreatic juice • Absorption 40-80% in normal individuals • Bacteria may produce enough to meet human requirements, but absorption is being studied. • Carried through lymph in chylomicrons
Deficiency Disease	
Deficiency Symptoms	Children: hemorrhagic disease of newborns Adults: defective blood clotting
Groups at Risk	• Newborn infants – injection at birth recommended • People who have been injured or are treated chronically w/antibiotics • Fat malabsorption
Food Sources	Good sources in rank order: Synthesized by intestinal bacteria; green leafy vegetables, soy beans, beef liver
Recommended Intake	• AI for adults: men: 120 μg/d; women: 90 μg/d
UL	No adverse effects have been reported; so UL was not set.
Enzymes/ Hormone Associated	
Key Nutrient Interactions	• Excess A interferes with K absorption • Excess E also antagonizes – perhaps through absorption or metabolism.

	Calcium
Function	Structural component of bones and teeth, role in cellular processes, muscle contraction, blood clotting, enzyme activation. • Mineralization ○ 99% of Ca in bones & teeth ○ 60-66% of bone wt. Due to hydroxyapatite& Ca-phosphate. • Binds to Ca binding proteins found in bone like osteocalcin (BGP) • Blood clotting • Nerve induction, muscle contraction • Intracellular Ca^{2}+ usually very low • Intracellular Ca^{2}+ causes reactions like smooth & skeletal muscle contraction
% Absorption.	Two routes: one is active/saturable; second is passive/paracellular Net Ca absorption from both routes is ~ 25-35%.
Deficiency Disease	
Deficiency Symptoms	Rickets, osteomalacia, osteoporosis, tetany. • Low levels of free ionized Ca^{2+} in blood may result in tetany • Osteoporosis ○ Type 1 – postmenopausal women 51-65, affects vertebrae/wrist. ○ Type 2 – "senile" – men/women > 75; also affects hip, pelvis, humerus/tibia
Groups at Risk	• High fiber diets • Fat malabsorption • Immobilization • Thiazide diuretics
Food Sources	• Milk, cheese, yogurt, ice cream (?) • Tofu • Fish with bones (salmon, sardines), clams, oysters • Turnip greens, broccoli, kale • Legumes, dried fruit
Recommended Intake	RDI • Ages 9-18 1300 mg/d • Adults 19-30 1000 mg/d • Adults 51-70 1200 mg/d
UL	2500 mg/d
Enzymes/ Hormone Associated	Adenylate, cyclase, kinases, protein kinase, Ca^{2+} Mg^{2+} ATPase, others.
Key Nutrient Interactions	• Caffeine and alcohol are positively assoc. w/risk of fracture in middle aged women. • Ca supplements decrease absorption of iron & other trace min.

	• Lead absorption is inversely related to dietary Ca intake. • Ca reduces the absorption of fatty acids & the reabsorption of bile acids. • Higher intake of dairy products is assoc. w/lower lipid stores.

	Phosphorus
Function	Structural component: bone, teeth, cell membranes, phospholipids, nucleic acids, nucleotide coenzymes, ATP-ADPphosphate transferring system in cells, pH regulation. 85% in skeleton, 14% in muscle; 2nd to Ca in abundance. • Skeletal Tissue ○ Calcium phosphates ○ Hydroxyapatite ($Ca_{10}[PO_4]_6[OH]_2$) • High-energy bonds (ATP, etc.) • Nucleic Acids (DNA, RNA) • Phospholipids • Acid/Base Balance
% Absorption.	• Stimulated by Vit D as calcitriol • Phosphorus from phytic acid (phytate) is less available • Aluminum or Mg hydroxides reduce absorption
Deficiency Disease	
Deficiency Symptoms	Neuromuscular, skeletal and himatologic and renal manifestations, rickets, osteomalacia, anorexia.
Groups at Risk	
Food Sources	Rank order: Meat, poultry, fish, eggs, milk, milk products, nuts, legumes, cereal grains, chocolate. Widely distributed in foods • Animal products, nuts, legumes, cereals
Recommended Intake	• RDA ○ Ages 9-18: 1250 mg/d ○ Adults: 700 mg/d
UL	UL • Ages 9-18: 4 g/d • Adults: 3 g/d
Enzymes/ Hormone Associated	Activates many enzymes in phosphorylation and dephosphorylation.
Key Nutrient Interactions	

	Magnesium
Function	Component of bones; role in nerve impulse transmission, protein synthesis, enzyme activation • Bound to phospholipids as part of cell membranes • Stabilizes structure of ATP • Cofactor or activator of more than 300 enzymatic reactions
% Absorption.	• 30-65% absorbed • Absorption is greater when intakes are low or status is poor • Fiber and fat malabsorption decrease absorption
Deficiency Disease	
Deficiency Symptoms	Depression, muscle weakness, tetany, abnormal behavior, convulsions, growth failure. • Associated with alcoholism or renal disease • Nausea, vomiting, weakness, cardiac arrhythmia, etc.
Groups at Risk	Excessive vomiting or diarrhea, alcoholism, diuretic use, diabetes mellitus, burns.
Food Sources	Rank order: nuts, legumes, cereals, grains, soybeans, parsnips, chocolate, molasses, corn, peas, carrots, seafood, brown rice. Coffee, tea, cocoa, nuts, legumes, whole-grains, green leafy vegetables, whole grains.
Recommended Intake	RDA • Men, 19-30 400 mg/d • Women, 19-30 310 mg/d • Men >31 420 mg/d • Women >31 320 mg/d
UL	UL (from nonfood sources) 350 mg/d for age 8 and above
Enzymes/ Hormone Associated	Hydrolysis and transfer of phosphate groups by phosphokinase; important in numerous ATP-dependent enzyme reactions
Key Nutrient Interactions	

