Question 1:
A 14-year-old youth has had intermittent periumbilical and lower abdominal pain, some bloating, and increased flatus for 2 years. He denies a relationship of the pain to food or drink, and a milk-free diet did not relieve his symptoms. He has had no fevers, diarrhea, constipation, bleeding, or other systemic problems and his growth is normal. He eats a regular diet, including diet soft drinks and sugar-free gum. His family is intact and he denies undue stress in his school or social life. He also denies alcohol, drug use, or smoking. Physical examination is normal, including heme occult negative rectal examination. Screening laboratory tests including complete blood count, ESR, liver enzymes and amylase, and urinalysis are normal. Which one of the following would be the most likely etiology of the abdominal complaints in this teenager?

A. lactose intolerance
B. excessive sorbitol intake
C. irritable bowel syndrome
D. teenage stresses
E. acid-peptic disease

Suggested answer: B or C. Sorbitol is a FODMAP (fermentable oligo-, di-, and monosaccharides and polyols), metabolized by colonic bacteria to produce short chain fatty acids and gas. Sorbitol is commonly found in diet soft drinks and sugar-free gum. When taken in excess, sorbitol produces enough gas to produce abdominal pain and bloating as in this patient. Sorbitol can also cause a persistent, osmotic diarrhea.

Irritable bowel syndrome, the most commonly diagnosed gastrointestinal condition, is diagnosed by the presence of 3 things: i) chronic abdominal pain, ii) altered bowel habits (constipation or diarrhea, which is may or may not be present in this patient), and iii) no organic cause. The etiology of IBS in unclear; however, one hypothesis is that bacteria cause IBS, by fermenting FODMAPs in the colon. FODMAPs have been shown to produce IBS symptoms in clinical trials. Treatment for IBS is broad, and includes a strong physician-patient relationship, avoiding certain foods (lactose, allergens, gluten), anti-spasmodics, anti-depressants, anti-diarrheal agents, and/or antibiotics.

This patient does not have lactose intolerance, as a milk-free diet did not relieve his symptoms. He should resume drinking milk, or at least receive calcium and Vitamin D supplements to support growth. In addition, the patient does not report excessive stress, and does not have typical GERD symptoms.

Question 2:
A 9-year-old girl has been losing hair for about 2 years and now presents with a large mass in her epigastrum. Her parents separated about 3 years ago. The patient and her siblings have been spending part of each week at each parent's home. A plain film of the abdomen reveals a large mass in the stomach. Endoscopy reveals a trichobezoar. What do you now recommend to the family?

A. administer meat tenderizer orally
B. endoscopic removal of bezoar under anesthesia
C. abdominal CT scan to rule out gastric tumor
D. surgical consultation for removal of bezoar

E. reassurance that the bezoar will pass

Suggested answer: D. Trichobezoars usually occur in young women with psychiatric disorders, and in some cases may extend through the small bowel and even cecum (Rapunzel syndrome). Phytobezoars (from vegetable matter) are responsive to enzymatic dissolution, including cellulase, papain, and carbonated soda. Trichobezoars are resistant to enzymes and must be removed manually. Endoscopy can be attempted but often fails, with the endoscopic tools becoming snared in the strands of hair. Surgical removal is more effective. All patients should receive psychiatric therapy to prevent the problem from reoccurring.

Question 3:

Among the hepatitis viruses, the hepatitis B virus (HBV) is unique because:

A. liver injury is mediated through the immune system
B. the presence of antibodies to HBV indicates protective immunity
C. it has similarities to human retroviruses because it is a DNA virus which replicates through an RNA intermediate
D. it is the only agent to cause fulminant hepatic failure
E. it has a glycoprotein coat enclosing a viral nucleocapsid

Suggested answer: C. HBV is a DNA virus that enters the hepatocyte nucleus and is read by host-cell machinery to make RNA particles. The RNA particles in turn are exported to the cytoplasm, where HBV-encoded reverse transcriptase converts them to new viral DNA particles. Infection can be acute and cause fulminant hepatic failure; however, chronic infections characterized by a series of stages are more common. First, in the "immune tolerant" phase, the host allows HBV infection and replication as seen by high HBV DNA levels and HBeAg positivity. Second, in the "immune clearance" phase, the host mounts an immune response against infected hepatocytes, signified by the appearance of anti-HBe, disappearance of HBe-Ag, transaminase elevation, and hepatitis symptoms. In some cases, the host clears the virus completely (anti-HBs appears, HBsAg disappears); in other cases, the virus becomes latent and can reactivate/stimulate the "immune clearance" phase at unpredictable times. The virus has a glycoprotein envelop enclosing a proteinaceous nucleocapsid.

HAV is an RNA virus that never enters the nucleus; rather, in the cytoplasm, it makes more particles using its own RNA-dependent RNA polymerase. Infections are acute and can cause fulminant hepatic failure. Infections have a biphasic pattern, first with viral replication (akin to the HBV "immune tolerant" phase") quickly followed by immune attack of virus and cells harboring the virus (akin to the HBV "immune clearance" phase, and characterized by appearance of anti-Hep A IgM and hepatitis symptoms). The virus does not have an envelope, but does have a proteinaceous nucleocapsid surrounding the RNA.

HCV is an RNA virus like HAV but has an envelope. It also never enters the nucleus, but rather enters the cytoplasm, takes over the cell's ribosomal machinery, and converts the cell into a factory producing viral proteins that generate more viral nucleic acid and particles. Viral particles then bud off the cells (using the cell's plasma membrane for an envelope) and infect other cells. Acute infections are mild or even asymptomatic, and fulminant hepatic failure is rare. Chronic infections are more common, and occur when the host cannot completely clear

the infection. This long-term, low-level battle between host and virus leads to liver inflammation, cirrhosis, and hepatocellular carcinoma.

HDV is an RNA virus with an envelope like HCV; however, the envelope has HBsAg, making HDV replication possible only in cells also infected with HBV. HDV enters the nucleus, and host-cell RNA polymerases use the original HDV strand to make more RNA particles. Acutely, HDV is thought to cause cytopathic damage to hepatocytes and may be confused with HBV reactivation (see above). Fulminant hepatic failure is possible. Chronically, the host immune response to HDV infected cells causes hepatocyte damage.

HEV is an RNA virus without an envelope, similar to HAV. The life cycle is less well-understood, but HEV appears to never enter the nucleus (similar to HAV). Instead, in the cytoplasm, the virus makes more particles using its own RNA-dependent RNA polymerase. Infections are usually acute and can cause fulminant hepatic failure. Chronic infections have only been reported in solid-organ recipients taking post-transplant immunosuppression.

Question 4:

Common routes of the spread of hepatitis A virus include all of the following except:

A. consumption of contaminated water or food
B. close personal contact
C. infants in daycare centers
D. homosexual men by sexual contact
E. transfusion of packed red blood cells

Suggested answer: E. Hepatitis A is shed in bile, found in stools, and spread fecal-orally. Hence, it can be spread through consumption of contaminated water/food, close personal contact (without proper hand-washing), infants in close proximity in a day care, and other close contact such as anal-oral sexual contact. Interestingly, infants that acquire HAV infection have a less severe course, perhaps because of a less developed immune system. HAV is not spread through blood transfusions.

Question 5:

Serological changes associated with being a healthy carrier of the hepatitis B virus are:

A. HBsAg positive, HBeAg positive, HBV DNA negative by hybridization assay, with normal serum aminotransferases
B. HBsAg positive, HBV DNA negative by hybridization assay, anti-HBe positive, with normal serum aminotransferases
C. HBsAg negative, anti-HBs positive, anti-HBe positive
D. HBsAg negative, anti-HBs negative, anti-HBe positive
E. HBsAg positive, HBV DNA positive by hybridization assay, HBeAg negative, with only slightly elevated serum aminotransferases

Suggested answer: E. Inactive carries are those who were once infected with Hepatitis B and mounted a successful immune response against it. During the infection or "immune tolerant" phase, these patients had HBV antigens and DNA in their serum (HBsAg positive, HBeAg positive, HBV DNA virus positive) but have not yet mounted an immune response (anti-HBe

negative as well as anti-HBs negative). During the immune response or "immune clearance" phase, these patients developed antibodies against the virus (anti-HBe positive) as well as a clinical picture of hepatitis (elevated transaminases). Their immune response is effective but not complete, rendering them carriers with evidence of the virus still present (HBsAg positive, HBV DNA hybridization positive) but also evidence of a successful response (anti-HBe positive causing HBeAg negativity). Carriers may also have slightly elevated aminotransferases. Had their immune response been complete, the patients would be cured of the disease and be anti-HBs positive, HBsAg negative, anti-HBe positive, HBeAg negative, and HBV DNA negative.

Question 6:

All of the following statements about hepatitis E are true, except:

A. outbreaks of hepatitis E tend to be very large because of the high rate of secondary (case-to-case) spread
B. cases of hepatitis E in the United States are rare
C. infection with hepatitis E virus (HEV) in pregnancy is associated with high mortality rate
D. anti-HEV appears to be protective, and prospects for developing a vaccine are good
E. HEV is not closely related in structure or function to any of the other viral hepatitis agents

Suggested answer: A. While the seroprevalence of HEV is ~20% in the US, symptomatic HEV infection is rare (perhaps because most infections may be with the less virulent genotype 3). HEV is acquired through contaminated water and rarely spreads person-to-person, making it less readily transmissible than HAV. Following HEV infections, humans develop anti-HEV IgM and then anti-HEV IgG. There are no HEV vaccines readily available yet, though some are being developed. HEV has a unique genome and structure and is the only member of the genus hepevirus in the family Hepeviridae.

HEV is most dangerous during pregnancy. For unclear reasons, women infected in the third trimester have an increased risk of hepatic failure and mortality (15-25% mortality rate). This may because the virus replicates faster in the pregnancy state. Furthermore, infants born to infected mothers are also at risk, with some presenting with massive hepatic necrosis shortly after birth.

Question 7:

Recognized complications of acute hepatitis A include all of the following except:

A. fulminant hepatic failure
B. relapsing hepatitis C
C. chronic hepatitis
D. cholestatic hepatitis
E. triggering autoimmune hepatitis

Suggested answer: B. HAV most commonly causes an acute, self-resolving hepatitis. However, it has been associated with a variety of other presentations: i) fulminant hepatic failure (rare); ii) relapsing, chronic hepatitis characterized by HAV-caused hepatitis interspersed between long periods without symptoms (prognosis is excellent, with no reports of cirrhosis or chronic liver disease); iii) cholestatic hepatitis characterized by prolonged jaundice, itching, and laboratory

abnormalities, which eventually self-resolves with supportive care; and iv) triggering of autoimmune hepatitis, which develops months after the initial HAV infection.

Question 8:
A 45-year-old woman is undergoing treatment for chronic hepatitis C with the combination of interferon (3Φ three times a week) and ribavirin (1000 mg per day). Prior to therapy she was found to have cirrhosis but there was no evidence of hepatic decompensation. Her baseline blood count was hemoglobin 13.9 g/dL, MCV 89, total white cell count 4200/mm^3, platelet count 92,000/mm^3. After 6 weeks of therapy, her blood count was hemoglobin 9.9 g/dL, MCV 102, total white cell count 2500/mm^3, platelet count 47,000/mm^3. The best course of action is:

A. decrease the dose of ribavirin to 600 mg/day
B. decrease the dose of interferon to 1.5Φ three times a week
C. administer recombinant human erythropoietin
D. decrease the dose of both ribavirin (to 600 mg/day) and interferon (to 1.5Φ three times a week)
E. check serum levels of folate and vitamin B_{12} and correct if deficient

Suggested answer: D. This patient is being treated with interferon and ribivarin, which implies she has either genotype 2, 3, or 4 (genotype 1 is treated with interferon, ribivarin, and a protease inhibitor). Interferon strengthens the innate and adaptive immune response, whereas ribivarin is a nucleoside analog.

80% of patients taking interferon and ribivarin have side-effects. Anemia usually appears in the first 12 weeks, caused by ribivarin-induced hemolysis (ribivarin is concentrated in erythrocytes leading to oxidative damage) and interferon-related bone marrow suppression to blunt a compensatory response. Neutropenia and thrombocytopenia occur soon after treatment initiation and are due to interferon-related bone marrow suppression. Ribivarin dose reduction would treat the anemia, whereas Interferon dose reduction would treat the thrombocytopenia. Erythropoietin is another medication that has been shown to improve the anemia, possibly without needing to reduce the ribivarin dose.

Question 9:
An 18-year-old Asian woman is being treated for hepatitis B. Prior to therapy she was found to have ALT 198 U/L, AST 91 U/L, normal bilirubin, albumin, and prothrombin time. Liver biopsy results showed chronic hepatitis B, grade 3, stage 3. After 12 weeks of therapy, serum ALT is found to have increased to 1,082 U/L, bilirubin 2.1 mg/dL but albumin and prothrombin time remain normal. Apart from some fatigue, the patient is tolerating interferon well. The best course of action is:

A. check for antinuclear antibodies and total immunoglobulin level in serum and consider instituting corticosteroid therapy
B. stop interferon
C. recheck lab work again in 2 weeks time
D. add lamivudine to the regimen
E. ask the patient to skip three scheduled doses of interferon

Suggested answer: C. Interferon and the antiviral lamivudine are used to treat HBV infection in children. Interferon is dosed for 16 weeks, has numerous side effects, and leads to serological conversion (presence of anti-HBe positive and HBeAg negative) in 40% (genotypes A and B) to 5-15% (genotypes C and D) cases. Lamivudine is taken indefinitely and has similar rates of seroconversion after 2 years (~30-35%). Lamivudine, however, induces viral resistance, with rates greater than 60% reported after 3 years of use.

This patient is taking interferon. Interferon causes a rise in AST/ALT in 30-40% of cases, likely because it stimulates the immune system to destroy infected hepatocytes. Hence, this rise is a sign the medication is working. Had the patient been taking lamivudine, a rise in AST/ALT could also signify development of viral resistance. Interferon does induce autoantibodies that can be symptomatic (i.e. hypothyroidism, hyperthyroidism) but this is less common. Interferon should not be stopped, because the patient's fatigue is only mild. Adding lamivudine to the interferon regimen may decrease viral load faster, but has not been shown to produce better virological outcomes after the 16 week course has finished. (On the other hand, combination therapy with lamivudine plus interferon, versus lamivudine alone, may prevent development of viral resistance.)

Question 10:
All of the following are primary cellular components of the immune system and the gut mucosa except:
A. Peyer's patches
B. lamina propria lymphocytes
C. intrapithelial lymphocytes
D. IgG-secreting B lymphocytes
E. IgA-secreting B lymphocytes

Suggested answer: D. The gut is the largest lymphoid organ in the body. Specialized epithelial cells, called M cells, sit above Peyer's patches and sense luminal antigens. The M cells then stimulate naïve B and T cells in the Peyer's patches. The naïve cells undergo a long maturation process, during which they take a long circular course to eventually return to the gut mucosa (Peyer's patches → regional lymph nodes → lymphatics → thoracic duct → systemic circulation → exit in the lamina propria). In the lamina propria, they reside and perform their immune surveillance functions. In addition, special memory T-cells called intraepithelial lymphocytes are anchored to the epithelial layer. They respond to a subset of luminal antigens, and secrete cytokines to mediate the inflammatory response.

B cells that mature into plasma cells ultimately residing in the lamina propria have special functions. They mainly secrete IgA2 and very little IgM and IgE, but virtually no IgG. IgA2 differs from the IgA1 made by plasma cells in the circulation. IgA2 molecules are dimeric and secreted into the luminal space only after transiting through epithelial cells (via endocytosis followed by exocytosis). Furthermore, IgA2 molecules are essentially non-inflammatory because they bind antigens but do not activate complement. As a result, IgA2 molecules neutralize antigens without triggering excessive inflammation to the countless number of gut antigens.

Question 11:

Cells from intestinal lymphoid tissues migrate to all of the following immune tissues except:
A. gastrointestinal mucosal immune tissues
B. pulmonary mucosal immune tissues
C. genitourinary tract
D. lactating mammary glands
E. skin

Suggested answer: E. The "common mucosal immune system" refers to the interconnected mucosal organs that house IgA2 secreting plasma cells (which initially started as naïve B cells in Peyer's patches). These mucosal organs include the lamina propria of the small intestine, the salivary and lacrimal glands, the lactating mammary glands, the genitourinary tract, and the lungs. Migration to these areas is mediated by specific cell adhesion molecules.

Question 12:
Which one of the following most accurately reflects the epidemiologic features of inflammatory bowel disease?
A. the prevalence is approximately 100 cases per 100,000 general population
B. the prevalence is approximately 1,000 cases per 100,000 general population
C. non-Jews are more likely to develop Crohn's disease than Jews
D. people who smoke are less likely to get Crohn's disease
E. people who smoke are more likely to get ulcerative colitis

Suggested answer: A. The epidemiology of inflammatory bowel disease has been well studied. In North America, UC has prevalence of 27-246 per 100,000 persons, and Crohn disease has a prevalence of 26-201 per 100,000 persons. There is a negative correlation between smoking and UC, and a positive correlation between smoking and Crohn disease recurrence. People of Jewish descent have a higher risk of developing Crohn disease compared to non-Jews, highlighting the partly-genetic etiology of the disease.

Question 13:
Which one of the following extraintestinal manifestations of inflammatory bowel disease do not parallel the course of intestinal inflammation and do not improve in parallel with improvement in intestinal symptoms?
A. peripheral arthritis
B. apthous ulcers
C. spondylitis and sacroiliitis
D. erythema nodosum
E. uveitis and iritis

Suggested answer: C. Arthritis is the most common extra-intestinal complications of IBD. Peripheral arthritis usually involves large joints, does not cause synovial destruction, and parallels the course of intestinal symptoms. Central axial arthritis, such as ankylosing spondylitis (characterized by back and progressive spinal stiffness) is similar to primary sclerosing cholangitis in that it does not follow the course of intestinal disease. Treatments for axial arthritis include NSAIDs (despite concern for inducing worsening intestinal inflammation),

methotrexate, sulfasalazine, and/or anti-TNF therapy. Apthous ulcers, erythema nodosum, uveitis, and iritis often (but not always) parallel intestinal disease.

Question 14:

All of the following urinary tract complications may occur as a consequence of Crohn's disease except:

A. calcium oxalate renal stones
B. calcium phosphate renal stones
C. uric acid renal stones
D. ureteral obstruction due to retroperitoneal fibrosis
E. fistulous communication between the terminal ileum and the bladder

Suggested answer: B. There are two general mechanism by which Crohn disease affects the renal system. First, transmural inflammation can affect the underlying ureters, causing occlusion usually on the right side and hydronephrosis. Inflammation can also create fistulas between inflamed bowel and the bladder, promoting cystitis and urinary tract infections.

Second, Crohn disease is associated with calcium oxalate and uric acid renal stones. Calcium oxalate stones form when the ileum is affected, preventing proper absorption of fats. Unabsorbed long-chain fatty acids compete with the insoluble calcium oxalate for calcium. Without calcium, oxalate binds sodium, becomes soluble, is absorbed by the colon ("enteric hyperoxaluria"), and eventually re-precipitates as calcium oxalate stones when excreted in the urine. Calcium is an effective treatment. Uric acid stones form secondary to bicarbonate loss with diarrhea. With low serum bicarbonate, the kidneys excrete acid in compensation. Uric acid, which is soluble in alkalotic conditions, precipitates as stones in the low pH urine.

Question 15:

All of the following statements regarding the release of mesalamine (5-aminosalicylate) by the following delivery systems are true except:

A. the dose form Pentasa releases throughout the small and large intestine beginning in the duodenum and continuing through to the rectum
B. the dose form Asacol releases beginning in the terminal ileum and cecum and continuing through to the rectum
C. the dose form olsalazine (Dipentum) releases throughout the colon beginning in the cecum and extending to the rectum
D. mesalamine administered as a Rowasa suppository extends to the left colon and splenic flexure
E. no exception

Suggested answer: A. Sulfasalazine is used to treat topical inflammatory bowel disease. It is metabolized by colonic bacteria into two components: 5-ASA, which has anti-inflammatory properties, and sulfapyridine, which has anti-bacterial products. More recently 5-ASA products alone have been developed, because many patients are intolerant to the sulfapyridine component. Sulfasalazine and 5-ASA behave similarly in trials, suggesting that the sulfapyridine anti-bacterial function has little significance.

Because ingested 5-ASA is rapidly absorbed in the jejunum, enemas have been used to deliver medication directly to the colon. In addition, two delayed release preparations have been made. The first involves coating 5-ASA with resins or microgranules, which dissolve and release 5-ASA in settings of pH>7 (distal small bowel and colon). Pentasa and Asacol have this coating. The second involves dimerizing 5-ASA, so that it is only released after bacterial cleavage (in the colon). Olsalazine (Dipentum) is an example of this dimer form. Importantly, neither delivery system has proven more efficacious over the other.

Question 16:
All of the following agents are effective for both induction of remission and maintenance of remission in patients with ulcerative colitis except:

A. oral mesalamine formulations including Asacol and Pentasa
B. sulfasalazine
C. olsalazine (Dipentum)
D. rectal mesalamine (Rowasa enemas and suppositories)
E. no exception

Suggested answer: E. For mild to moderate ulcerative colitis, sulfasalazine and 5-ASA preparations have been shown effective in inducing and maintaining remission (compared to placebo controls). There were no significant differences between sulfasalazine versus 5-ASA, or among the different 5-ASA preparations. Furthermore, for distal colitis, 5-ASA enemas achieve remission in as many as 90% of cases and maintain remission in as many as 75% of cases. When combined, oral plus enema therapy is more efficacious in inducing and maintaining remission when compared to either agent alone.

Question 17:
All of the following side effects associated with azathioprine and 6-mercaptopurine are idiosyncratic reactions except:

A. pancreatitis
B. leukopenia
C. fever
D. rash

Suggested answer: B. Idiosyncratic reactions are those that occur rarely, are unpredictable, and are dose-independent. For AZA and 6-MP use, these include pancreatitis, fever, rash, and pneumonitis. Leukopenia, on the other hand, is an intended side-effect used to reduce host cell inflammation. Leukopenia occurs when the 6-MP metabolites are shunted away from TPMT-mediated production of 6-MMP (which causes hepatotoxicity). Instead, 6-MP is metabolized through a different pathway to 6-TG. 6-TG accumulates in tissues, inhibits purine metabolism and subsequent DNA/RNA synthesis, and prevents lymphocyte proliferation. If too much, 6-TG can cause severe leukopenia and dangerous host immunosuppresion.

Question 18:
All of the following statements are true with respect to the treatment of inflammatory bowel disease with azathioprine and 6-mercaptopurine except:

A. controlled clinical trials have demonstrated that azathioprine doses of 2.0-2.5 mg/kg/d and 6-mercaptopurine at doses of 1.0-1.5 mg/kg/d are effective
B. these agents are thought to be relatively slow acting requiring up to 3 months or more to reach the full clinical effect
C. these agents are effective for the treatment of Crohn's disease including patients with chronically active disease, patients with fistulas who are steroid dependent and patients who require maintenance of remission therapy
D. these agents are not useful in patients with ulcerative colitis for maintenance of remission
E. none of the above

Suggested answer: D. Both 6-MP and its pro-drug AZA have been used successfully to treat UC and Crohn disease. AZA's molecular weight is >2 times that of 6-MP, and ~88% of AZA converts to 6-MP, so dosing for AZA is ~2 times that of 6-MP. The drugs require 3-6 months to achieve their full effect, so they are better at maintaining – rather than inducing – remission. They have been tested numerous times in clinical trials, with results supporting their ability to increase remission maintenance by ~40-70% and decrease corticosteroid requirements in ~70% of patients with corticosteroid-dependent disease.

Question 19:
All of the following statements regarding the use of methotrexate for the treatment of inflammatory bowel disease are true except:
A. methotrexate administered as a 25 mg intramuscular dose weekly is effective for inducing remission in patients with active Crohn's disease and for steroid sparing
B. methotrexate administered at doses of 15-25 mg/week orally or intramuscularly is effective for induction of improvement and remission in patients with active ulcerative colitis
C. there is no controlled clinical trial data to indicate that methotrexate is effective for maintenance of remission in patients with Crohn's disease
D. there is no controlled clinical trial data to indicate that methotrexate is effective for maintenance of remission in patients with ulcerative colitis
E. no exception

Suggested answer: B and C. Methotrexate blocks inflammation, perhaps by inhibiting methylation reactions vital for immune cells to function and proliferate. Methotrexate has been best studied in Crohn disease, with results seen with the intramuscular (versus oral) form. In Crohn disease, intramuscular methotrexate has been found to induce remission (25 mg q week) and maintain remission (15 mg qweek) in clinical trials. Studies with oral preparations have been less promising, and positive controlled clinical trial data for UC is lacking. Methotrexate side effects include nausea, vomiting, and abdominal distress, relieved in part by folic acid. Chronic methotrexate can also cause liver toxicity, but the doses given for IBD are not high enough to warrant surveillance liver biopsies.

Question 20:
Which one of the following statements is false with respect to the use of cyclosporine in patients with inflammatory bowel disease?

A. cyclosporine administered as a continuous intravenous infusion at a high dose of 4 mg/kg/d is effective for severely active ulcerative colitis
B. cyclosporine administered orally at a dose of 5 mg/kg/d is ineffective for the induction of improvement or remission in patients with active Crohn's disease
C. cyclosporine administered orally at a dose of 5 mg/kg/d is ineffective for maintenance of remission in patients with Crohn's disease
D. cyclosporine is slow acting and thus is not useful as a bridge therapy to other slower acting medications such as 6-mercaptopurine, azathioprine, or methotrexate
E. none of the above

Suggested answer: D. Cyclosporin binds cyclophilins to inhibit calcineurin and subsequent transcription of pro-inflammatory cytokines. Cyclosporin has a rapid onset of action, allowing it to be used as a bridge to 6-MP, AZA, or methotrexate therapy. In ulcerative colitis, cyclosporin (4 mg/kg/day continuous infusion) can prevent colectomy in severe, steroid-refractory cases. More recent data shows that lower dose infusions (2 mg/kg/day) may have similar potency with a possible (but not proven) decrease in side-effects. On the other hand, in Cohn disease, low dose oral cyclosporin (5 mg/kg/day) does not induce remission and higher doses and/or parenteral administration have yet to be properly tested. Cyclosporin does have significant side effects limiting its use, including opportunistic infections, nephrotoxicity, seizures (especially if cholesterol levels are low), peripheral neuropathy, and anaphylaxis.

Question 21:
The gene product of the hemochromatosis locus, HFE is:
A. a component of the ferritin complex which stores iron
B. a surface molecule that associates with the transferrin receptor
C. a divalent cation transport protein
D. a component of the endoplasmic reticulum
E. a subunit of the apotransferrin molecule

Suggested answer: B. Hereditary hemochromatosis is caused by mutations in the HFE (high Fe) locus. HFE is a transmembrane protein expressed in intestinal crypt and liver cells. It controls liver absorption in two proposed ways:

i) expressed in crypt cells → in crypts, binds transferrin receptor and promotes uptake of transferrin-bound iron from the circulation → enterocytes have high transferrin bound iron → enterocytes down-regulate the apical iron transporter DMT1 ("divalent metal transporter 1", a divalent cation transport protein) → enterocytes migrate up to villi but without DMT1 cannot absorb iron
ii) expressed in liver cells → increases liver hepicidin expression → liver hepicidin travels to enterocytes and downregulate basal transporter ferroportin → without ferroportin, iron is absorbed by villi enterocytes but cannot be transported into the circulation → enterocytes sloughed into lumen and absorbed iron lost

Question 22:
The liver disease that results from mutations in the Wilson's disease gene is associated with which one of the following?

A. inability to take up copper from the plasma ceruloplasmin pool
B. dysfunction of a copper transporter that is embedded in the canalicular membrane
C. inability to transport copper from the cytosol to the trans-Golgi network
D. copper-dependent antibody mediated immune reactions
E. abnormal primary structure of the ceruloplasmin molecule

Suggested answer: C. Wilson's disease is caused by a mutation in the copper-transporting adenosine triphosphatase (ATPase) gene (ATP7B). ATP7B has at least two functions: i) coordinates transport of copper from the cytoplasm, through the trans-Golgi network to vesicles, and eventually out into the bile cannaliculi via exocytosis; and ii) promotes the binding of copper with apoceruloplasmin to form ceruloplasmin, which is secreted into the bloodstream. Without ATP7B, copper is neither excreted into the bile nor the circulation (via ceruloplasmin). As a result, copper levels rise in hepatocytes, ultimately leading to oxidative damage and spilling of copper into the circulation.

Question 23:
A young adult with a life-long history of mild jaundice, but no bilirubinemia or evidence of chronic hepatitis or hemolysis is likely to have a genetic defect in:
A. sinusoidal bilirubin uptake pump
B. MRP2 (canalicular multispecific organic anion transporter)
C. bilirubin-UGT
D. UDP glucuronic acid synthetase
E. cholesterol 7-á-hydroxylase

Suggested answer: C. This patient has Gilbert's syndrome, which is caused by reduced uridine diphosphoglucuronate glucuronosyltransferase (UGT) activity. Normally, hepatocytes take up unconjugated bilirubin through the sinusoidal space. Hepatocytes then conjugated the bilirubin using bilirubin-UGT and excrete it into the cannalicular space. This process is independent of bile acid secretion, so isolated defects in bilirubin production/secretion should not lead to the liver damage often seen with defects in bile acid secretion.

The bilirubin conjugation process can be impaired at many steps. First, hepatocyte uptake of unconjugated bilirubin can be blocked by drugs. Second, hepatocyte conjugation can be impaired by defects in UGT activity. Gilbert's syndrome is caused by mutations in the regulatory elements controlling UGT expression and has mild, jaundice phenotypes. Crigler-Najjar syndrome, on the other hand, is caused by mutations in the gene itself, and can result in severe kernicterus-like phenotypes. Third, hepatocytes can have impaired secretion of bilirubin after it is conjugated. Dubin-Johnson syndrome results from mutations in MRP-2, which transports conjugated bilirubin from the cytoplasm to the cannalicular space. Rotor syndrome results from defective hepatocyte storage of conjugated bilirubin, leading to leakage into the cytoplasm.

Question 24:
Alagille syndrome is differentiated from other causes of cholestasis by:
A. typical facies and cardiovascular abnormalities
B. high unconjugated bilirubin levels

C. Unusually high transaminases plus high alkaline phosphatase
D. high hepatic copper content
E. the frequent finding of coexistent pulmonary fibrosis

Suggested answer: A. Alagille's syndrome is an autosomal dominant disease in the Notch signaling pathway. It has an incidence of 1:40,000 to 1:100,000, with variable penetrance and variable presentation. Common findings include paucity of bile ducts, characteristic facies (triangular face with pointed chin and broad forehead), pulmonic stenosis, Tetrology of Fallot, posterior embryotoxin, and butterfly vertebrate. Conjugated bilirubin, not unconjugated bilirubin levels, can be high, with pruritis often the most bothersome symptom. High hepatic content is more characteristic of Wilson's disease (though Alagille's patients may have increased copper staining on biopsies, secondary to poor excretion), and Hepatitis C infection is associated with increased risk of idiopathic pulmonary fibrosis.

Question 25:

Alpha- l-antitrypsin deficiency leads to liver injury by way of:

A. uncontrolled proteolytic enzyme activity in the portal tracts
B. chronic pancreatitis and focal biliary cirrhosis
C. inability to transport divalent cations into the endoplasmic reticulum
D. accumulation of abnormal glycoprotein in the liver cells
E. Pulmonary fibrosis and the development of cardiac cirrhosis

Suggested answer: D. A1AT "deficiency" refers to a deficiency of A1AT in lung tissue, leading to unchecked elastase activity and pulmonary damage over many years. A1AT is produced in and secreted by hepatocytes. However, in many forms of A1AT such as Z and M alleles, a misfolded protein is made that polymerizes in the endoplasmic reticulum, cannot be secreted, and accumulates abnormally in hepatocytes. This, in turn, can lead to liver damage. Accumulated A1AT protein can be detected by with periodic acid-Schiff (PAS) reagent staining on liver biopsy. Importantly, patients with deletions in the A1AT gene will not have liver disease, because there will be no protein to abnormally accumulate.