	Sodium
Function	Water, pH and electrolyte regulation, nerve transmission, muscle contraction. • 30% on bone surface • Major cation of extracellular fluid
% Absorption.	95% absorbed; excess should be excreted by kidneys
Deficiency Disease	
Deficiency Symptoms	Anorexia, nausea, muscle atrophy, poor growth, weight loss.
Groups at Risk	
Food Sources	Rank order: Table salt, meat, seafood, cheese, milk, bread, vegetables (abundant in most foods except fruits). Major source in diet is added salt Processed foods ~75% of total Na
Recommended Intake	• 115 mg/d for obligatory losses • Nat. Research Council has suggested 500 mg/d (salt is 39% Na, thus ~1250 mg/d (4.5-12.5 g salt) • Estimated Na intakes ~1800-5000 mg/d (4.5-12.5 g salt)
UL	
Enzymes/ Hormone Associated	Na^+/K^+-ATPase. Renal excretion & retention under the control of aldosterone
Key Nutrient Interactions	

	Potassium
Function	Water, electrolyte, and pH balances, cell membrane transfer. 98% intracellular – major intracellular cation
% Absorption.	Over 90% absorbed
Deficiency Disease	
Deficiency Symptoms	Muscular weakness, mental apathy, cardiac arrhythmias, paralysis, bone fragility.
Groups at Risk	
Food Sources	Rank order: avocado, banana, dried fruits, orange, peach, potatoes, dried beans, tomato, wheat bran, dairy products, eggs. Fruits and vegetables are good sources of K
Recommended Intake	NRC recommends 2000 mg/d, but suggests that 3500 mg/d might be better
UL	
Enzymes/ Hormone Associated	Pyruvate kinase, Na^+/K^+-ATPase. Excretion regulated by aldosterone
Key Nutrient Interactions	Hyperkalemia - can cause cardiac arrest Hypokalemia – from vomiting/diarrhea Potassium is not as calciuric as Na.

	Sulfur
Function	Component of sulfur-containing amino acids, thiamin, biotin, lipoic acid.
% Absorption.	
Deficiency Disease	
Deficiency Symptoms	Unknown
Groups at Risk	
Food Sources	Protein foods (meat, poultry, fish, eggs, milk, cheese, legumes, nuts.
Recommended Intake	
UL	
Enzymes/ Hormone Associated	
Key Nutrient Interactions	

	Chloride
Function	Primary anion, maintains pH balance, enzyme activation, component of gastric hydrochloric acid. Most abundant anion in extracellular fluid • Negatively charged ion • Part of gastric HCl • Exchange for HCO_3^- in RBC
% Absorption.	Cl is almost completely absorbed – tends to follow Na Major route of excretion is kidney
Deficiency Disease	
Deficiency Symptoms	In infants: loss of appetite, failure to thrrive, weakness, lethargy, severe hypokalemia, metabolic acidosis
Groups at Risk	
Food Sources	Average consumption – far in excess of requirement Table salt, seafood, milk, meat, eggs
Recommended Intake	NRC recommends 750 mg/d; needs may be higher in very high tremperatures
UL	
Enzymes/ Hormone Associated	
Key Nutrient Interactions	

	Iron
Function	
% Absorption.	• 10-15% absorption • Strongly affected by iron status • Low iron stores increase absorption
Deficiency Disease	Iron Deficiency Anemia – RBCs are microcytic and hypochromic. Serum transferring receptors are high.
Deficiency Symptoms	• Pallor, listlessness • Behavioral disturbances, impaired performance on some cognitive tasks, short attention span • Decreased work capacity • Impaired immune system, etc. • Iron depletion – plasma ferritin drops & iron absorption increases • Iron Deficient Erythropoiesis – Plasma iron and transferring saturation decrease and EPP increases
Groups at Risk	• Infants and young children – low iron in milk, rapid growth & low stores • Adolescents in growth spurt • Females during childbearing years • Pregnant women – expanding blood volume, demands of fetus placenta, blood losses
Food Sources	• Ferric (Fe^{+3}) and ferrous (Fe^{+2}) • Western diet – 5 to 7 mg Fe/1000 kcal • Heme iron – from hemoglobin & myoglobin – meat, fish, poultry. 50-60% of iron in MFP is heme • Non-heme iron – from plant & dairy food, 40% of iron in MFP, in enriched products • Good sources of iron – red meats, enriched foods, whole grains, beans, dark green leafies, dried fruits • Dairy products tend to be low in iron • Organ meats are high but not popular
Recommended Intake	• Men 8 mg/d of iron • Women 19-50 18 mg/d of iron • Women > 50 8 mg/d of iron • Women, pregnancy 27 mg/d of iron
UL	Adults: 45 mg/d of iron
Enzymes/ Hormones	
Key Nutrient Interactions	• Ascorbic acid • Copper – need certuloplasmin • Zinc - 25:1 molar ratio of non-heme iron to Zn diminishes Zn absorption • Lead inhibits heme synthesis

	• Iron deficiency associated with dec. Se • Iron deficiency causes increase in lead absorption.

	Zinc
Function	• Part of many metalloenzymes (>70-200) • Growth and cell replication • Bone formation • Skin integrity • Cell-mediated immunity & host defense
% Absorption.	• Gastric acidity important • Carrier-mediated with passive absorption of high intakes • Enhancers include: citric acid, histidine, cysteine, glutathione, picolinic acid • Inhibitors include: phytate, oxalate, polyphenols, fibers, some other nutrients
Deficiency Disease	
Deficiency Symptoms	• Body reserves quickly exhausted • Some Zn metalloenzymes decrease with deficiency and some are conserved • Growth retardation – an early sign • Poor wound healing, dermatitis • Hypogeusia, nightblindness • Delayed sexual maturation
Groups at Risk	
Food Sources	
Recommended Intake	Women: 8 mg/d Men: 11 mg/d
UL	Adults: 40 mg/d
Enzymes/ Hormone Associated	• Carbonic anhydrase • Alkaline phosphatase • Alcohol dehydrogenase • Carboxypeptidase A, aminopeptidase • Superoxide dismutase – cytoplasm • Polymerases, kinases, nucleases, transferases, phosphorylases, transcriptases, phospholipase C, Δ-aminolevulinic acid dehydratase
Key Nutrient Interactions	• Zinc & Vitamin A (alcohol dehydrogenase, synthesis of RBP) • Copper (via metallothionein) • Folate (digestion requires Zn dependent enzyme) • Lead (interferes with heme synthesis)

	Copper
Function	• Ceruloplasmin – oxidase enzyme ○ Oxidizes Fe^{2+} to Fe^{3+} for transport ○ Also manganese • Superoxide dismutase in cytosol • Cytochrome c Oxidase • Lysyl oxidase • Amine oxidases and others
% Absorption.	• Usual absorption – 30-50%; lower % with higher doses • Organic acids increase absorption • Zinc interferes (via metallothionein), as do iron & Vit C
Deficiency Disease	• Hypochromic anemia • Neutropenia
Deficiency Symptoms	• Hypopigmentation of skin • Impaired immune functions • Bone abnormalities, especially demineralization
Groups at Risk	• Excessive Zn intakes •]Malabsorption syndromes • Menkes syndrome
Food Sources	• Richest sources – organ meats & shellfish • Nuts, seeds, legumes, dried fruits are also good sources • Endogenous copper from saliva & gastric & pancreatic secretions
Recommended Intake	RDA for adults: 900 μg/d
UL	10mg (10,000 μg)/d
Enzymes/ Hormone Associated	
Key Nutrient Interactions	• Ascorbic acid • Zn – induction of intestinal metallothionein • Iron – anemia with Cu deficiency • Se and others

	Selenium
Function	• Chemistry similar to sulfur; not a metal • Functions not completely understood • Cofactor for glutathione peroxidase • Necessary for iodine metabolism
% Absorption.	• Compounds like selenmethionine are absorbed like the amino acid • 50-80% absorption of selenoamino acids
Deficiency Disease	Diseases in livestock Keshan & Kashin-Beck's disease in China
Deficiency Symptoms	
Groups at Risk	• TPN patients, if not supplemented • Interacts in thyroid deficiency
Food Sources	• Animal products better sources than plants. • Vastly different soil concentrations
Recommended Intake	• Adults: 55 μg/d
UL	400 μg/d
Enzymes/ Hormone Associated	
Key Nutrient Interactions	

	Chromium
Function	• Potentiates action of insulin - perhaps by affecting insulin receptor • Increases cellular uptake of insulin • In diabetics in China, Cr improved impaired glucose tolerance - dietary Cr intakes not known. • Chromium may also improve lipid profiles
% Absorption.	• 0.5 - 2% • Absorption is dose dependent -- 2% of 10 microgram doses and 0.5% of 40 microgram doses • Enhancers: amino acids, soluble chelators, vitamin C • Inhibitors: alkalinity, phytates
Deficiency Disease	
Deficiency Symptoms	results in insulin resistance and hyperinsulinemia trauma and metabolic stress appear to increase the need for chromium
Groups at Risk	• Vegetarians who don't eat whole grains or brewer's yeast. • People who eat only refined grains and sugars.
Food Sources	• meats, whole grains, brewer's yeast
Recommended Intake	• AI women 19-50 25 micrograms/day • women > 51 20 micrograms/day • men 19-50 35 micrograms/day • men >51 30 micrograms/day
UL	Not possible to determine
Enzymes/ Hormone Associated	Potentiates insulin activity Binds to transferrin in blood
Key Nutrient Interactions	Refining sugar and grains can decrease Cr content. Heating acidic foods in stainless steel can increase their Cr concentration.

	Iodine
Function	• Iodide used for synthesis of thyroid hormones • Carried in blood by thyroid-binding globulin, albumin and transthyretin (prealbumin) • Free T_4 and T_3 interact with receptors • Affect gene expression & metabolic rate
% Absorption.	• Absorbed efficiently • Thyroid hormones absorbed unchanged • Selectively concentrates in thyroid glands (70-80%)
Deficiency Disease	Goiter • Problem in many countries • Prevalence >10%, called endemic goiter • Iodine deficiency in a fetus can cause cretinism - mental deficiency, hearing loss, deaf mutism, motor disorders • Iodizing salt is of some use
Deficiency Symptoms	Goiter deaf/mutism - iodine deficiency - children born of iodine-deficient mothers
Groups at Risk	• People who don't use iodized salt • Goiter belt across the midwest. • People who live in areas with low soil concentrations of I.
Food Sources	• Seafood • Dough conditioners
Recommended Intake	• RDA - 150 micrograms/d for men and women
UL	1,100 micrograms/day
Enzymes/ Hormone Associated	• Free T_4 and T_3 interact with receptors • Thyroxin - key hormone for affecting rate of metabolism
Key Nutrient Interactions	Goitrogens • Substances in the diet that interfere with iodide metabolism (these augment TSH & thyroid gland enlargement) • Substances like thiocyanate in cassava cause international nutrition problems • Goitrin in cabbage, cauliflower, broccoli, turnips, brussel sprouts, rutabaga, etc.