Question 1:
A 10 month old boy undergoes resection of hepatoblastoma limited to the right lobe of his liver. He has no underlying liver disease and completed his chemotherapy prior to surgery without complication.

Assuming that his post-operative course is unremarkable, which of the following best describes the regenerative response of the residual liver segment to resection.

A. The liver mass will be restored only after infusion of hepatocyte stem cells
B. The liver mass will be restored only after the remaining hepatocytes have undergone 12 rounds of cell doubling
C. The liver mass will be stored only after the remaining hepatocytes have undergone 1-2 rounds of replication
D. The liver mass will be restored only after infusion of recombinant hepatocyte growth factor
E. The liver mass will be restored only after infusion of TNF-α

Suggested answer: C. Liver regeneration is thought to proceed through one of two routes: i) in healthy tissue, such as following resection, proliferation of all cell types; and ii) in diseased tissue proliferation of stellate cells, oval cells, or other cells with stem-cell properties. In the above question, the cells in the remaining normal liver (hepatocytes, cholangiocytes, endothelial cells, etc) will divide soon after resection to restore the missing liver mass. 1-2 rounds of replication is sufficient to double the liver mass.

Hepatic growth factor has mitogenic, anti-apoptotic, and anti-inflammatory properties, and in experimental settings does promote liver regeneration. TNF-alpha, among other things, promotes hepatic endothelial cell proliferation and also has been used in experiments to promote the regenerative program. However, neither compound has proven clinical utility in regeneration, and neither is administered following liver resection.

For a review, see Michalopoulos GK. Liver Regeneration. J Cell Physiol. 2007 Nov; 213(2):286-300.

Question 2:
An 8 year old young girl is referred to you for evaluation of increased weight. The patient and her parents want to know her risk for developing obesity in adulthood. She has no other complaints. Her school performance is good and she gets along well with peers. Her mother is 34 years old and her body mass index is 24.5. Her father is 36 years old and his body mass index is 32. Physical examination shows that her body mass index is greater than 95th percentile for age and sex. Examination is otherwise normal and she has no biochemical evidence of endocrine disease.

Of the following, what is the most accurate answer to the parent's question.

A. Her risk of obesity as an adult is 1 in 5, similar to that of the general population
B. She has a 2 fold increased risk of obesity by age 30 compared to her peers
C. Her increased weight likely reflects the prepubertal growth surge.
D. Weight before puberty does not correlate with risk of obesity during adulthood.
E. Since one of her parents is obese, she has an 90% likelihood of obesity by age 30

Suggested answer: B. Many childhood factors have been studied to determine whether they predict adult obesity, including childhood obesity after age 3, parental obesity, television time, birthweight, and in utero insults. The patient in this question has two important risk factors: she is obese (BMI > 95%) and at least one of her parents is obese. As a result, her risk for obesity increases above that of the

population. The exact increase may be anywhere from 2-4 times depending on the population studied. A child having one obese child is thought to have a 50% increased chance of becoming obese as an adult.

See Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. N Engl J Med. 1997 Sep 25;337(13):869-73.

Question 3:
The emergency room calls about a 2 year old who swallowed some toilet bowl cleaner. Mom says she was cleaning the bathroom and thought the toddler was in another room. She turned around and saw her son with the bottle at his lips. He did some coughing, crying, and spitting. 2 hours later, physicians in the ED say that the lips look red and perhaps there is a burn on the posterior oropharynx. The child appears well. The next appropriate step would be:

A. send home with follow up in GI clinic in 1 month
B. send home with UGI in 1 month and follow up as needed
C. observe in ED for 6 hours and if no symptoms send home
D. admit NPO with EGD the next morning
E. admit NPO on steroids and antibiotics with EGD the next morning.

Suggested answer: D. Toilet bowl cleaners are acidic, allowing them to dissolve stains made from minerals found in pipe water. Acid ingestions cause coagulation necrosis. Acids pass quickly through the GI tract, so symptoms commonly occur in the stomach and small intestine (though oropharynx and esophageal lesions can also occur). EGD should be performed within 12-36 hours of the ingestion (the delay allows time for some damage to occur, so that it can be visualized during endoscopy).

In contrast to acid ingestions, base ingestions cause liquefaction necrosis. The base reacts with stomach acid to create heat, which burns the mucosa. Symptoms can present in the oropharynx; however, lack of oropharynx findings does not mean that more distal (i.e. esophagus) mucosa is intact. Alkaline ingestions have a 1000-fold lifetime risk of developing esophageal carcinoma.

Question 4:
A 13 year old young woman developed recurrent seizures one year after receiving a liver transplant one year ago because of acute liver failure. She has been started on treatment with dilantin after she was determined to have an idiopathic seizure disorder. The family is concerned that dilantin may affect the metabolism of tacrolimus. Which of the following is the most likely effect of dilantin on tacrolimus pharamcokinetics?

A. Decreased tacrolimus level due to competition with dilantin for intestinal absorption
B. No effect
C. Decreased tacrolimus level due to activation of the CYP3A4 by dilantin
D. Increased tacrolimus level due to inhibition of the CYP3A4 by dilantin
E. Increased tacrolimus level due to competition with dilantin for renal excretion

Suggested answer: C. Numerous medications affect the cytochrome P450 3A4 system, the major enzymes involved in clearing Tacrolimus. Azole antifungals, calcium channel blockers, and macrolides inhibit the P450 system, thereby increasing the Tacrolimus levels. Antiseizure agents (such as dilantin) and anti-TB agents can induce the P450 system and decrease Tacrolimus levels.

Question 5:

A 16 year old young woman with steroid-dependent Crohn's disease has a 3 week history of increased diarrhea and weight loss. Her disease is well-controlled when she is taking prednisone at 40 mg each day. When her dose of prednisone is decreased below 20 mg each day, she has an exacerbation of symptoms. On examination, her body mass index is 17 and she has mild tenderness to palpation throughout her abdomen. Endoscopic and radiologic evaluation show inflammatory disease primarily in the jejunum and ileum. You recommend that treatment be started with mercaptopurine and discuss potential nutritional intervention. Which of the following nutritional interventions is most likely to promote recovery?

A. Complete bowel rest and institution of total parenteral nutrition
B. Complete bowel rest and institution of peripheral parenteral nutrition
C. Oral zinc supplementation
D. Elemental diet delivered by nasogastric tube
E. Supplement present diet with a lactose free formula

Suggested answer D. This patient is having a flare of small bowel Crohn's. There are two things to consider when making a nutrition plan: i) stopping the flare, and ii) reversing the malnutrition. In terms of stopping the flare, both TPN/bowel rest and enteral nutrition (elemental or non-elemental) have produced remission rates up to 80% in some studies. However, relapse rates are generally higher after enteral nutrition vs. prednisolone. In terms of reversing malnutrition, sufficient enteral nutrition is hard to achieve via PO feedings and usually needs an NG tube. Parental nutrition via IV bypasses this, but has increased cost, greater chance of mixing error, and risk of line infection. Because this patient has no contraindication to using the gut, enteral feeds are preferable. No consistent differences have been found between elemental or non-elemental formulas.

Supplements (choice E) are controversial, as they may simply displace other foods and result in no net gain in calorie consumption.

Question 6:
A 10 month old boy with biliary atresia has developed progressive jaundice and is listed for liver transplantation. His 27-year-old mother has been evaluated and found to be a suitable living liver transplant donor. When discussing the procedure for transplantation with the family, the surgeon explains that only the left lateral segment of the mother's liver will be removed and transplanted into the recipient. Which of the following describes the segment(s) of the liver to be used for transplantation in this case?

A. Segments 5,6,7, and 8
B. Segments 2,3, and 4
C. Segment 4
D. Segment 1
E. Segments 2 and 3

Suggested answer: E. Left lateral segment transplants comprise segments 2 and 3. The left lateral segment represents approximately 20-25% of total volume, and includes the left hepatic vein, left branch of the portal vein, and left branch of the hepatic artery. In split liver transplantation, the left lateral segment goes to a child, whereas the right graft (segments I and IV to VIII, including the vena cava, right branch of the hepatic artery, and portal vein) goes to an adult.

Question 7:
In addition to the regulatory mechanisms intrinsic to the epithelium itself, electrolyte transport is regulated by all of the following pathways except:

A. Endocrine and paracrine regulation

B. ATP
C. Enteric neural regulation
D. Intestinal immune system

Suggested answer: A. Electrolyte transport is controlled by a number of processes. The enteric nervous system controls electrolyte transport, as acetylcholine and vasoactive intestinal polypeptide from nerve endings stimulate epithelial cells to secrete chloride, which in turn leads to water in the lumen for food lubrication. Paracrine factors (from immune and other surrounding cells) also control electrolyte transport. For example, histamine from mast cells increases chloride secretion and decreases bicarbonate secretion; prostaglandins from myofibroblasts, on the other hand increase secretion of both. ATP has a central role in electrolyte transport, providing the energy to create gradients of cations (i.e. Na+/K+ ATPase). Classic endocrine hormones are not thought to be major regulators of electrolyte transport.

Question 8:
Which of the following is not a feature of Reye's syndrome?

A. elevated transaminases
B. cholestasis
C. encephalopathy
D. microvesicular steatosis
E. vomiting

Suggested answer: B. Reye's syndrome involves mitochondrial defects in fatty acid oxidation, caused by a double insult of viral infection (flu, gastroenteritis) and mitochondrial toxins (i.e. salicylates). It is best characterized as an event occurring after aspirin is given for a viral illness, and presents as vomiting/lethargy followed by encephalopathy and hepatocyte damage (ALT and AST 3X > normal). Liver biopsies show microvesicular steatosis without necrosis, and electron microscopy shows mitochondrial changes. Bilirubin levels are usually normal or only slightly increased, and if cholestasis is present other diagnoses should also be considered.

Question 9:
What is the most sensitive indicator for renal cyclosporine toxicity?

A. cyclosporine level
B. blood pressure
C. GFR calculated using creatinine
D. Creatinine
E. GFR based on inulin

Suggested answer: E. Cyclosporine binds with cyclophilin, which in turn inhibits calcineurin. Active calcineurin normally dephosphorylates nuclear factor of activated T cells (NFAT-1), allowing it to enter the nucleus and promote transcription of IL-2 and other pro-T and B cell cytokines. Hence, cyclosporine is known as a calcineurin inhibitor (Tacrolimus works in a similar way, binding to its partner FK-506 binding protein to inhibit calcineurin).

Cyclosporine causes two forms of renal toxicity: acute and chronic. Acute toxicity is characterized by afferent and efferent arteriole vasoconstriction, secondary to endothelial cell dysfunction. This results in a drop in GFR and acute renal failure. Chronic toxicity occurs from vasoconstriction leading to ischemia and structural changes in the kidneys. Acute toxicity is reversible by withdrawing the medication, whereas chronic toxicity is thought to be permanent.

Clinically, patients with cyclosporine toxicity present with decreased GFR. They have hypertension secondary to sodium/volume retention, as the kidneys try to preserve perfusion in the setting of arteriole constriction. The lowered GFR also leads to an increase in BUN and creatinine. Hence, the most sensitive test to determine toxicity would be one that identifies an impaired GFR. Inulin, an inert substance that is freely filtered through the glomerulus and not reabsorbed, is used to accurately determine GFR.

Question 10:
A 7 month old infant is brought to you for evaluation because of recurrent vomiting and lethargy for 3 months. Dietary history reveals that she was exclusively breastfed until 5 months and her diet now consists of cereal, fruits, fruit juice, and vegetables. What enzyme deficiency is likely?

A. fructose-6-phosphate
B. triokinase
C. aldolase B
D. lactase
E. sucrase isomaltase

Suggested answer C. This patient tolerates lactose from breast milk but does not tolerate foods with sucrose/fructose (lactose is a disaccharide made from glucose and galactose, whereas sucrose is a disaccharide made from glucose and fructose). Sucrose is digested by the brush border enzyme complex sucrose isomaltase, which has both sucrase and alpha1,6 dextrin hydrolyzing activity. Deficiencies in this enzyme result in sugar malabsorption and diarrhea.

Fructose, once transported into the enterocytes by facilitate diffusion, becomes phosphorylated to fructose-1-phosphate by fructokinase. Aldolase B then controls the fate of the molecule, cleaving it into products that enter the glycolytic, gluconeogenic, or glycogen synthesis pathways. Without this enzyme, fructose-1-phosphate accumulates. Such patients with hereditary fructose intolerance develop poor feeding, vomiting, lethargy, hypoglycemia, failure to thrive, liver disease, and proximal renal tubular dysfunction when fed sucrose or fructose.

Question 11:
Cobalamin (Vitamin B12) absorption may be impaired in each of the following conditions EXCEPT:

A. pernicious anemia
B. cholestatic jaundice
C. Crohn's ileitis
D. Zollinger-Ellison syndrome
E. Small bowel bacterial overgrowth
F. Pancreatic insufficiency

Suggested answer: B. Vitamin B12 (cobalamin) comes mainly from the cobalamin-containing meats, but gut bacteria produce small amounts that are absorbed. The absorption of B12 from foodstuffs is a well-characterized process. First, cobalamin must make it through the acidic stomach, by binding to haptocorrin (R binder) at low pH. Most of the gastric haptocorrin originates from saliva. In the duodenum, pancreatic proteases activate in the presence of bicarbonate, hydrolyze haptocorrin, and liberate cobalamin. The cobalamin in turn binds to intrinsic factor (made by gastric parietal cells) and becomes resistant to pancreatic proteases. The cobalamin/intrinsic factor complex binds to an ileal brush border receptor and enters enterocytes.

Given this sequence, B12 absorption can be impaired at multiple steps. Pernicious anemia leads to low intrinsic factor, due to autoimmune attack on parietal cells. Zollinger-Ellison syndrome causes the duodenum to be too acidic, preventing protease activation and degradation of the haptocorrin/cobalamin complex. In the same way, pancreatic insufficiency prevents degradation of haptocorrin/cobalamin. Bacterial overgrowth in the small intestine disrupts the cobalamin/intrinsic factor interaction, and ileal disease affects cobalamin/intrinsic factor binding at the ileal brush border. Cholestasis does not alter B12 absorption. Bile does contain haptocorrin, but salivary haptocorrin is clinically the most important.

Question 12:
True statements regarding the Schilling test include each of the following EXCEPT:

A. The stage I test result is normal in patients receiving acid suppressive therapy
B. The Schilling test relies on normal renal function for adequate interpretation
C. The stage II test result is abnormal in healthy patients who have undergone total gastrectomy
D. Results may be abnormal in patients with small bowel bacterial overgrowth

Suggested answer: C. In patients with B12 deficiency, the Schilling test is used to determine which step in the absorption process is impaired. There are 4 steps to the test. Step 1 involves feeding radiolabeled B12 and measuring the amount excreted in the urine, as an indicator of how much is absorbed. Unlabeled B12 is injected concurrently that saturates tissue B12 receptors, ensuring that labeled B12 passes to the urine. Step 2-4 then repeat the first step with various adjuncts: step 2 adds intrinsic factor (if test becomes normal, then assume IF deficiency or pernicious anemia), step 3 adds antibiotic (if test becomes normal, then assume small bowel overgrowth), and step 4 adds pancreatic enzymes (if test becomes normal, then assume pancreatic insufficiency).

The Schilling test should be normal in patients with acid suppression, as too much acid (not too little) disrupts B12 absorption by interfering with pancreatic protease activation. The Schilling test relies on normal renal function to excrete radiolabeled B12, and results are impaired with bacterial overgrowth (hence step 3 of the test). Patients without a stomach should have impaired B12 absorption because of reduced IF levels; however, step 2 provides supplemental IF and bypasses this defect.

Question 13:
Folate supplementation is indicated in all of the following situations EXCEPT:

A. Anticonvulsant therapy with phenytoin or carbamazepine
B. Celiac sprue
C. Chronic sulfasalazine therapy
D. Pancreatic insufficiency
E. Methotrexate therapy

Suggested answer: D. Folate is absorbed via a sodium-dependent carrier, after being hydrolyzed from polyglutamate to monoglutamate forms by brush border enzymes. Once inside epithelial cells, folic acid becomes methylated and reduced into its metabolically active form 5-methyltetrahydrofolate. Celiac sprue impairs brush border activity. Phenytoin impairs brush border enzyme activity converting polyglutamate to monoglutamate forms, and sulfasalazine interferes with absorption through the carrier. Methotrexate prevents reduction of folate that enters cells into its active form, by inhibiting dihydrofolate reductase (DHFR). Pancreatic enzymes are not involved in folate absorption.

Question 14:
Brush border saccharidase activity is decreased by:
A. A diet rich in sucrose

B. Fasting
C. Diabetes mellitus
D. Pancreatic exocrine insufficiency
E. Intestinal bacterial overgrowth

Suggested answer: E, There are 3 brush border saccharidases: sucrase-isomaltase, lactase-phlorizin hydrolase, and maltase-glucoamylase. The brush border, and subsequently the saccharidases, are destroyed by proteases created by overgrowing bacteria. Lactase-phlorizin hydrolase expression can be increased in infants by enteral feeds, but fasting has never been proven to decrease activity. In adults, all enzymes except lactase can be induced by substrate (lactase expression declines with age in the majority of people, and persistence of lactase expression is an autosomal recessive trait). Pancreatic amylase is important to start alpha1,6 digestion of starch, which is continued by sucrase-isomaltase and lactase-phlorizin hydrolase. However, salivary amylase can compensate in settings of pancreatic insufficiency.

Question 15:
Which of the following is not a recognized disease association of hepatitis C viral infection?

A. Cryoglobulinemia
B. Porphyria cutanea tarda
C. Membranoproliferative glomerulonephritis
D. Diabetes mellitus
E. Increased risk of myocardial infarction

Suggested answer: E. There are many extrahepatic manifestations of Hepatitis C. Cryoglobulinemia occurs when Hepatitis C-antibody complexes form in the blood. "Mixed" cryoglobulinemia refers to complexes with IgG against the Hepatitis C antigen and IgM against the IgG. To diagnose cryoglobulinemia, blood samples must be kept warm because the complexes precipitate when cooled.

Porphyria cutanea tarda is a common skin manifestation of Hepatitis C. As a result of liver dysfunction, the UROD gene (uroporphyrinogen decarboxylase) is impaired, heme synthesis is halted, and porphyrins build up. The porphyrins collect in the skin absorb visible violet light, producing free radicals that damage nearby tissue. In the skin, the most common findings are erosions, blisters, and scarring.

Membranoproliferative glomerulonephritis is also seen with Heptitis C, perhaps from a vasculitis produced by the antibody-antigen complexes. Diabetes mellitus (adult-onset, insulin resistant) is 4X more likely in Hepatitis C patients for unknown reasons. Some have speculated that the antibody response induced by Hepatitis C results in an autoimmune attack of the pancreas. No association between Hepatitis C and myocardial infarction has been demonstrated.

Question 16:
All of the following statements regarding the pathogenesis of diarrhea in patients with Zollinger-Ellison syndrome are true EXCEPT:
A. Hypergastrinemia leads to colonic hypersecretion of fluid and electrolytes.
B. Acid hypersecretion leads to extreme acidification of the duodenum, resulting in inactivation of pancreatic enzymes and concomitant steatorrhea.
C. Extreme acidification of the small intestine can lead to mild disruption of enterocyte integrity, resulting in mild malabsorption.
D. Gastric hypersecretion can lead to significant volume overload of the small intestine.

Suggested answer: A. Zollinger-Ellison syndrome is a disorder of acid hypersecretion, caused by tumors (commonly pancreatic) secreting gastrin. Children have increased gastric secretions, as well as diarrhea

secondary to acid osmotic load, mucosal damage, and pancreatic lipase inactivation. Most changes from acid hypersecretion occur in the small intestine rather than the colon.

Question 17:
The following statements regarding the management of foreign bodies in the stomach are true EXCEPT:

A. The clinician should consider removing objects that are more than 2 cm in diameter or more than 5 cm in length, because they are unlikely to pass through the duodenum.
B. In the case of battery ingestion, levels of heavy metal in the blood and urine should be measured.
C. Batteries that have passed through the esophagus to the stomach should always be removed.
D. Between 80% to 90% of ingested foreign bodies that reach the stomach will pass without specific therapy.

Suggested answer: B. When disk button batteries are swallowed, X-ray imaging must be done to determine the location of the battery. 90% of batteries pass spontaneously within 14 days. When batteries lodge in the esophagus, they must be removed immediately as even 1 hour of contact has been shown to be injurious (and 4 hours of contact can erode through all esophageal layers). Injury occurs from electrolyte leakage, liquefaction necrosis secondary to alkali leakage such as sodium or potassium hydroxide, mercury toxicity, pressure necrosis, and direct current flow causing low voltage burns. Batteries found in the stomach can be removed if they are not passed after 1 week. Levels of heavy metals are not routinely measured in battery ingestion, as serum levels have never been reported to be high enough after battery ingestion to cause toxicity.

Question 18:
All of the following are treatments for symptomatic bezoars EXCEPT:

A. Cellulase
B. Acetylcysteine
C. Atropine
D. Mechanical fragmentation at the time of endoscopy

Suggested answer: C. Bezoars refer to a mass trapped in the gastrointestinal tract (usually the stomach). Removing the mass can be accomplished via mechanical fragmentation or enzymatic digestion. Mechanical digestion involves breaking the bezoar into small pieces, so that it can pass through the intestinal tract. This approach risks causing pylorous/ intestinal obstruction. For digestion, the enzymes used depend on the constituents of the mass, and include cellulase (which digests cellulose) and acetylcycteine (which splits disulfide bonds in proteins). Atropine does not have digestive activity.

Question 19:
All of the following are potent acid secretagogues EXCEPT:

A. Coffee
B. Decaffeinated coffee
C. Milk
D. Alcohol

Suggested answer: C. Secretagogues are substances that cause the secretion of other substances, i.e. acid by parietal cells. Alcohol and coffee directly stimulate parietal cells through uncharacterized mechanisms. Alcohol also impairs gastric mucosa which contributes to acid-mediated damage. Caffeine increases cAMP levels in parietal cells leading to increased acid production. However, coffee independent of caffeine also stimulates parietal cells, consistent with observations that both caffeinated

and decaffeinated coffee increases acid production. Milk is not a secretagogue; rather, it is thought to neutralize stomach acid because it has a pH higher than that in the stomach.

Question 20:
A 21 year old woman who has had type I diabetes for 12 years had a 2-year history of intermittent nausea and vomiting that has worsened in the past 3 months. A scintigraphic scan to evaluate solid-phase gastric emptying shows 8% emptying at 2 hours (normal, 42% to 80%). All of the following statements are true EXCEPT:

A. This condition is usually associated with other peripheral and/or autonomic neuropathies.
B. Delays in gastric emptying correlate well with symptoms of nausea and vomiting in this condition.
C. Findings on gastrointestinal manometry may include loss of fed and fasting antral motility and increased phasic and tonic pyloric motility.
D. A gastric acid analysis may show a reduction in acid production in response to sham feeding.
E. The delay in gastric emptying may be exacerbated by periods of worsening hyperglycemia.

Suggested answer: B. While delayed gastric motility is best-documented in long-standing diabetics, a few case reports have documented the phenomenon in children as well. The mechanism is thought to be diabetic neuropathy of the vagal nerve. Patients feel fullness and bloating, though symptoms of nausea and vomiting correlate poorly with delayed gastric emptying. Furthermore, with poor vagal input, acid secretion decreases during sham feeding, migrating motor complexes are reduced (but cells of Cajal are normal in number), antral contractions are less frequent, and the pylorous has increased tone. Interestingly, in addition to the chronic diabetic changes, episodes of hyperglycemia in normal and diabetic patients can cause delayed gastric emptying.

For further discussion, see Kashyap P, Farrugia G. Diabetic gastroparesis: what we have learned and had to unlearn in the past 5 years. Gut. 2010 Dec;59(12):1716-26.

Question 21:
Which of the following statements concerning management of the above case is TRUE?

A. Avoidance of a high fat diet might reduce symptoms.
B. Increasing the oral dose of erythromycin might worsen the nausea.
C. The efficacy of domperidone in reducing nausea may be partially explained by CNS effects on dopamine receptors in the brain stem.
D. Endoscopic destruction of a gastric bezoar may alleviate symptoms temporarily.
E. All of the above statements are correct.

Suggested answer: E. In order to improve gastric motility, a number of approaches are available. The first is to improve glycemic control. The second is to use motility agents, including erythromycin, domperidone (a dopamine receptor antagonist), cisparide, and IV grehlin. Erythromycin can be titrated up as tolerated, until side-effects such as diarrhea, nausea, or vomiting occur. Removing any bezoars that have formed secondary to poor motility may also improve symptoms, as well as avoiding meals that further slow gastric motility, i.e. high fat meals.

Question 22:
A one month old infant boy recovery from heart surgery develops post-prandial emesis. He was the product of a 35 week gestation. He was found to have congenital heart disease and received prostaglandin E1 for 21 days to maintain patency of his ductus arteriosus prior to surgery. Post-operatively he did well. He began feeding with a standard infant formula 2 days ago.

A. Chest X-ray
B. Upper GI
C. Upper endoscopy
D. Change to elemental formula
E. Begin treatment with H2 blocker

Suggested answer: C. Post-prandial emesis occurs for a number of reasons, including simple reflux, malrotation, milk allergies, dysmotility, and pyloric stenosis. In the setting of heart disease, gastric hypoperfusion must also be considered which may delay motility and/or decrease intestinal barrier function, allowing large protein epitopes to enter the bloodstream and cause allergies. Finally, with chronic prostaglandin use, case reports have documented antral hyperplasia and gastric outlet obstruction. Unlike pyloric stenosis which involves muscle, this phenomenon involves the mucosa. The condition reverses with drug withdrawal. Endoscopy could diagnose this definitively, as well as rule-out allergic causes. (Upper GI could also suggest antral hyperplasia but could not distinguish it from pyloric stenosis).

Question 23:
A 17-year-old girl presents with a complaint of a fatigue and jaundice for 4 weeks. She has enlargement of her liver, scleral icterus and 5 fold elevation of serum transaminases. Her INR is 1.2. Her hepatitis A, B, and C serologies are negative but her anti-nuclear antibody titer is 1:640. She has not taken medications. Review of systems reveals that she has had loose stools for 6 months and that she has lost 5 pounds.

Which of the following is the most appropriate next step?

A. Observe for six months
B. Measure anti-mitochondrial antibody titers
C. Colonoscopy
D. Liver biopsy
E. UGI and small bowel follow through

Suggested answer: D. This patient has liver disease and a positive ANA titer (1:640 is lower limit of abnormal), making type I autoimmune hepatitis likely. Her liver disease also accompanies intestinal disease suspicious for possible inflammatory bowel disease. Indeed, approximately <1% of children with ulcerative colitis develop autoimmune hepatitis and 3-5% develop primary sclerosing cholangitis. The first step is to confirm he liver diagnosis with a liver biopsy, looking for mononuclear and plasma cell infiltrates in the portal tracts. Next, a colonoscopy can be performed to further investigate the possibility of inflammatory bowel disease.

Question 24:
The gastric mucosa is a hostile environment for most bacteria. Helicobacter pylori is highly adapted to survival in the gastric mucosa. Which of the following is most likely explanation for the survival of H.pylori in the acidic environment of the gastric mucosa?

A. Expression of a vacuolating cytotoxin which impairs acid secretion
B. Production of urease
C. Inhibition of histamine stimulated acid secretion
D. Inhibition of the H+/K+ pump
E. Strong adhesion to the mucosal surface

Suggested answer: B. Helicobacter pylori are uniquely situated to handle the acidic environment of the stomach. H. pylori has a urease, which hydrolyzes urea into carbon dioxide and ammonia, and the ammonia in turn buffers the stomach pH. H. pylori uses adhesins to adhere to the mucosal surface, as well as a vacuolating cytotoxin (VacA) to create channels in which nutrients can escape from mucosal cells to feed the bacteria. Proton pump inhibitors block the H+/K+ pump, and ranitidine inhibits histamine-induced parietal cell acid secretion.

Question 25:
What is one of the primary differences between pediatric enteral formulas and adult enteral formulas?

A. Pediatric formulas have less protein/same volume
B. Pediatric formulas utilize different sources of carbohydrates
C. Pediatric formulas are only made with hydrolyzed protein
D. Pediatric formulas utilize only LCT to enhance fat absorption

Suggested answer: A. Pediatric formulas (versus adult formulas) have more fat but decreased protein and carbohydrates. They utilize similar carbohydrates, are made full proteins, pepstides, or amino acids, and use various triglycerides (including long chain fatty acids to prevent essential fatty acid deficiency) for the fat component.

Question 1:
A 5-month-old infant has been fed only goat milk. Laboratory studies reveal: hemoglobin concentration, 9.5 g/dL; mean corpuscular volume, 98 fL; white blood cell count, 4200/mm3; and reticulocyte count, 0.2%.

For initial treatment, it would be MOST appropriate to recommend dietary supplementation with

A. ascorbic acid
B. folic acid
C. iron
D. pyridoxine
E. vitamin B12

Suggested answer: B. Goat's milk can be used for infants suffering from cow's milk protein allergy. Goat's milk contains only trace amounts of the allergenic protein alpha-S1-casein normally found in cow's milk (however, goat's milk contains equivalent amounts of another allergenic protein beta-lactoblobulin). Goat's milk is also deficient in other vitamins, including vitamin D (supplemented in cow's milk and formulas), vitamin B12, and especially folate. Goat's milk contain 6 ug/L folate, whereas breast milk contains 45 ug/L and cow's milk 50 ug/L. Hence, infants drinking goat milk are most susceptible to folate deficiency and resulting megoblastic anemia.

Of note, milk from other animals have been tested on children with cow's milk protein allergy, with better results (see Vita et al. Ass's milk in children with atopic dermatitis and cow's milk allergy: crossover comparison with goat's milk. Pediatr Allergy Immunol (2007) 18: 594-8).

Question 2:
The basal energy or metabolic requirement for children is calculated MOST accurately by considering

A. body surface area
B. creatinine-height index
C. serum protein concentration
D. total lymphocyte count
E. triceps skinfold thickness

Suggested answer: E. The basal metabolic rate (BMR) is the amount of energy used by an organism at rest. In children it includes the energy of growing, and differs between boys and girls in accord with the sex differences in the intensity and duration of the adolescent growth spurt. BMR is measured by the heat given off per unit of time, and is expressed as calories released per kilogram of body weight (or per square meter of body surface area) per hour. BMR is a function of an organism's fat free mass (FFM), as this comprises the bulk of active metabolic tissue.

BMR correlates best with body surface area. Creatinine-height index may estimate lean body mass/FFM, and hence correlate with BMR, but it is not well validated in children. Triceps skinfold thickness measures subcutaneous fat, not FFM. Certain methods using multiple skin fold measurements to estimate FFM ("Dauncey" method and the "Durnin/ Womersley" method) are fraught with multiple problems.

Question 3:
Of the antibodies found in human colostrum and milk, the immunoglobulin (Ig) that is MOST likely to prevent organisms from adhering to the infant's intestinal mucosa is

A. IgA

B. IgD
C. IgE
D. IgG
E. IgM

Suggested answer: A. Infants passively acquire many antibodies from their mothers ("passive humoral immunity"). During gestation, they receive maternal IgG transplacentally. After birth, they receive IgA from colostrum and breast milk, which provides local protection in the gut but does enter the systemic circulation. They also receive IgG from breast milk, which can bind to transepithelial Hc receptors and enter the circulation. Infant do not receive IgE, IgM, or IgD (an immunoglobulin associated with IgM) passively from their mothers.

Question 4:
A 3-year-old boy, who has sustained second- and third-degree burns of the esophagus from ingesting a lye solution, requires placement of a gastrostomy tube for nutritional support. The parents are counseled about the risks and benefits of tube feedings.