	Manganese
Function	• glycosyl transferases - collagen synthesis • Arginase - involved in urea formation • Superoxidase dismutase - prevents lipid peroxidation in mitochondria • And, other roles
% Absorption.	• Absorption is higher when iron status is poor • Fiber & phytate may decrease absorption • Accumulates in mitochondria • Easier to absorb from water than from food. Absorption % is higher.
Deficiency Disease	No worry of vegetarian for toxicity.
Deficiency Symptoms	Causes neurological defects (like Parkinson's disease). In rats - neonatal ataxia (lack of balance/wobble) due to defects in inner ear (collagen synthesis)
Groups at Risk	• Very rare in humans • miners • in liver failure, Mn accumulates • Japan - storing old batteries - Mn got into water table - causes Parkinson-like symptoms.
Food Sources	• whole-grain cereals, dried fruits, nuts, leafy vegetables, tea
Recommended Intake	• AI women, all ages 1.8 mg/day men, all ages 2.3 mg/day
UL	11 mg/day from food, water & supplements
Enzymes/ Hormone Associated	
Key Nutrient Interactions	Fe and Mn major conflict.

	Molybdenum
Function	• Not too much known about metabolism
% Absorption.	
Deficiency Disease	
Deficiency Symptoms	
Groups at Risk	
Food Sources	• Best sources are legumes, nuts and whole grains
Recommended Intake	• RDA for men and women = 45 micrograms/d
UL	• 2 milligrams (2000 micrograms)/d
Enzymes/ Hormone Associated	
Key Nutrient Interactions	

	Fluoride
Function	• 1942 - recognized inverse relationship between dental caries & fluoride intake • Nearly 50 yrs of drinking water fluoridation in U.S. Controversy: what if add too much? Mottled teeth < 6 yrs. old. Lubbuck, Tx. - mix water. One faucet to drink; one for other uses. Small towns - not safe for pregnant women and children to drink the water. • Bound in bone and teeth by apatite - replaces OH groups • Optimal water concentrations are 1-2 ppm
% Absorption.	•
Deficiency Disease	
Deficiency Symptoms	
Groups at Risk	
Food Sources	• Tea and fish bones • Ready-to-use infant formulas have fluoride
Recommended Intake	• AI for males 4 mg/day • females 3 mg/day
UL	• > 8 yr 10 mg/day
Enzymes/ Hormone Associated	
Key Nutrient Interactions	Adverse Effects: • Mottling of teeth • Skeletal fluorosis

241. How is absorption of fat-soluble vitamins different from absorption of water-soluble vitamins?

The absorption and transport of the fat-soluble vitamins, in contrast to that of the water-soluble vitamins, are closely associated with the absorption and transport of lipids. As with dietary lipids, optimal fat-soluble vitamin absorption requires the presence of bile salts. Similarly, the transport of the fat-soluble vitamins in the body occurs initially by chylomicrons. Moreover, the fat-soluble vitamins are stored in body lipids, although the amount stored varies widely among the four fat-soluble vitamins.

The body handles the water-soluble vitamins differently from the way it handles the fat-soluble vitamins. They are absorbed into portal blood, in contrast to fat-soluble vitamins and, with the exception of cyanocobalamin (vitamin B_{12}), they cannot be retained for long periods by the body. Any storage occurring results from their binding to enzymes and transport proteins. Water-soluble vitamins are excreted in the urine whenever plasma levels exceed renal thresholds.

242. Explain the structural relationship between beta-carotene and vitamin A.

β-carotene is a precursor (provitamin) to vitamin A. Carotenoids, like β-carotene, typically possess at least one unsubstituted β-ionone ring. Most carotenoids can be converted into retinal.

243. Where does most conversion of carotene to vitamin A occur?

Much β-carotene is converted to retinal & retinal in the intestinal mucosa.

244. What are key differences between retinoic acid and retinol? What impact do these differences have on safety?

Retinoic acid is a metabolite of retinal. Retinol is a vitamin A alcohol. Retinoic acid, in contrast to retinol, is picked up by the portal vein and transported in the plasma bound tightly to albumin. A and carotenoids (retinal) are transported by chylomicrons in lymph to tissues & the liver. Retinol is 70-90% absorbed. β-carotene is 20-50% absorbed. Therefore, vit A is more toxic than β-carotene. 13-cis retinoic acid (Acutane) has teratogenic effects (10x RDA can become toxic). β-carotene toxicity is not as likely.

245. Explain the relationship between retinol and rhodopsin.

Vit A combines with opsin to form rhodopsin. Light breaks down rhodopsin, frees all trans retinal and sends a signal to the optic nerve.

246. Explain the relationship between exposure to sunlight and vitamin D status.

Ultraviolet light on the skin converts 7-dehydrocholesterol to previtamin D_3 (cholecalciferol or calciol). You make it in your skin.

247. What is the most active form of vitamin D and how and where is it formed?

Following hydroxylation in the liver, 25-OH D3 bound to DBP is released into the blood and taken up by the kidney. In the kidney, a second hydroxylation of 25-

OH D_3 occurs at the 1 position, resulting in 1,25-$(OH)_2D_3$ (also called calcitriol), which is considered the active vitamin.

248. What does the most active form of vitamin D do?

Calcitriol, 1,25-$(OH)_2D_3$, synthesized in the kidney, is considered the active form of vitamin D and functions like a steroid hormone. Vitamin D interacts with cell membrane receptors and with nuclear vitamin D receptors to influence gene transcription.

249. What are the relationships between vitamin D and parathyroid hormone?

- As a hormone, calcitriol functions in the body with parathyroid hormone (PTH) in the homeostasis of blood calcium concentrations. Calcitriol also has a role in cell differentiation, proliferation, and growth.
- With PTH, calcitriol enhances Ca and P reabsorption in the distal renal tubule.
- PTH, alone or with calcitriol, mobilizes Ca and P from bone -- to keep blood Ca constant.
- Calcitrol may suppress PTH.

250. For which vitamins are there concerns about toxicity?

- A - hypervitaminosis; teratogenic effects of 13-*cis* retinoic acid (Acutane)
- D - (most likely of all when RDI chronically exceeded; anorexiz, n&v, FTT,Htn.)
- E - (least likely, but toxicity in premature infants suggests there is an UL)
- Folic acid - supplements > 5000 µg can mask B12 deficiency; >400 µg is drug.
- Niacin (B_3) - large doses given for high cholesterol, but undesirable side effects.
- B6 (sensory & peripheral neuropathy w/ 1-6g pyridoxine/d

251. What is carotenemia?

The presence of high levels of carotene in the blood, which result in an abnormal yellow appearance of the plasma and skin.

252. Where is tocopherol stored?

In foods of animal origin, vitamin E, primarily α-tocopherol, is found concentrated in fatty tissues of the animal. Absorbed tocopherol is incorporated into chylomicrons in the enterocyte and is transported through the lymph into circulation. Tocopherol is distributed to the tissues primarily by the LDLs and may play a role in protecting the LDLs from oxidation in the process. There is no single storage organ for vit E. The largest amount of the vitamin is concentrated in an unesterified form in the adipose tissue, with smaller amounts in liver, lung, heart, muscle, adrenal glands, and brain.

253. What effect does vitamin E have on the cell membranes?

Vitamin E maintains membrane integrity. It is an antioxidant - prevents oxidation of PUFA in phospholipids & hemolysis of RBCs. The cell membrane is particularly susceptible. Lungs, brain, and erythrocytes. Removal of peroxides & superoxide radicals. Vitamin E reacts with peroxyl radicals to terminate chain reactions.

254. What is a fat soluble vitamin that functions as an antioxidant?
Vitamin E (more effective), and vitamin A.

255. What biochemical reaction is affected by vitamin K and what is its relationship to Ca?
Blood clotting. Vitamin K binds calcium. Prothrombin binds Ca and forms thrombin, which catalyzes the proteolysis of fibrinogen to yield fibrin.

256. What factors decrease calcium absorption? Why?
Decreased by:

- Estrogen deficiency
- Fiber & phylate
- Oxalate (spinach, celery, berries, tea, cocoa)
- Competition with other divalent cations.

257. Describe the mechanism (hormones) by which calcium homeostasis is maintained.
Calcium us regulated by:

- PTH
    - In kidney:
        - Increases synthesis of calcitriol
        - Increases reabsorption of Ca by tubules
    - In bone
        - Stimulates degradation of bone (synergy w/PTH)
    - In intestine
        - Indirectly affects by stimulating formation of calcitriol in kidney.
- Calcitriol
    - In intestine:
        - Absorption increased by calbindin synthesis
    - In kidney:
        - With PTH may enhance Ca reabsorption
    - In bone:
        - With PTH may increase Ca resorption.
- Calcitonin
    - o Lowers serum Ca2+ by preventing Ca mobilization from the boner.
    - o Inhibits osteoclast activity.

258. When does peak bone mass occur?
By 35 years.

259. For what ages is the RDA for calcium 1000 mg? When is it higher?

RDA:	Ages 9-18	1300 mg/d	Higher
	Adults 19-30	1000 mg/d	
	Adults 51-79	1200 mg/d	Higher

260. How does exercise affect bone mass?

Weight-bearing activity results in loss of bone mass.

261. What effects do aluminum and magnesium hydroxide gels have on phosphate levels in the blood?

Hypophosphatemia, can occur with the chronic use of aluminum salts.[61-64] Along with phosphate loss, there is the potential for development of osteomalacia and osteoporosis. This occurs because aluminum binds to phosphate in the gut, which in turn prevents phosphate absorption.[65] Phosphate depletion leads to bone demineralization.

Identify advantages and disadvantages of their use.

Antacids. Antacids are salts (e.g., magnesium hydroxide, aluminum hydroxide, aluminum phosphate, calcium carbonate, and sodium bicarbonate) that react with gastric acid to increase the pH in the stomach and the duodenal bulb. Current uses include the treatment of gastritis, gastroesophageal reflux, peptic ulcer disease, hyperphosphatemia, calcium deficiency states, and hypomagnesemia. Aluminum toxicity is observed in patients with decreased renal clearance and chronic use of aluminum salt antacids.[58,59] The manifestations are neurologic and include myoclonus, encephalopathy, and seizures.[60] Additionally, constipation, bowel obstruction, bezoar formation, and electrolyte abnormalities, such as hypocalcemia and hypophosphatemia, can occur with the chronic use of aluminum salts.[61-64] Along with phosphate loss, there is the potential for development of osteomalacia and osteoporosis. This occurs because aluminum binds to phosphate in the gut, which in turn prevents phosphate absorption.[65] Phosphate depletion leads to bone demineralization. Patients who use aluminum hydroxide on a regular basis and complain of weakness or bone pain should be evaluated for calcium and phosphate depletion. In addition, these patients should have directed skeletal radiographs to look for osteomalacia and pathologic fractures.[66] Aluminum toxicity is treated with chelation therapy and hemodialysis.[67]

262. What is the primary function of magnesium?

- Bound to phospholipids as part of cell membranes.
- Stabilizes structure of ATP.
- Cofactor or activator of more than 300 enzymatic reactions.

263. Why is magnesium high in green leafy vegetables?

Chlorophyl"s center is Mg (like hemoglobin's center is Fe).

264. What is the major intracellular cation?

Potassium is the major intracellular cation. 98% intracellular.

265. What is the typical consumption of sodium in the U.S?

Estimated Na intakes ~1800-5000 mg/d (4.5-12.5 g salt). We consume way more than is required.

266. What are the most common ways that people lose excessive amounts of electrolytes such as sodium and potassium?

The chief cause of deficiency arises through alimentary disturbance such as severe diarrhea and vomiting. Diarrhea, vomiting, profuse sweating. major burns.

267. From what general sources do we get most of our dietary sodium?

Added Table salt. Processed foods ~ 75% of total Na.