In your discussion, you tell them that the MOST frequent complication of enteral feeding is

A. clogging of the feeding tube
B. diarrhea
C. electrolyte disturbances
D. gastric irritation
E. hypoalbuminemia

Suggested answer: B. Gastrostomy tubes (G tubes) allow for nutrition in patients with oral or esophageal disease. There are many complications with G tubes, including aspiration, electrolyte imbalances (i.e., refeeding syndrome), and fluid imbalances as most formulas only contain 70-80% water. Other long term complications may include dysmotility, as the procedure attaches the stomach to the abdominal wall. The most frequent complication is osmotic diarrhea. Diarrhea results when the rate of feeding exceeds the gut's capacity to absorb, leading to increased sugar delivery to the colon where it is metabolized by bacteria into osmotically active substances.

Question 5:
A 1,220 gm infant develops necrotizing enterocolitis. After the infant recovers, the BEST type of formula to use to initiate feedings is

A. 20 calories/oz elemental formula
B. 20 calories/oz premature formula
C. 20 calories/oz standard infant formula
D. 24 calories/oz premature formula
E. 27 calories/oz premature formula

Suggested answer: D. Breast milk has many advantages over formula, including the prevention of NEC. Multiple studies have demonstrated that infants started on expressed breast milk (from their mother or a donor) have lower NEC rates compared to those started on formula. He current recommendations are to "prime" the with breast milk early. It is unclear whether the rate of milk increase affects NEC rates.

Despite the benefits of breast milk, breast milk does not have enough calcium and phosphorous for preterm infants. Preterm formulas account for this deficiency and have adequate amounts. For the patient in the vignette, the infant should first undergo "priming" with human milk. When a rate of 100 cc/kg is achieved, the human milk can be fortified to 24 kcal/ounce and advanced to reach a goal of 150-

180 cc/kg/day. If human milk is unavailable, elemental formula (better) or preterm formula fortified to 24 kcal can be used (there is no data favoring 20 kcal formula over 24 kcal formula).

Question 6:
A TRUE statement regarding anthropometric measurements in the assessment of nutritional status is:

A. Acute changes in weight reflect changes in muscle mass
B. Arm circumference is the best screening tool for malnutrition
C. Single measurements are the most sensitive indicators of nutritional problems
D. Standard growth curves are equally applicable to all ethnic groups
E. Standard growth curves overestimate the early gains to be made by breastfed infants

Suggested answer: B. Mid-upper arm circumference (MUAC) is an easy way to screen for malnutrition, applicable to all children >1 year of old or >6 months old and taller than 65 cm. To measure MUAC, measure the circumference (to the nearest millimeter) at the midpoint of the left arm, half-way between the tip of the shoulder (olecranon) and the tip of the elbow (acromium). MUAC compared to BMI is less affected by edema. Despite the ease of MUAC, the most sensitive indicators of nutritional problems account for multiple variables, such as social factors in addition to anthropometric calculations. Acute changes in weight usually reflect fluid shifts, not changes in muscle mass.

Standard growth curves are convenient ways to compare a child's height and weight with same-aged children in the population. There are CDC and WHO growth curves. The CDC curves reflect growth of US children over the last 30 years, whereas the WHO curves reflect growth of children all over the world, including Brazil, Ghana, India, Norway, Oman, and the United States. Initially, the CDC recommended using the CDC growth curves for all children in the US. Now, however, they recommend using the WHO growth curves for children <2 years old, because the WHO growth curves better account for breast feeding. When the curves for <2 years old are compared, the WHO curve (more breast fed infants) starts off faster but plateaus quicker. As a result, the CDC curve overestimates the percentiles for breast fed infants early and underestimates their percentiles later. The CDC recommends switching to the CDC curve at age 2, resulting in a situation where a child may be overweight at age 2 on the WHO curve but normal on the CDC curve.

Question 7:
An 8-month-old girl recently recovered from a gastrointestinal illness. When the mother reintroduced the formula, cereal, and baby foods the child had been eating before the illness, the girl developed persistent, watery diarrhea; abdominal distention; flatulence; and recurrent abdominal pain.

Of the following, the MOST likely cause of this patient's problem is

A. cow milk allergy
B. gluten sensitivity
C. lactose intolerance
D. new-onset infectious enteritis
E. persistent infectious enteritis

Suggested answer: C. This patient suffers from secondary/acquired lactose intolerance. It occurs after a viral infection, in which intestinal brush border (and their disaccharidases such as lactase) are destroyed. As a result, lactose will not be digested in the small intestine, will pass to the colon, and will be metabolized by gut bacteria into gas and osmotically active substances. Lactase is the last disaccharidase to return to normal function after injury, so secondary lactose intolerance may last for months.

Question 8:
In humans, vitamin E functions PRIMARILY as a:

A. coenzyme of carboxylase
B. component of rhodopsin
C. membrane antioxidant
D. methyl donor
E. regulator of calcium absorption

Suggested answer: C. Vitamin E is a fat-soluble antioxidant that stops production of reactive oxygen species normally formed when fat undergoes oxidation. Biotin (Vitamin B7) is a coenzyme for many carboxylases. Vitamin A is a component of rhosopsin, the photopigment used in black/white vision. Folic acid (Vitamin B9) and colbalamin (Vitamin B12) are methyl donors. Vitamin D is a regulator of calcium absorption.

Question 9:
Zinc is MOST easily absorbed from:

A. casein-dominant, cow milk-based formula
B. cow milk
C. human milk
D. soy-based formula
E. whey-dominant, cow milk-based formula

Suggested answer: C. Zinc bioavailability has been studies by labeling zinc with a radioisotope, mixing it into various milk/formula preperations (human milk, cow's milk, cow's milk formula, and soy protein formula), and assaying it on newborn sucking rates. Zinc bioavailability was 28% in human milk, 24% from cow's milk formula, 15% from cow's milk, and 10% from soy formula.

Cow's milk-based formula is the first choice for infants who are not breast fed. Cow's milk has 50% more protein, and the ratio of whey protein to casein protein is 20:80 (compared to 70:30 in human milk). Caesin is composed of proteins held together in granular structures called micelles, precipitates out in the acidic environment of the stomach, but is nicely digested in the alkaline environment of the small intestine, providing a slowly absorbed source of amino acids. Whey, on the other hand, consists mainly of beta-lactoglobulin (major component of bovine whey, and allergenic), alpha-lactalbumin (major component of human whey), albumin, immunoglobulins, hormones, and growth factors. It is easily digested in the acidic environment of the stomach and produces a rapid surge in plasma amino acids. Pasteurization destroys many of the immunoprotective properties of whey.

The ratio of whey to casein in popular formulas are as follows: 100:0 in Carnation Good Start Supreme, 60:40 in Enfamil Lipil, and 48:52 in Similac Advance.

Question 10:
An infant boy born at term is delivered at home without medical supervision. At 48 hours of age, he is brought to the emergency room because of a bloody discharge from the umbilical cord and bloody stools.

Until the results of laboratory studies are available, the BEST initial management is to administer intravenous

A. ampicillin and gentamicin
B. cryoprecipitate
C. factor VIII concentrate
D. fresh frozen plasma
E. vitamin K

Suggested answer: E. Newborns are vulnerable to hemorrhagic disorders secondary to Vitamin K deficiency. Very little Vitamin K is transferred transplacentally, and the storage of Vitamin K in the neonatal liver is also limited. Furthermore, until the gut is colonized with bacteria (especially Bacteroides species), there is very little microbial production of Vitamin K. Breast milk also contains little Vitamin K. To prevent bleeding, Vitamin K is administered intramuscularly immediately after birth in the US. With a Vitamin K injection, the incidence of Vitamin K deficiency-related bleeding varies from 0.25-1.7% in the first week of life.

Question 11:
Physical examination of a 2-year-old malnourished girl reveals a "rachitic rosary."

Among the following, the indicator MOST likely to be associated with this child's problem is:

A. bronchopulmonary dysplasia
B. chronic hepatitis
C. galactosemia
D. sucrase-isomaltase deficiency
E. tyrosinemia

Suggested answer: E. "Rachitic rosary" refers to prominent knobs of bone at the costochondrial joints. It is associated with rickets, and is caused by excessive urinary losses of calcium and phosphate and/or defect in renal hydroxylation of 25-OH Vitamin D3 into 1,25-diOH Vitamin D3. Tyrosinemia can involve renal tubules, leading to a Fanconi-like syndrome with normal anion-gap, metabolic acidosis, hyperphosphaturia, hypophosphatemia, and Vitamin D resistant rickets. Galactosemia is characterized by inability to metabolize galactose, and is caused by mutations in one of 3 genes. It can involve renal tubular dysfunction and a Fanconi-like syndrome, but (unlike this case) typically presents with jaundice and seizures in the first few days of life. Sucrase-isomaltase deficiency leads to improper digestion of sucrose, resulting in sucrose delivery to colonic gut bacteria. It is characterized by diarrhea and malnutrition.

Question 12:
The immunoglobulin (Ig) MOST abundant in human milk is:

A. IgA
B. IgD
C. IgE
D. IgG
E. IgM

Suggested answer: A. Human milk contains all the immunoglobulins (M, A, D, G, E), but secretory IgA is the most abundant. sIgA from breast milk is an important source of passive immunity before the neonate generates its own sIgA; furthermore, assuming the mother and child share the same environment and flora, breast milk sIgA will confer protection against the relevant organisms. sIgA is packaged in breast milk in acid-resistant packages, allowing it to survive the acidic stomach and makes its way to the

intestines. Early milk contains 2 g/L IgA, 0.12 g/L IgM, and 0.34 g/L IgG. Mature milk contains 1 g/L IgA, 0.2 g/L IgM, and 0.05 g/L IgG.

Question 13:
An infant born at term has a Coombs positive ABO blood group incompatibility. On the third day of life, laboratory findings include: venous hemoglobin concentration, 14 gm/dL, and total serum bilirubin level, 10.8mg/dL.

Among the following, the MOST appropriate therapy is

A. blood transfusion
B. expectant follow-up
C. intravenous administration of immune globulin
D. therapeutic iron supplementation
E. vitamin K supplementation

Suggested answer: B. This child is at risk for elevated unconjugated bilirubin requiring phototherapy, given his Coombs positive/ABO blood group incompatibility status. Currently, his total serum bilirubin level is 10.8 mg/dL which is below the recommended phototherapy range for a healthy, full-term newborn. His future care should include expectant follow-up, as well as at least one bilirubin fractionation measured early to ensure that the there is no elevation in conjugated bilirubin.

Question 14:
A 1, 450 gm infant is not growing well on 24 calories/oz premature formula. The caloric density is increased to 27 calories/oz by the addition of medium-chain triglycerides.

Of the following complications, this change in formula is MOST likely to produce:

A. bloody stools
B. diarrhea
C. gastric distention
D. increased gastric emptying time
E. steatorrhea

Suggested answer: B. This patient is being fed a formula with increased osmolarity, and is at risk for an osmolar diarrhea. Medium-chain triglycerides (MCTs) are considered more easily absorbed than that other fatty acids, because they are absorbed directly into the enterocyte and carried through the portal circulation to the liver (they do not travel through lymphatics). Furthermore, MCTs do not require bile acids, lipase, or co-lipase for their absorption. Recently, studies have challenged the benefits of MCTs, showing infants fed long chain fatty acids grew just as well as those taking MCTs.

Question 15:
Which of the following drugs administered to the mother is MOST likely to have an adverse effect on the infant who is breast feeding?

A. Furosemide
B. Gentamicin
C. Hydralazine
D. Metronidazole
E. Penicillin

Suggested answer: D. Metronidazole is secreted in breast milk in small quantities, just as furosemide, gentamicin, hydralazine, and penicillin are. None of the medications have been shown to pose a risk to the infant. However, metronidazole poses a theoretical risk of cancer to children, as it increases the risk of certain cancers in mice and rats. As a result, some practioners will recommend mothers to stop breast feeding for 12 to 24 hours after taking metronidazole.

Question 16:
During the first 4 months of life, the USUAL caloric requirement (in Kcal/kg per day) for appropriate postnatal growth in the healthy term infant who is formula fed is

A. 90
B. 105
C. 120
D. 135
E. 150

Suggested answer: B. Newborns need extra calories to support rapid growth. On average, a 0-3 month bottle fed infant will take from 90-135 kcal/kg/day to achieve an increase in weight of 25 to 30 g/day (135-202.5 cc/kg/day). A 3-12 month infant requires approximately 100 kcal/kg/day. Hence, on average, during the 4 months of life a child will need 105 kcal/kg/day.

Question 17:
Medium-chain triglycerides account for 40 to 50% of the fat content of formulas fed to low-birthweight infants.

Of the following, the BEST explanation for this practice is that:

A. absorption of medium-chain triglycerides is similar to that of butterfat
B. low-birthweight infants have a large pool of bile acids
C. low-birthweight infants have increased capacity to synthesize bile salts
D. medium-chain triglycerides cause less steatorrhea
E. medium-chain triglycerides require micelle formation for absorption

Suggested answer: D. Preterm infants have low intraluminal bile salts, and all infants have low pancreatic lipase (their salivary lipase compensates). Medium chain triglycerides (MCTs) can be absorbed directly into enterocytes and passed to the liver via the portal vein. Their absorption is not dependant on bile salts, pancreatic enzymes, chylomicron formation, or lymphatic transport. Recently, studies have challenged the benefit of MCTs over long-chain fatty acids by showing that MCTs offered no extra growth advantage in preterm infants. MCTs carry the risk of increased urinary dicarboxylic acid excretion, which is produced after incomplete beta oxidation of MCTs.

Question 18:
A 31/2-year-old boy with chronic diarrhea and failure to thrive is diagnosed with cystic fibrosis. Neurologic examination reveals absent deep tendon reflexes, truncal ataxia, and muscle weakness. A nutrient deficiency is suspected.

Given this constellation of findings, what additional physical sign is MOST likely to be present in this child?

A. Desquamating skin lesions
B. Ophthalmoplegia

C. Positive Trousseau sign
D. Purpura
E. Stooped posture

Suggested answer: B. Vitamin E deficiency is characterized by neurological and neuromuscular findings, including ophthalmoplegia. Vitamin A deficiency can present as desquamating skin lesions and night blindness. Vitamin D deficiency can present with hypocalcemia leading to a positive Trousseau sign (spasms of the hand when blood flow if occluded via a blood pressure cuff). Vitamin D deficiency can also lead to vertebral fractures producing a stooped posture. Vitamin K deficiency leads to bleeding seen as petechiae (<3 mm) or purpura (3-10 mm).

Question 19:
Which of the following amino acids, present in adequate amount in cow milk-based formula, must be added to soy-based infant formula?

A. Isoleucine
B. Leucine
C. Lysine
D. Methionine
E. Valine

Suggested answer: D. Methionine is a sulfur-containing essential amino acid, and is two times more abundant in cow's milk than soy milk. Methionine supplementation improves the biological quality of soy protein, by improving weight gain, urea nitrogen excretion, and albumin synthesis. Hence, supplementation began in the early 70s; before that, infants feeding soy formulas were at risk for severe hypoalbuminemia and edema. In addition to methionine, carnitine (fatty acid transport), and taurine (neurodevelopment, bile acid conjugation) are also supplemented in soy protein.

Question 20:
A 2-year-old child has undergone resection of the terminal ileum because of an ileal-ileal intussusception. Of the following nutrients, which is MOST likely to become deficient in this patient?

A. Folic acid
B. Thiamine
C. Vitamin A
D. Vitamin B12
E. Vitamin K

Suggested answer: D. Vitamin B12 is exclusively absorbed in the terminal ileum. Vitamin B12 (cobalamin) comes mainly from cobalamin-containing meats, but gut bacteria produce small amounts that are absorbed. The absorption of B12 from foodstuffs is a well-characterized process. First, cobalamin must make it through the acidic stomach, by binding to haptocorrin (R binder) at low pH. Most of the gastric haptocorrin originates from saliva. In the duodenum, pancreatic proteases activate in the presence of bicarbonate, hydrolyze haptocorrin, and liberate cobalamin. The cobalamin in turn binds to intrinsic factor (made by gastric parietal cells) and becomes resistant to pancreatic proteases. The cobalamin/intrinsic factor complex binds to an ileal brush border receptor and enters enterocytes.