268. What is the estimated safe minimum intake of sodium for an adult? How much salt is this?

115mg/d of Na is probably sufficient to replace obligatory losses and provide for growth.

269. Why do vegetarians tend to have higher potassium intakes than the rest of the population?

Fruits and vegetables are good sources of K. Vegetarians tend to eat more fruits and vegetables than the rest of the population.

270. We give little attention to the body's need for chloride? Why?

Cl is the most abundant anion in extracellular fluid. It is almost completely absorbed -- tends to follow Na, and the average consumption is far in excess of requirement.

271. Is achlorohydria usually due to a dietary deficit of chloride?

No. Achlorohydria is an abnormal condition characterized by the absence of hydrochloric acid in gastric secretions. It occurs most commonly in atrophy of the gastric mucosa, gastric carcinoma, and pernicious anemia. It is also found in severe iron deficiency anemia. Protein digestion is severely impaired.

272. Where in the hemoglobin molecule is iron bound?

Heme iron must be hydrolyzed from the globin portion of hemoglobin or myoglobin prior to absorption. Iron is bound to the porphyrin ring. The heme iron, unlike nonheme iron, remains soluble because of both degradation products of the globin and, if in the small intestine, the alkaline pH of the small intestine. Thus, heme containing the iron bound to the porphyrin ring is readily absorbed intact as a metalloporphyrin into the mucosal cell of the small intestine.

273. What effect does oxidation state have on the absorption of iron?

Iron, a metal, exists in several oxidation states varying from Fe^{6+} to Fe^{2-}, depending on its chemical environment. The only states that are stable in the aqueous environment of the human body and in food are the ferric (Fe^{3+}) and the ferrous (Fe^{2+}) forms. Absorption of iron is improved if the iron is present as ferrous iron. Ferrous iron transverses the glycocalyx and brush border of the intestine better than ferric iron. Ferrous iron then binds to receptors on the intestinal mucosal cell for absorption across the brush border.

274. What dietary factors impact iron absorption?

Overall absorption of iron is strongly affected by iron status. If Fe is depleted, it goes up.

The body controls how much of the nutrient enters. It's not perfect, though.

- Enhancers: (may increase from 2-3% to 8%)
  - Some acids, sugars, meat, fish, poultry, ascorbic acid
- Inhibitors:
  - Polyphenols, oxalic acid, phytates, EDTA, phosvitin, 300-6-- mg Ca & others.
  - Rapid transit, malabsorption, excess antacids, decreased gastric acidity.

275. What are iron storage compounds?

- Storage iron = that iron not needed in a functional capacity -- liver, bone marrow, and spleen (waiting to be used)
- Ferritin is primary storage form of iron in cells
- Hemosiderin -- another iron storage protein -- with iron overload.

Genetics & polymorphisms: hemechromotosis - excess Fe storage problem.

276. Why is iron deficiency anemia high in infants and children?

Low iron in milk, rapid growth & low stores. Typically born with low Fe stores. Particularly at risk is premature infant because Fe deposits are made in the last few months. Adolescents in growth spurt -- tissue growth.

277. Explain differences in heme and nonheme iron absorption?

Heme iron (derived from hemoglobin and myoglobin in MFP) is absorbed intact into the enterocyte and hydrolyzed within the intestinal cell to yield ferrous iron. Nonheme iron (from plants, i.e. nuts, fruits, vegetables, grains and tofu and dairy products such as milk, cheese, eggs), following release from food components, is typically present in the stomach in the ferric state. Ferric iron may or may not be reduced in the stomach to the ferrous state. Non-heme iron is less well absorbed.

278. Does iron status influence iron absorption?

Yes. Overall absorption of iron is strongly affected by iron status. If Fe is depleted, it goes up. The body controls how much of the nutrient enters. It's not perfect, though.

279. Where is iron stored in the body?

1. • Storage iron = that iron not needed in a functional capacity -- liver, bone marrow, and spleen (waiting to be used)
2. • Ferritin is primary storage form of iron in cells
3. • Hemosiderin -- another iron storage protein -- with iron overload.

Genetics & polymorphisms: hemechromotosis - excess Fe storage problem.

280. Why are parasites so detrimental to iron status?

Iron losses increase in the presence of intestinal parasites because parasites use the iron for their own growth.

281. What protein carries iron in the blood stream?

Iron is attached in the ferric state to transferrin in the blood. Binding of iron by protein prevents the use of iron by bacteria for their own growth. Most iron in the plasma is from hemoglobin destruction & release from storage.

282. What is the best measure of iron stores?

Ferritin can be measured in serum. It can estimate Fe stores. Radio-immune assay.
1mg ferritin/L in serum = 10 mg body iron stores.)

283. Where are red blood cells synthesized?

Production of the RBCs occurs in the bone marrow.

284. What is hemochromatosis?

The term hemochromatosis is used to indicate iron overload or toxicity, which is coupled with tissue damage. Hemochromatosis is most often seen in aduly Caucasian males and begins to occur around 20 years of age. The condition is characterized by increased (at least two times normal) iron absorption with deposition of iron as hemosiderin in the parenchymal cells of the liver and other organs such as the heart, causing damage to the tissues. It is a genetically (autosomal recessive) transmitted ideopathic trait.

285. Is hemoglobin a sensitive measure of iron stores? Why or why not?

Numerous measurements are used for the assessment of iron nutriture. The most common indices are hemoglobin and hematocrit, which indicate the presence of anemia. Hemoglobin measures the amount of Hb per unit. Hematocrit measures the proportion of the total blood volume that is RBCs. These measures are not too useful with mild deficiency, but are better with severe deficiency. Ferritin as a measure of iron stores is more helpful. Evaluation of iron stores is much more valuable because iron deficiency occurs in three stages beginning with depletion or iron stores.

- Stage 1 - depletion of iron stores in the liver, spleen, and bone marrow.
- Stage 2 - Plasma ferritin concentrations diminish and the number of transferrin receptors on the cell surface increases, representing an up-

regulation to enable cells to better compete for iron that is bound to transferrin.

- Final stages - anemia occurs as indicated by low blood hemoglobin concentrations. Blood hemoglogin concentrations of < 12 g/dL and 14 g/dL for females and males, respectively, are suggestive of iron deficiency anemia. Hematocrit concentrations of <37% and 40% for women and men, respectively, also are typical of iron deficiency anemia. Serum ferritin and transferrin saturation remain depressed, free protoporphyrin remains elevated. Serum iron (which includes the iron on transferrin, but not in ferritin) is diminished, TIBC is elevated, and hemoglovin, hematocrit, MCH, MCHC, and MCV are lower than normal. Red blood cells are pale (hypochromic) and small (microcytosis).

286. What dietary factors affect the bioavailability of zinc?

- Gastric acidity is important.
- Carrier-mediated with passive absorption of high intakes.
- Enhancers include: citric acid, histidine, cysteine, glutathione, picolinic acid.
- Inhibitors include: phytate, oxalate, polyphenols, fibers, some other nutrients.

287. Identify a zinc dependent enzyme which would explain the dramatic effect of zinc on growth?

- Alkaline phosphatase - hydrolyzes monoesters of phosphates.
- Alcohol dehydrogenase - conversion of alcohols to aldehydes such as retinol to retinal.
- Carboxypeptidase A, aminopeptidase - digestion of protein.
- Superoxide dismutase - in cell cytoplasm, catalyzes the removal of superoxide radicals.
- Phospholipase C - catalytic activity to release PO_3 from phospholipids.
- Polymerases, kinases, nucleases, transferases, phosphorylases, transcriptases, phospholipase C, δ-aminolevulinic acid dehydratase - paramount to nucleic acid synthesis are the zinc metalloenzymes DNA and RNA polymerase and deoxythymidine kinase. Physiological functions of zinc include tissue or cell growth (i.e., regulation of protein synthesis), cell replication, bone formation, skin integrity, cell-mediated immunity, and generalized host defense.

288. Why are vegetarians at risk in terms of zinc status? Would this include all types of vegetarians?

Zinc is found in food complexed with amino acids that are part of peptides and proteins, and with nucleic acids. Very good sources of zinc are red meats (especially organ meats) and seafood (especially oysters and mollusks). Animal products are thought to provide between 40% and 70% of zinc consumed by most people in the US. Other good sources of zinc include poultry, pork, and dairy products. Whole grains (especially bran and germ) and vegetables (leafy and

root) represent good plant sources of zinc. Zinc from plant sources is not only lower in content but also absorbed to a lesser extent than from meat. Lacto-ovo-vegetarians get zinc from eggs, milk, and cheeses, so would not be at risk in terms of zinc status.

289. What good source of copper do you most commonly consume?

Nuts, seeds, legumes, dried fruits.

290. What protein is the carrier for copper in the blood stream?

Ceruloplasmin carries copper in the blood and delivers it to tissues. Ceruloplasmin - oxidase enzyme oxidizes Fe^{2+} to Fe^{3+} for transport.

291. Identify dietary substances that facilitate or inhibit copper absorption.

- Usually bound to a.a. in proteins. Active & passive absorption. Usually 30-50%; lower % with higher doses.
- Organic acids increase absorption. Cu takes on the absorptive characteristics of whatever it binds to.
- Zinc interferes (via metallothionein), as do iron & vitamin C.

292. What is metallothionein?

Metallothionein serves as a cellular storage site for metals, primarily zinc, but also copper cadmium, and mercury. Metallothionein is found in most tissues of the body, including the liver, pancreas, kidney, intestine, and red blood cell. Liver and RBC metallothionein-bound zinc diminishes as dietary zinc intake decreases and is thus thought to reflect zinc status or stores. Zinc and possibly other minerals appear to affect the gene expression of metallothionein.

293. What problems might be expected if there were inadequate amounts of the trace mineral which is a cofactor for superoxide dismutase?

SOD found in the cell cytoplasm requires two atoms each of both zinc and copper for function; zinc appears to have a structural role in the enzyme. This important enzyme catalyzes the removal of superoxide radicals, Ox-. 2O2- + 2H+ ---> H2O2 + O2 Superoxide radicals can cause peroxidative damage of phospholipid components of cell membranes. In other words, without SOD, superoxide radicals can form more destructive hydroxyl radicals that damage both unsaturated double bonds in fatty acids in cell membranes and other molecules in cells. SOD therefore assumes a very important protective function. SOD is found in most cells of the body. Increased peroxidation of cell membranes is found with copper deficiency.

For lysyl oxidase?

Lysyl oxidase is secreted by connective tissue cells and serves to generate cross-linking between connective tissue proteins including collagen and elastin. The cross-linking is needed to stabilize the extracellular matrix. Specifically, lysyl oxidase catalyzes the removal of the epsilon amino group of lysyl residues of a polypeptide and the oxidation of the terminal carbon atom of an aldedhyde. Lysyl oxidase activity decreases with inadequate copper intake. Thus, collagen cross-

linking appears to be affected by dietary copper (i.e., synthesis of collagen). Collagen is found in the tendons, ligaments, and the fascia. It is found in connective tissue, including skin, bone, ligaments, and cartilage. It represents 30% of total body protein.

294. Can you think of reasons why large doses of zinc might impair wound healing?

Excessive intakes of zinc can result in a copper deficiency due to the competition of these two minerals for intestinal absorption. Elimination of excess zinc by the body is a slow process and will continue to inhibit copper absorption until it is eliminated. Primary functions of copper in the body are for collagen, and wound healing. So, large doses of zinc might impair wound healing by causing competition for copper absorption.