Question 21:
Of the following, the MOST beneficial formula for patients with gastrointestinal allergy, short gut syndrome, or cystic fibrosis is:

A. a protein hydrolysate
B. carbohydrate free
C. lactose free
D. low in iron
E. soy based

Suggested answer: A. A protein hydrolysate formula provides proteins in the form of small peptides. As such, they are less allergenic and less likely (vs. full proteins) to cause allergies in patients with gastroenterology allergies such as cow's milk protein allergy. They are also less likely to cause allergies in children with poor gut integrity, such as those with short gut syndrome. Protein hydrolysate formulas requires less peptidase digestion because they are pre-digested, making them ideal for patients with Cystic Fibrosis or patients with other reasons for pancreatic sufficiency. Sugars such as lactose have nothing to do with allergy, but may cause an osmotic diarrhea in patients with malabsorption. Soy proteins are both allergenic and require pancreatic enzymes to fully digest.

Question 22:
Of the following fatty acids, which MUST be added to cow milk-based infant formula?

A. Arachidic
B. Linoleic
C. Oleic
D. Palmitic
E. Stearic

Suggested answer: B. There are 2 essential fatty acids for humans: alpha-linolenic acid (ALA, an omega-3 fatty acid) and linoleic acid (LA, an omega-6 fatty acid). LA is the only fatty acid whose amount is required to be stated on formulas. ALA and LA are not independently added, but rather part of the vegetable oils mixed in formulas to provide fatty acids.

ALA is converted to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are anti-inflammatory. LA is used to make arachidonic acid (ARA) which is a precursor to prostaglandins and other proinflammatory mediators. Both DHA and ARA are supplemented in available formulas.

Question 23:
A 2-year-old boy with developmental delay receives daily tube feedings. Among the following, the side effect MOST likely to result from high osmolality or high carbohydrate content of these feedings is:

A. diarrhea
B. fecal impaction
C. gastritis
D. mucosal atrophy
E. occlusion of the feeding tube

Suggested answer: A. High osmolality and high carbohydrate content formulas can both lead to diarrhea. High osmolality results in high osmolar concentration in the colon, which draws water into the lumen creating loose stools. High carbohydrate contents can result in excess carbohydrates reaching the colonic gut bacteria. The bacteria ferment the carbohydrates into osmotically-active short chain fatty acids, which also attract water in the lumen to produce diarrhea.

Question 24:
When the composition of colostrum is compared to that of mature human milk, colostrum is found to be LOWER in:

A. ash
B. immunoglobulin A
C. polymorphonuclear leukocytes
D. sodium
E. total fat

Suggested answer: E. Colostrum is the first stage of breast milk and lasts for many days after birth. Colostrum is high in protein (especially immunoglobulins), fat-soluble vitamins, and minerals ("ash"). Compared to mature milk, it has higher concentrations of protein, sodium, potassium, and chloride. It has lower fat concentrations than that found in mature milk.

Question 25:
The RECOMMENDED daily dose of vitamin D for a healthy 1-week-old, preterm infant taking oral feedings is (in IU):

A. 4
B. 40
C. 100
D. 400
E. 1,000

Suggested answer: D. Vitamin D is best known for its role in calcium homeostasis; however, it is also a hormone that has far ranging effects in the host. Because infants often receive inadequate sunlight, and because breast milk has low concentration of Vitamin D, infants are advised to supplement their milk/formula feeds with Vitamin D supplementation. The current recommendation for preterm or term neonates is to supplement with 400 IU/day.

Question 1
Which of the following statements regarding parenteral nutrition (PN)-associated complications and toxicity is true?

A. Premature infants develop protein toxicity rapidly with early introduction of PN.
B. The most common feature of neonatal PN-associated liver disease is steatosis.
C. Experimental models have demonstrated impaired pulmonary function and displacement of bilirubin from albumin binding sites with excessive intravenous (IV) lipid administration.
D. PN-associated liver disease usually presents within one week of initiating PN.

Suggested answer: C. Parenteral nutrition has many associated complications. In general, within 1-2 weeks LFTs become elevated and micro/macro steatosis develops. Cholestasis (conjugated bili > 1.5 mg/dL), extramedullary hematopoiesis, fibrosis and then cirrhosis ensue. Moderate fibrosis is present after approximately 40 months of parenteral nutrition. Cholestasis is the prominent initial finding in infants (steatosis and extramedullary hematopoiesis resolves), whereas steatosis is most prominent in adults.

Specific macronutrient complications include: i) protein toxicity with time, perhaps from amino acids such as methionine, cysteine, and tryptophan, as documented in premature infants receiving 3.6 g/kg/day vs. 2.5 g/kg/day; ii) glucose toxicity leading to steatosis, especially with GIRs>12.6; and iii) lipid toxicity, possibly through phytosterols in lipid preparations. Lipids have also been shown to alter pulmonary membrane diffusion and displace bilirubin from albumin.

Question 2
Which of the following metabolic alterations is most commonly seen with re-feeding syndrome?

A. Hyperlipidemia secondary to increased serum ketone bodies
B. Wernicke's encephalopathy secondary to thiamine deficiency
C. Severe hypophosphatemia affecting myocardial and respiratory function
D. Hypernatremia and hypertonic dehydration affecting mental status

Suggested answer: C. Refeeding syndrome occurs within 4 days when transitioning from the starving to the fed state. During starvation, the body metabolizes protein and fat, and uses little insulin. Protein/fat catabolism leads to low total body phosphate stores, even if serum levels are normal. With feeding, the body starts metabolizing sugar and generates large amounts of insulin. The insulin surge promotes cellular uptake of phosphate, resulting in profound hypophosphatemia. The low phosphate impairs ATP production resulting in a myriad of symptoms, from non-specific signs to rhabdomyolysis, leukocyte dysfunction, respiratory failure, cardiac failure, hypotension, arrhythmias, seizures, coma, and even sudden death. Hypophosphatemia can also rarely cause Wernicke's encephalopathy, but thiamine deficiency (not associated with refeeding syndrome) is a more likely cause.

Question 3
Which of the following statements is false concerning failure to thrive (FTT)?

A. FTT is a term used to describe infants and children whose growth deviates from that expected for their sex and age.
B. It is a symptom not a diagnosis
C. Dysfunction of any organ system may result in FTT.
D. It is a common disorder that may affect 10-20% of outpatients.
E. The majority of patients with FTT have organic causes.

Suggested answer: E. There is no consensus definition for FTT. It usually refers to children with abnormally low weight for age and gender. Others suggest that it should include failure in other aspects of development as well. Still other definitions for older children are: <75% median weight/height, <2 standard deviations below mean weight/height, or weight that crosses 2 percentiles. FTT accounts for 1-5% of pediatric hospital referrals and 10-20% of outpatient visits. Usually an organic cause is not found, though oro-motor dysfunction is increasingly becoming recognized as a common cause for FTT.

Question 4

A 29 year-old male is referred from an optometrist for evaluation. The patient's liver profile shows AST 78 IU/L, ALT 92 IU/L, Bili 1.4 mg/dL, Alk Phos 88 IU/L, and albumin 3.4 g/dL. The photo of the patient's eyes is attached. All of the following statements are true except: 3.18.04

A. The patient's diagnosis is Wilson's disease if the ceruloplasmin is low.
B. This finding on the eye exam can be seen in primary biliary cirrhosis and autoimmune hepatitis.
C. The pigmentation will disappear with effective therapy.
D. Neurologic symptoms typically do not occur in the absence of this finding.
E. The mechanism that causes the disorder associated with this finding occurs as a result of over-absorption of copper.

Suggested answer: E. Wilson's disease, the commonest metabolic cause of ALF in children over 3, results from defective copper trafficking out of hepatocytes. The disease is caused by a mutation in ATB7B, which moves copper ions against concentration gradients i) into the Golgi (for formation of ceruloplasmin) and ii) out of the cell. As a result, serum ceruloplasmin is low, though it may sometimes be normal or high because ceruloplasmin is also a negative acute phase reactant. Other diagnostic tests include a blood smear for hemolysis, low alkaline phosphatase, and raised urine copper before and after pencillamine challenge. The best diagnostic test is elevated copper levels on liver biopsy.

Kayser-Fleisher rings are gold or gray/brown rings in the peripheral cornea representing copper/sulfur deposits. They are usually (but not always) present in older patients with neurological problems, such as mood disorders/depression (adolescents), bradykinesia (pseudo-parkinsonian Wilson's), multiple sclerosis with tremor (pseudo-sclerotic Wilson's) , or dyskinesia. Treatment reverses KF rings. Some treatments include pencillamine which binds free copper for urinary excretion, and zinc which traps copper in enterocytes to be lost in the gut lumen when the cells are sloughed.

Serum copper is not a reliable test for Wilson's disease. Serum copper reflects a combination of free copper and copper bound to ceruloplasmin. Therefore, in Wilson's disease it may be high (from free copper released when hepatocytes lyse) or low (because of poor ceruloplasmin production).

Question 5

All of the following medications can cause acute cholestasis resembling obstructive jaundice except:

A. Erythromycin estolate
B. Nitrofurantoin
C. Sulindac
D. Amoxicillin-clavulanic acid
E. Chlorpromazine

Suggested answer: C. Most drug-induced liver disease is cytotoxic. However, some drugs induce hepatitis-cholestasis disease characterized by jaundice, itching, elevated alkaline phosphatase, and histological evidence that resembles obstructive jaundice. Drugs that cause this include erythromycin, chlorpromazine, nitrofurantoin, and amoxicillin-clavulanic acid. Eosinophils can be seen on liver biopsies, suggesting a hypersensitivity/allergic etiology. Sulindac is an NSAID that can also cause cholestasis through inhibiting cannilicular secretion of bile acids. Rather than an obstructive picture, histology shows more hepatocellular damage as the retained bile damages hepatocytes.

Question 6

A 17 year-old female is gravida 21 weeks. She presents with nausea, emesis and jaundice. Her medications are prenatal vitamins. Her laboratory exam is significant for ALT 639 IU/L, AST 459 IU/L, bilirubin 4.8 mg/dL, Alk Phos 320 IU/L, and albumin 3.4 g/dL. The most likely cause of her jaundice is:

A. Intrahepatic cholestasis of pregnancy
B. Viral hepatitis
C. Acute fatty liver of pregnancy
D. Hyperemesis gravidarum
E. Drug-induced hepatitis

Suggested answer: B. The most common cause of jaundice in pregnancy is viral infection, with HSV and Hepatitis E most concerning for the developing fetus. In the case of Hepatitis B infections, the newborn needs active (vaccine) and passive (immunoglobulins) immunoprophylaxis. Intrahepatic cholestasis of pregnancy usually has more itching than jaundice, and occurs in the 3rd trimester when hormone levels are highest (estrogen inhibits BSEP and progesterone inhibits MDR3). Mutations in BSEP and MDR3 may also manifest for the first time during pregnancy. Acute fatty liver of pregnancy presents more severely, and hyperemesis gravidarum has extreme nausea and vomiting. Prenatal vitamins should not cause hepatitis.

One algorithm is as follows: 1) rule out viral hepatitis; then 2) if ALT>1000, consider medication toxicity (Tylenol); 3) if ALT<1000 and with renal failure or DIC, consider acute fatty liver of pregnancy; 4) if ALT<1000 with RUQ pain, consider stones; and 5) otherwise if ALT<1000 consider hyperemesis gravidarum or other drugs.

Question 7

A 10-old male with HIV on HART therapy is evaluated for elevated liver enzymes (ALT 119 IU/L, AST 101 IU/L, bilirubin 1.3 mg/dL, Alk Phos 390 IU/L). A liver biopsy showed numerous blood-filled cysts that do not have an endothelial lining. This liver biopsy finding is most likely secondary to:

A. Cytomegalovirus
B. Protease inhibitors
C. Rochalimaea hensalae
D. Caroli's disease
E. Congenital factors (e.g., cystic Von Meyenburg complexes)

Suggested answer: C. Peliosis hepatis refers to blood filled cavities in the liver that develop from neo-angiogenesis. Peliosis often also occurs in the spleen. The neo-angiogenesis is induced by Bartonella spp. infection (formerly Rochalimaea, such as those that cause Cat Scratch disease) in the setting of HIV/AIDS (CD4<100). In HIV negative individuals, hepatis peliosis can be caused by anabolic steroids, Castleman's disease, Hodgkin's lymphoma, leukemia, or other malignancies. Diagnosis is made by visualizing gram-negative bacilli in blood or biopsy specimens, and cultures are seldom positive.

Caroli's disease and cystic von Meyenburg complexes are both developmental diseases associated with polycystic kidney disease. Caroli's disease has numerous dilated intrahepatic bile ducts lined with defective cholangiocytes. Cystic von Meyenburg complexes are benign cystic tumors, also referred to as bile duct hamartomas.

Question 8
All of the following statements regarding coagulation disorders in cirrhosis are true except:

A. Thrombopoietin is decreased in patients with cirrhosis.
B. Factor VIII is not depressed until the late stages of cirrhosis.
C. Bleeding is a common cause of death in patients with cirrhosis who undergo abdominal surgery.
D. Thrombotic complications are rare in patients with cirrhosis because of thrombocytopenia and decreased clotting factor levels.

Suggested answer: D. Coagulopathies accompany liver disease, as hepatocytes synthesize both pro- and anti- coagulation factors. As a result, bleeding is a common cause of death in cirrhotic patients who undergo surgery, while thrombotic complications such as DVTs and PEs also occur. Factor VIII is high (made in spleen in lymph nodes) in cirrhosis and is not depressed until late stages. The liver also makes thrombopoietin, which promotes megakarocytes to make platelets. Thrombopoietin is low in cirrhosis, and, along with platelet congestion in the spleen from portal hypertension, explains thrombocytopenia in cirrhotic patients (liver transplant restores thrombopoietin levels to normal).

Question 9
Which of the following statements concerning esophageal varices is not true?

A. Esophageal variceal bleeding ceases spontaneously in 40% of patients.
B. The mortality from an episode of variceal hemorrhage is 30%.
C. Overall mortality is not significantly reduced with beta-blocker prophylaxis.
D. A hepatic venous portal gradient (HVPG) of greater than or equal to 20 mm HG predicts a poorer one-year survival in a patient who has bled from varices.
E. Sclerotherapy is an effective method of preventing first time variceal bleeding and reducing mortality.

Suggested answer: E. Variceal bleeding must be managed effectively, as the mortality from variceal hemorrhage is 30-50%. Varices are unlikely to bleed when the HVPG is less than 12, whereas 1/3 of patients in one study bled if the gradient was greater than 12. Prophylactic measures such as beta blockers have been shown to prevent bleeds but have not improved mortality from variceal hemorrhage. Prophylactic sclerotherapy or banding has not become standard practice. Prophylactic sclerotherapy did reduce variceal bleeding but increased congestive hypertensive gastropathy in one study (no difference in survival). In another study, 42% of patients bled after prophylactic sclerotherapy.

In the event of bleeding, only 40-50% episodes stop spontaneously. Sclerotherapy and band ligation have proven effective measures to stop bleeding temporarily, and are considered standard measures to stabilize a patient ahead of liver transplant.

Question 10
All of the following drugs can cause microvesicular steatosis except:

A. Tetracycline
B. Aspirin
C. AZT
D. Alcohol
E. Troglitazone
F. Valproic acid

Suggested answer: E. Troglitazone is a PPARg agonist used to treat DM2, that has since been pulled off the market for causing hepatitis. Histology shows hepatocellular injury, and liver failure can ensure within 1-7 months. The other choices (tetracycline, aspirin, AZT, alcohol, and valproic acid) can all affect mitochondria and cause mircovesicular steatosis, analogous to that seen with aspirin in Reye's syndrome.