295. What is the major extracellular cation?

Sodium.

296. What is the major intracellular cation?

Potassium.

297. What are the most important elements/compounds contributing to osmotic pressure of the extracellular fluid?

Osmotic pressure of plasma and interstitial fluid - largely due to protein molecules.

298. Is protein concentration higher in the plasma or in the interstitial fluid? What are the major proteins involved?

ISF is much lower in protein than is plasma. (Therefore, plasma attracts water.)

299. How does the concentration of protein in plasma affect edema?

Reabsorption force is primarily plasma osmotic pressure. Albumin is small. Several g./100 ml. so lots of osmotic pressure. Must move water against gravity from feet to heart, so this helps get water into the blood. Sodium increases osmotic pressure and draws water into the blood stream. Without it, fluid accumulates in the lower limbs.

300. What are the major systems that control our fluid and electrolyte balance?

- Hypothalamus via antidiuretic hormone (ADH or vasopressin)

- Renin-angiotensin-aldosterone (aldosterone produced in adrenal cortex).

- Both of the above exert their effects through the kidney.

301. What organ or tissue is most important for regulation of water balance?

Kidney.

302. What is antidiuretic hormone?

- Water-conserving hormone
- Increases reabsorption of water in distal convoluted tubule & collecting duct.

303. What regulates the release of ADH?

- Hormone released from storage in response to:
  - Increased ECF osmolarity
    Plasma is ECF so retain more water in blood if osmolarity in plasma

  - Decreased intravascular volume
    Secrete ADH ---> retain water ---> increase blood volume.

304. How does ethanol affect the release of ADH?

Secretion is inhibited by alcohol ---> increases urination because in interferes with ADH.

305. What is the stimulus for secretion of aldosterone?

Release stimulated by:

- Increased angiotensin II (under normal conditions).
- Decreased atrial natriuretic peptide (ANP)
- Increased potassium (K^+)
- Decreased sodium (maintain blood volume)

306. What is rennin?

- Proteolytic enzyme

- Release stimulated by decreased renal perfusion pressure
- Hydrolyzes angiotensinogen to angiotensin I (affects aldosterone to increase BP)

307. What effect does aldosterone have on Na concentration in the blood? What is the overall result of increased aldosterone secretion?

Sodium reabsorption is increased by aldosterone.

308. How effective is the sensation of thirst in controlling water balance?

It is not sensitive enough to protect an athlete in timely fashion. You become fairly dehydrated before you feel thirst, and you can override the sensation instead of stopping to drink. Elderly persons lose the acuity of the thirst sensation and may become dehydrated before they actually feel thirsty.

309. Is most of the glomerular filtrate resorbed OR excreted?

The glomerulus filters ~130mL/min or >187,000 mL/d, and the kidney only produces ~1400mL or urine, so <u>>99% of the filtrate is reabsorbed</u>.

310. Is Na the only nutrient which has been implicated in hypertension?

Potassium intake has been linked to reduction in blood pressure.

311. Does metabolism generate mostly acidic or mostly basic compounds?

Metabolism of energy nutrients continually produces <u>acid,</u> therefore urine pH is below neutral. Should always be acidic.

312. What are three different mechanisms by which the body can control acid base balance?

Buffers

Respiratory regulation of pH

Renal regulation of pH

313. Explain how impaired breathing can change acid/base balance.

If plasma pH rises (less carbonic acid), respiratory rate is decreased (breathe more slowly and pH decreases). With emphazema or asthma, there is a potential for change in blood pH (build up of acid in the blood). A rapid drop makes the blood too acidic. The renal system kicks in, but the person can go into acidosis.

314. How does the respiratory center in the brain respond to acidity of the extracellular fluid?

If plasma CO2 increases

- More carbonic acid is formed which decreases pH
- Respiratory rate increases (body tries to reduce CO2).

The more CO_2 produced, the more acid. Breathe more rapidly. Remember RQ = CO_2/O_2.

315. Do diabetic patients tend to have acidosis or alkalosis? Why?

Acidosis. Ketone bodies are acidic. They are short: acetone & butyric acid.

316. Identify conditions that would cause respiratory acidosis or respiratory alkalosis?

Respiratory acidosis: inability to exhale CO_2 (emphazema, asthma).

Respiratory alkalosis: hyperventilation (breathe off too much CO_2).

317. What is carbonic anhydrase and what is its role?

Enzyme responsible for getting rid of CO_2.

318. What hormones affect the reabsorption of Ca in the kidney?

Renal reabsorption of Ca is closely linked to PTH.

319. What happens in the glomerulus?

- Filter to remove water and other substances < 50,000 daltons
- Water, glucose, amino acids, metabolic wastes make up glumerular filtrate.
- Large particles are not filtered except in disease states.
- Filtrate passes to tubules where some materials are salvaged.

320. What is a placebo effect?

A placebo is a non-active ingredient. The placebo effect does not mean no effect, however. The pt. may feel better from paying attention to diet or other variables.

321. Distinguish between prospective and retrospective research?

Prospective studies - follow up over time.

Retrospective research - Looking back, for instance at people who died from cancer. How are they similar? Compare with age-related controls. Retrospectively, what was different in the groups?

322. What is a double-blind study?

Neither the researcher nor the subjects know which group is control and which is experimental.

323. Give examples of qualitative and quantitative research.

Qualitative -data are verbal (historical research, descriptive survey)

Quantitative - data are numerical (analytical surveys, experimental methods)

324. Does epidemiological research demonstrate relationships or cause and effect?

Study of distribution of condition in population and the factors that influence the distribution. It is an exciting way to point to areas for study. The porblem is that it does

not demonstrate cause and effect; just relationship. There are lots of conflicting relationships. It raises questions, but doesn't define whether it affected your results.