Question 11
A 14 year-old female presents for evaluation of jaundice and fatigue. She has been taking phenytoin for six years for a seizure disorder and levothyroxine for three years for hypothyroidism. Her review of systems is positive for amenorrhea (three months). Laboratory exam shows ALT 684 IU/L, AST 388 IU/L, bilirubin 6.1 mg/dL, Alk Phos 199 IU/L, total protein 8.2 g/dL, albumin 3.1 g/dL, and PT 16 seconds. The most likely explanation for her illness is:

A. Phenytoin liver toxicity
B. Autoimmune hepatitis
C. Hyperthyroidism
D. Primary Biliary Cirrhosis
E. Choledocholithiasis

Suggested answer: B. This patient likely has autoimmune hepatitis. She has some early symptoms of AIH, such as fatigue and amenorrhea. Other extra-hepatic symptoms include low grade fever, skin rash, and joint pain. She has a pre-existing history of likely autoimmune thyroid disease. And her total protein is elevated in the context of a low albumin, suggesting she is making copious immunoglobulins as would occur in autoimmune states. Phenytoin toxicity and PBC are not associated with amenorrhea. Hyperthyroidism usually does not elevate liver numbers. Choledocholithiasis would present with RUQ pain.

Question 12
Which of the following statements concerning hereditary hemochromatosis (HH) is false?

A. The phenotypic expression in the United States is 1/200-1/250.
B. HH is the most common, identified, genetic disorder in Caucasians.
C. The genetic defect causes an excessive absorption of iron.
D. Compound heterozygosity (C282Y, H63D) accounts for 3-5% of cases.
E. HH should be considered in any male patient with transferrin saturation greater than 60 percent.

Suggested answer: B. Hereditary hemochromatosis is a disease of excessive gut iron absorption. Iron (in the form of free iron or attached to heme) is processed by the brush border and then stored in enterocytes as ferritin. The enterocytes can either pass the iron into the circulation via the transporter ferroportin or carry the iron into the intestinal lumen and out of the body when the cells are sloughed. Iron that passes

through the ferroportin channel is carried to the liver via the portal circulation and stored in zone 1 hepatocytes. Kupffer cells in the liver store iron from the systemic circulation, whereas reticulendothelial cells in the spleen store iron from spent red blood cells.

Hereditary hemochromatosis is most commonly caused by the HFE (high Fe) gene. The gene controls liver hepcidin expression. Hepcidin is a hormone which negatively regulates ferroportin. With mutant HFE, then, hepcidin levels are low. As a result, ferroportin activity is increased, and more iron stored in the enterocyte is allowed to enter the systemic circulation, even when excess iron is already present. The iron becomes deposited in various end organs, where it causes a series of systemic complications. The iron binds to its carrier transferrin, so a transferrin saturation >60% in males and >45-50% in females should be concerning for hemochromatosis.

The genetics of HFE are complex. The incidence of HFE homozygosity in Caucasian/Celtic populations is as high as 1:150-1:200. However, phenotypic expression ranges from 1:2 to 1:150, depending on the what symptoms are accepted as consistent with disease (in the 1:2 study, many of the symptoms were general and could be found in control subjects as well). As a result, the incidence of HH based on phenotype may be as rare as 1:200 (incidence of homozygosity) X 1:150 (incidence of symptoms in homozygous individuals) = 1:30,000. This is rarer than the 1:3200 incidence of CF, which is the most common identified genetic disorder in Caucasians.

Question 13
All of the following statements regarding TPN liver disease are true except:

A. TPN liver disease is commonly associated with the development of gallbladder stones and sludge.
B. TPN liver disease is usually cholestatic in adults and associated with steatosis in infants.
C. TPN liver disease usually resolves following institution of enteral nutrition if cirrhosis has not developed.
D. Low birth-weight infants are more susceptible than adults to TPN liver disease.
E. The combination of CCK and ursodiol does not reduce mortality from TPN-related liver disease.

Suggested answer: B. Liver disease is a mjor complication of TPN. Clinical cholestasis develops in 25% of premature infants on TPN, with low birth-weight infants and those developing sepsis at highest risk. Steatosis is transient in infants, whereas it is the defining characteristic in adults. 100% of infants on TPN for more than 6 weeks develop calcium bilirubinate sludge (stones are much less common). Studies have shown that CCK does not reduce gallstones, cholestasis, or mortality. Ursodiol can improve liver numbers initially, but has not been shown to improve liver histology or mortality.

Question 14
Pellegra is associated with what vitamin deficiency?

A. Riboflavin
B. Thiamin
C. Ascorbic acid
D. Pyridoxine
E. Niacin

Suggested answer: E. Vitamin B1 (thiamine) deficiency causes “beri beri,” characterized by confusion, peripheral paralysis, muscle weakness, tachycardia, and cardiomegaly. Vitamin B2 (riboflavin) deficiency causes anemia, angular stomatitis, and seborrheic dermatitis. Vitamin B3 (niacin) deficiency causes pellagra, consisting of dermatitis, diarrhea, and dementia. Vitamin B6 (pyridoxine) deficiency causes tongue swelling, rash, and neuropathy. Vitamin B9 (folate) deficiency causes macrocytic anemia

and macroglossia. Vitamin B12 (cyanocobalmin) deficiency also causes macrocytic anemia. Vitamin C (ascorbic acid) deficiency causes bleeding gums, poor wound healing, and scurvy.

Question 15
A 24 month old infant who is TPN-dependent secondary to short gut syndrome has persistent anemia. She does have TPN-cholestasis but does not have esophageal varices. There has been no evidence of bleeding. On exam she is pale and mildly jaundiced. Her hemoglobin is 7.5 gm/dl and her MCV is 70. What deficiency would result in her persistent anemia?

A. Carnitine
B. Selenium
C. B_{12}
D. Copper

Suggested answer: D. Copper deficiency can occur with TPN use, especially because copper is often omitted from formulations to avoid excessive copper accumulation (copper is secreted via bile, and cholestasis impairs this secretion). Copper deficiency can cause iron anemia and microcytic anemia, because copper is needed for enzymes involved in iron absorption (i.e. copper-dependent ferroxidase). B12 deficiency causes megoblastic anemia, and can result from ileal resection in short bowel syndrome. Selenium deficiency occurs if it is not supplemented in TPN, and leads to cardiomyopathy and Keshan's disease (perhaps in association with Coxsackie virus infection).. Carnitine deficiency also occurs if it is not supplemented in TPN. Carnitine is needed to shuttle long chain fatty acids into the mitochondria, and without it myopathy (including cardiomyopathy) develops.

Question 16
What is not a result of ascorbic acid deficiency?

A. perifollicular hemorrhage
B. subperiosteal hemorrhage
C. hyperkeratotic hair follicles
D. cheilosis

Suggested answer: D. Ascorbic acid (Vitamin C) deficiency is associated with enlargement and hyperkeratosis of hair follicles, followed by proliferation of blood vessels around the follicle leading to perifollicular hemorrhage. Subperiosteal hemorrhage is also possible, especially in infants. Cheilosis/angular stomatitis is a characteristic of riboflavin (vitamin B2) deficiency.

Question 17
Vitamin A deficiency is manifested by all of the following symptoms except

A. keratomalacia
B. follicular hyperkeratosis
C. night blindness
D. xerosis
E. seborrhea dermatitis

Suggested answer: E. Vitamin A deficiency is characterized by night blindness, keratomalacia (dryness and keratinized epithelium of the cornea), xerosis especially of the conjunctivae and cornea, and follicular hyperkeratosis from blockage of hair follicles with keratin. Excessive vitamin A can cause seborrhea dermatitis.

Question 18
The standard deviation is defined as

A. The average of the squared differences between each observation and the mean.
B. Measure of the inaccuracy of the sample mean as a representative of the mean of the entire patient population from which the sample was drawn.
C. A standardized measure of variation used to compare dispersion for variables with different units of measurement.
D. Mean of the differences between each observation and their mean.

Suggested answer: C. Standard deviation measures how much variation there is in a data set from the mean. It quantifies the variability of the population. It can be viewed as a standarized measure of "dispersion," or variation, around the mean. One standard deviation below and above the mean accounts for 68.26% of the population, whereas two standard deviations below and above the mean accounts for 95.44% of the population.

If the data points represent the entire population, then the true mean can be calculated. In this case, the population variance is calculated by subtracting the value of each point from the mean, squaring the result, and then averaging it by dividing by the total number of values (choice A). The population standard deviation is then calculated by taking the square root of the population variance.

If data points represent a sample of the population, then the mean of the data points will estimate the true mean of the population. To account for this estimation, the variance of a sample is calculated by subtracting the value of each point from the mean, squaring the result, and then dividing by the total number of values minus 1. The sample standard deviation is calculated by taking the square root of the sample variance.

When the data points represent a sample of the population, the standard error of the mean can be calculated. It quantifies the how accurately the sample mean representing the true mean. In other words, it quantifies the certainty/uncertaintly of the calculated mean (choice B). It is calculated by dividing the sample standard deviation by square root of the number of data points (standard deviation of the sampling distribution of the mean).

Question 19
The following statement is false regarding a correlation coefficient r:

A. A correlation coefficient is a measurement of the strength of the linear association between two variables.
B. The correlation coefficient varies between -1 and +1.
C. It represents the proportion of the variability in an outcome variable that can be explained by its linear association with a predictor variable and vice versa.
D. It can only be used when the variables of interest are continuous.

Suggested answer: C. The Pearson's correlation coefficient r measures how well two continuous variables vary with one another. -1 reflects perfect negative correlation, +1 perfect positive correlation, and 0 no correlation. The square of the correlation (coefficient of determination) measures the amount of variance in one group that can be associated with the amount of variance in the other group (choice C). This question assumes r refers to the Pearson correlation coefficient; however, other correlation coefficients, like the Spearman rank correlation coeficient, does not require variables to be continuous.

Question 20

The following equation represents a linear regression line

A. r^2
B. $y = \beta_1 x_1 + \beta_2 x_2 + E$
C. $sd/\sqrt{n}$
D. $\text{logit } P(x) = \alpha + \beta E + \gamma_1 V_1 + \gamma_2 V_2 + \delta_1 E V_1$

Suggested answer: B. A linear regression line models the relationship between two variables using a line. A pre-requisite is that a correlation between two variables exists. The most common method for making the line is the method of least-squares. This method calculates the best-fitting line for the data by minimizing the sum of the squares of the vertical deviations from each data point to the line. Choice A is the coefficient of determination and choice C is the standard error of the mean.

Question 21

The following statements are true regarding sensitivity

A. Probability of testing positive if the disease is truly present
B. Probability of having the disease given the results of the test
C. Should not be increased relative to specificity when the penalty associated with misdiagnosis is high.
D. Can be increased by increasing the prevalence of disease in the screened population

Suggested answer: A. Sensitivity is the probability of a test being positive if the disease is truly present, whereas specificity is the probability of the test being negative if the disease is truly absent. These calculations do not depend on the prevalence of the disease. For screening tests (i.e. HIV screening tests), in which the goal is to catch all diseased individuals even at the risk of having false positives, sensitivity should be increased relative to specificity. In contrast to sensitivity and specificity, positive and negative predictive values reflect the probability of having or not having the disease given a test result. These values are influenced by the prevalence of the disease in the population.

Question 22

Using the following number set determine the mean, median, and mode

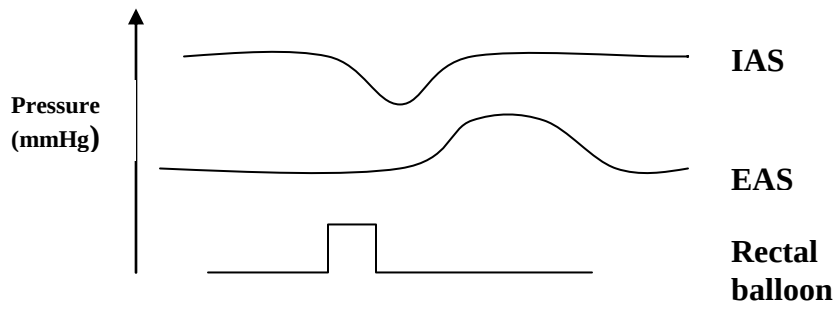
1, 2 ,3 ,4, 5 ,5 , 5

Suggested answer: Mean is (1+2+3+4+5+5+5)/7 = 3.57. Median is the middle number, or 4. Mode is the most common value, or 5.

Question 23

The reaction of the internal anal sphincter illustrated below is mediated via which pathway?

A. Cholinergic inhibitory
B. Cholinergic excitatory
C. Adrenergic inhibitory
D. Adrenergic excitatory
E. Interstitial cells of Cahal



Suggested answer: E. When the rectum is distended, the IAS relaxes to allow stools to descend and the EAS contracts to prevent defecation. The IAS relaxation is accomplished by non-adrenergic, non-cholinergic (NANC) nerves that release nitric oxide (NO), vasoactive intestinal peptide (VIP), and perhaps carbon monoxide. Rodent studies have also shown that Interstitial Cells of Cajal, the pacemaker cells throughout the gut stimulating slow waves of peristalsis, are located in the IAS and may be involved in IAS relaxation. (See *Gut* 2005;**54**:1107-1113. Interstitial cells of Cajal are involved in the afferent limb of the rectoanal inhibitory reflex)

Question 24
The pathogenesis of Hirschsprung's disease is thought to be related to which of the following?

A. Increased acetylcholine
B. Decreased glutamine
C. Decreased GABA
D. Decreased nitric oxide
E. Increased serotonin

Suggested answer: D. Hirschprung's disease is caused by lack of ganglion cells in the mucosal (Meissner's) and myenteric (Auerbach's) plexuses of the distal colon. These ganglion cells normally come from migrating neural crest cells during development, and mutations in genes involved in neural crest cell migration have been found in Hirschprung's patients. The classic manometry finding in Hirshprung's disease is absent IAS relaxation when the rectum is distended. The relaxation normally is mediated by nitric oxide, suggesting that nitric oxide-generating neurons are missing or defective in Hirschprung's disease.

Question 25
A 14 year old boy with biliary atresia who underwent a Kasai procedure at 5 weeks of age has progressed to end stage liver disease and is listed for liver transplantation. He has had 2 major variceal bleeds in the last 3 months and recently had a transjugular intrahepatic postosystemic shunt (TIPS) placed. The most likely complication following this shunt placement is:

A. Infection
B. Encephalopathy
C. Progressive liver failure
D. Stent migration

Suggested answer: B. The most common complication of the TIPS procedure is encephalopathy, as the procedure allows blood from the gut to bypass the liver filter and enter the systemic circulation directly. Encephalopathy happens in as many as 25-34% adult cases, and usually occurs immediately after the procedure. The second most common complication is shunt occlusion, which can develop within 24 hours of the procedure. Heart failure can also occur, as more blood is returned to right heart following TIPS. Stent migration has been reported, including cases in which the stent caused atrial puncture.

Question 1:
In the pediatric population, which of the following is the most common route of HCV transmission:

A. materno-foetal
B. IV drug use
C. blood products
D. sexual contacts
E. tattoos

Suggested answer: A. Since blood product screening started in 1991, most childhood HCV cases occur through perinatal transmission. Adolescents and adults acquire HCV through percutaneous (i.e. IV drug use) and non-percutaneous (i.e. sexual transmission) routes. Acute infections are often asymptomatic. Chronic infections, caused by incomplete immune-mediated attack against infected hepatocytes, lead to fibrosis and cirrhosis, and accounts for the most number of adult liver transplantations worldwide.

Question 2:
Which of the following is NOT associated with Wilson's Disease:

A. Fatty liver
B. High serum uric acid
C. Low serum zinc level
D. Low serum alkaline phosphatase
E. High serum bilirubin

Suggested answer: B. Wilson's disease is characterized by poor copper intracellular trafficking and extracellular transport, caused by a defect in the copper-transporting adenosine triphosphatase (ATPase) gene (ATP7B). It is the most common reason for fulminant hepatic failure in children greater than 3 years. The earliest histological changes include microvesicular and macrovesicular fatty deposition and glycogenylated nuclei, which progresses to inflammation and fibrosis.

Wilson's disease can present as a wide spectrum, from modest elevations in transaminases to acute hepatitis with high serum bilirubin levels. Wilson's disease also has characteristically low zinc and alkaline phosphatase levels, though the mechanism has not been completely resolved (zinc is a treatment in Wilson's disease, inducing metallothionein which traps copper in enterocytes). Uric acid levels are low in Wilson's disease, because copper accumulates in renal tubular cells. This causes a Fanconi-like syndrome and uric acid wasting into the urine.

Question 3:
Which statement is false:

A. 90% of Vit. A is stored within the liver
B. Vit. A deficiency Xeropthalmia is irreversible
C. Can cause a hypochromic microcytic anemia with low Fe but normal Fe stores
D. Hypervitaminosis A is associated with head aches

Suggested answer: B. Vitamin A comes from plant and animal sources. Vitamin A from plant sources is in the form of Provitamin A, which is converted to Vitamin A in a series of highly regulated steps that depend on whole-body Vitamin A status. Vitamin A from animal sources is already in the active form, so excessive intake can lead to Vitamin A toxicity. Once Vitamin A is absorbed, in enters the lymphatic system through chylomicrons, then the venous system at the thoracic duct where it is metabolized into remnants such as

apoliproteins B and E, and eventually endocytosed into the liver. 50-90% of total body retinol is stored in stellate (Ito) cells, and transports to other organs through the serum by binding to retinol binding protein.

Vitamin A deficiency is uncommon in the developed world, but the third most common nutritional deficiency world-wide. It presents as xerophthalmia (abnormal keratinization of conjunctiva secondary to poor lacrimal gland secretion), poor bone growth, non-specific skin problems, and decreased humoral and cell mediated immune function. Vitamin A deficiency can also lead to anemia, presumably by inhibiting the normal metabolism of iron. Supplementation can reverse many of these problems; however, advanced corneal scarring may be irreversible.

Vitamin A toxicity, on the other hand, presents with a myriad of symptoms, including dry skin, headaches, hepatomegaly, and increased CSF pressures (pseudotumor cerebri).

Question 4:
The most common route of transmission for new onset Hepatitis C in the pediatric population in United States and Europe is:

A. Drug Abuse
B. Male to male sex
C. Tainted blood supply
D. Vertical transmission

Suggested answer: D. Please see question1 in this set. Vertical transmission accounts for as much as 65% of pediatric cases of HCV infection.

Question 5:
Which of the following variables DOES NOT predict a higher likelihood of response to interferon therapy in children with chronic hepatitis B:

A. Active inflammation on liver biopsy
B. Higher interferon dose
C. Female gender
D. Low level of baseline HBV DNA
E. Elevated serum transaminase levels

Suggested answer: B. Interferon has at least two antiviral mechanisms: (1) increases expression of anti-viral genes, and (2) stimulates the immune system to eliminate HBV. The immune-stimulatory effects of interferon explains why responders first have a burst of elevated aminotransferases (presumably from the host immune system attacking infected hepatocytes), followed by normalization of aminotransferases, loss of serum HBV-DNA, and loss of viral antigens HbeAg and HbsAg.

Hence, interferon may help those children already trying to mount an immune response against infected hepatocytes (those with active inflammation on liver biopsy and those with ALT greater than or equal to 2 times the upper limit of normal). Furthermore, interferon may promote a better response when there is less virus to fight, i.e. in those with lower baseline serum HBV DNA levels. Interferon has also been shown to have a better response in females. Increasing interferon doses or priming with prednisone has not been shown to improve outcomes.

Question 6:
Which of the following is NOT a common feature of BOTH kwashiorkor and marasmus:

A. Irritability
B. Decreased serum lipoproteins
C. Markedly Depressed serum albumin
D. Increased susceptibility to infection
E. Anemia

Suggested answer: C. There are two subtypes of severe protein-energy malnutrition (PEM): kwashiorkor and marasmus. Kwashiorkor is characterized by muscle atrophy and increased body fat, secondary to poor protein intake in the setting of adequate energy intake. Marasums, on the other hand, is characterized by muscle wasting and depleted fat stores, secondary to inadequate intake of all nutrients. Severe PEM of both types produces a number of signs and symptoms: irritability, decreased serum lipoproteins, increased infection risk, and anemia. However, kwashiorkor classically presents with severely low serum albumin concomitant with edema. Marasmus presents with low-normal serum albumin with wasting but no edema.

Question 7:
Tyrosinemia is associated with:

A. Boiled cabbage smell
B. Mousey smell
C. Blue Cheese Vinaigrette smell
D. Resident post call smell
E. All of the above except D

Suggested answer: A. Tyrosinemia is caused by a defect in metabolizing tyrosine into its two products, acetoacetate (ketogenic) and fumarate (glucogenic). Five enzymes are involved in tyrosine metabolism, and defects in fumarylacetoacetate hydrolase (FAH) catalyzing the last enzymatic step leads to the most severe form of tyrosinemia (Hereditary tyrosinemia Type 1). Fumarylacetoacetate (FAA) accumulates, damaging renal and liver cells. FAA is metabolized into succinylacetoacetate and succinylacetone which are measured in the urine to make the diagnosis. Nitisinone, which blocks an earlier step in the tyrosine metabolism pathway, is used as treatment to prevent FAA accumulation.

Patients with tyrosinemia may present with a "boiled cabbage" smell. Others describe the smell as "rotten mushrooms" or "rancid butter." Patient with PKU (inability to break down phenylalanine) have a "mousy," "musty," "wolf-like," "barny," "horsey," or "stale" smell. Isovaleric acidemia patients have a "cheesy" "acrid" odor of "smelly feet."

Question 8:
Which statement about Hepatitis A is true:

A. Leading cause of fulminant hepatitis in Pediatrics
B. Has been associated with chronic hepatitis
C. Recurrence of the disease can occur up to 6 months after primary infection
D. Treatment for non-fulminant hepatitis A includes Lamivudine for 4 weeks
E. Severity of disease decrease with increasing age

Suggested answer: C. Hepatitis A is an RNA virus which replicates in hepatocytes and spreads. The virus per se does not cause symptoms; rather, cell-based immunity targeting infected hepatocytes leads to jaundice, elevated aminotransferases, and other symptoms. Older children are more severely affected, perhaps because they have a more developed immune response (70% under 6 years old are

asymptomatic, whereas 70% of older children/adults are symptomatic). Treatment is largely supportive, though vaccine and/or immunoglobulin administration to previously-unvaccinated exposed individuals has been shown to limit symptoms. Relapse can occur, typically only once within 6-9 months after the initial infection ("relapsing Hepatitis A"). HAV infection may also trigger autoimmune hepatitis in predisposed children, but HAV on its own has never been to cause a chronic infection.

Fulminant hepatitis occurs when the host's immune response is excessive. HAV infection accounts for only 1% of pediatric acute liver failure cases in the US (but up to 60% in Latin America).

Question 9:
Symptoms and signs NOT associated with Kwashiorkor (see picture) include:

A. Flaky paint sign
B. Hanover's sign
C. Flag sign
D. Proportional weight for height
E. Fatty liver

Suggested answer: B. Kwashiorkor is characterized by decreased protein intake but normal or above normal energy intake, and presents with edema and low serum albumin. Kwashiorkor patients have normal weight and height for age, anasarca, and dry, atrophic, peeling skin ("flaky-paint sign") with areas of hyperkeratosis and hyperpigmentation. They also have hepatomegaly (from fatty liver infiltrates) and a distended abdomen with dilated intestinal loops. The hair of kwashiorkor patients is dry, fargile, and hypopigmented. During periods of adequate protein intake, hair color is restored and produces bands of normal color (the "flag sign").

Question 10:
Acute lower GI hemorrhage in HIV infected patients is most often caused by:

a. CMV colitis
b. Lymphoma
c. Kaposi's sarcoma
d. Idiopathic chronic colitis
e. Nonspecific colitis

Suggested answer: C. HIV infected patients, especially those with low CD4 counts in the pre-HAART era, were especially vulnerable to GI problems of infectious or malignant origin. CMV colitis presents similarly to inflammatory bowel disease, with severe cases causing mucosal ulceration and hemorrhage.

Additionally, HIV-related non-Hodgkin's lymphoma frequently presents in the GI tract, with all segments from mouth to anus including biliary system vulnerable (vs. non-HIV related GI lymphomas, in which the stomach is most commonly affected). Severe cases may also produce rectal bleeding. The most common cause of GI bleeding in HIV patients is Kaposi's sarcoma. This malignancy is a vascular tumor caused by HHV-8, and appears as hemorrhagic nodules on colonoscopy. It has been associated with both upper and lower GI bleeds.

Question 11:
First line of treatment of esophageal candidiasis in HIV infected patient is:

A. Clotrimazole
B. Ketoconazole
C. Fluconazole
D. Amphotericin B

Suggested answer: C. Esophageal candidiasis presents with pain on swallowing, and occurs in HIV infected patients with CD4 counts <100 cells/ul. Unlike oropharyngeal thrush which can be treated with topical treatments such as clotrimazole, esophageal candidiasis always requires systemic antifungal therapy. Fluconazole is the intial treatment of choice, and has been shown to be more effective than ketoconazole in randomized trials. Amphotericin B must be given IV and has a number of side effects, making it a poor first choice.

Question 12:
Organisms causing intestinal microsporidiosis in AIDS patients is:

A. Encephalitozoon intestinalis
B. Cryptosporidium
C. Isospora belli
D. Enterocytozoon bieneusi

Suggested answer: A and D. Microsporidiosis is one of the commonest enteropathogens in HIV/AIDS patients. Microsporidiosis are small, spore-forming, intracellular organisms most closely related to fungi. In enterocytes, they distort villous architecture and impair absorption without much concomitant inflammation, leading to watery diarrhea. The most common species affecting humans is Enterocytozoon bieneusi (normally remain local), followed by Encephalitozoon intestinalis (can spread systemically via macrophages). Treatment is with albendazole, though it less effective for E. bieneusi.

Isospora belli and Cryptosporidium also affect immunocompromised patients. In contrast to microsporidiosis, they are protozoa. Both cause gastric/small bowel symptoms, and cryptosporidiosis is associated with voluminous watery diarrhea.

Question 13:
The most common non-opportunistic protozoon parasite is AIDS patients is:

A. Cryptosporidium
B. Gardia lamblia
C, Blastomyces hominis
D. Entamoeba histolytica
E. Toxoplasma gondii

Suggested answer: D. The most common gastrointestinal pathogens in HIV patients include Cryptosporidium parvum, Isospora belli, and Entamoeba histolytica. Of these, Cryptosporidium and Isospora are considered opportunisitc because they require the host to be immunocompromised to cause disease. Entamoeba histolytica, on the other hand, affects immunocompromised and immunocompetent individuals and is considered non-opportunistic.

Blastomyces dermatitidis (not hominis) is an opporunisitic fungus that typically does not affect the GI tract, whereas Blastocystis (not Blastomyces) hominis is a non-opportunistic protozoa whose role as a commensal versus pathogenic organism is still unclear. Giardia lamblia is a protozoan causing prolonged diarrhea in HIV/AIDS patients as well as immunocompetent patients. Finally, Toxoplasma gondii is an opportunistic protozoan that presents typically with encephalitis, pneumonitis, or chorioretinitis, but many also involve the gastrointestinal tract.

Question 14:
The most common opportunistic infection in HIV patients is:

A. Mycobacterium Avium Complex
B. Mycobacterium Tuberculosis
C. Salmonella Typhimurium
D. Clostridium Difficile

Suggested answer: B. While the statistics and definition differ in various studies (some report esophageal candidiasis and Pneumocystitis jiroveci as the most common opportunistic infections), Mycobacterium tuberculosis is one of the commonest opportunistic infections in HIV. Ongoing studies are investigating the relationship between TB and HIV, with results suggesting that TB may not only increase after HIV but lead to a more serious course of disease.

Other common opportunistic pathogens include Mycobacterium Avium Complex (MAC, comprising M. avium and M. intracellulare) causing chronic abdominal cramps and bloating, as well as Salmonella typhimurium causing hemtochezia, tenesmus, and lower abdominal cramps. Clostridium difficile is not an opportunistic infection, though it is very common in HIV patients presumably secondary to frequent antibiotic use.

Question 15:
Which of the following is NOT found in Wolman's disease (cholesterol ester storage disease)

A. Orange coloured liver
B. Lipid laden macrophages in the portal triad
C. Blueish hue to some hepatocytes
D. Diffuse steatosis
E. Inflammation

Suggested answer: C. Wolman disease is caused by a defect in lysosomal acid lipase (LAL). As a result, lysozymes receive endocytosed lipoproteins properly, but they cannot hydrolyze the triglycerides and cholesterol esters. The triglycerides and cholesterol esters accumulate inside cells, leading to bowel wall thickening (accumulation in enterocytes and macrophages) and severe life-threatening diarrhea and malnutrition. In Wolman disease, the adrenal glands are also calcified.

The liver in Wolman disease is enlarged and appears yellow/orange and greasy in appearance (the orange comes more from the cholesterol esters than the triglycerides). There is extensive fibrosis, associated with lymphoid infiltration and accumulation of triglycerides/cholesterol esters in hepatocytes, Kupffer's cells, and

portal area macrophages. In iron storage disorders, rather than Wolman disease, hepatocytes stained for iron may have bluish-hue reflecting excess ferritin in the cytoplasm.

Question 16:
A 5-month-old girl is referred for evaluation of poor growth and irritability. The history is significant for constant spitting up of formula. An upper gastrointestinal series reveals some gastroesophageal reflux but is otherwise normal. Which one of the following most likely explains these findings?

A. Prone positioning after feedings
B. Stress in the home
C. Immaturity with low pressures of the lower esophageal sphincter
D. Inappropriate relaxation of the lower esophageal sphincter
E. Pyloric stenosis

Suggested answer: D. This patient has gastroesophageal reflux disease (GERD) as opposed to uncomplicated reflux, because the reflux is causing pathological symptoms such as poor growth. She does not have anantomical defects such as malrotation, annular pancreas, or even pyloric stenosis because her UGI was normal. She may have cow's milk protein allergy, which can cause similar symptoms. However, the most common explanation for GERD is transient relaxations of the LES separate from the normal LES relaxation that occurs with swallowing.

The prone position has actually been shown to decrease reflux events, though in most cases the risk of SIDS outweighs risks caused by reflux. The patient is 5 months old and should not have an immature LES with consistently low pressures. Finally, stress in the home is more often correlated with adolescent, and adult GERD.

Question 17:
A 7-year-old girl who had undergone a surgical repair for long-segment Hirschsprung's disease in early infancy presents with a fever, abdominal distention, and bloody diarrhea for 2 days. Which of the following is the most likely diagnosis?

A. diversion colitis
B. enterocolitis
C. ulcerative colitis
D. colonic stricture
E. viral gastroenteritis

Suggested answer: B. This patient has Hirschsprung-associated enterocolitis (HAEC). The disease most commonly occurs within the year after correction though may occur before or many years after repair. It presents with diarrhea, fever, vomiting, and sometimes bloody stools. Imaging shows air-filled loops of bowel with no air in the rectosigmoid colon ("cut-off sign"). The pathogenesis is thought to be related to intestinal stasis and bowel overgrowth proximal to the agangiolic segment or proximal to an anastomotic stricture. Bacteria invade the intestinal wall, leading to disease. HAEC occurs in ~1/4 of patients with Hirschsprung's disease, and at one time had a mortality as high as 33%.

Diversion colitis is also caused by stasis; however, this patient does not have any blind loops of bowel. UC should have a more chronic course. Colonic (anastomotic) strictures are associated with HAEC, but HAEC can occur without strictures and strictures can exist without HAEC. Finally, viral gastroenteritis would not be expected to produce bloody diarrhea and the severe symptoms found in this case.

Question 18:
A 6-year-old boy just arriving from Eastern Europe has had malodorous diarrhea since early infancy, even though he was breast-fed. He is small, has some bruises from bumping into furniture going to the bathroom at night, and has recently developed some difficulty walking. Physical examination shows that he is small and undernourished, with depleted subcutaneous fat. He has a protuberant abdomen and 1+ edema in his lower extremities. He has no deep tendon reflexes in his lower extremities. Which one of the following explains the finding on the small intestinal biopsy from this patient?

A. gluten enteropathy
B. congenital lactase deficiency
C. abetalipoproteinemia
D. glucose-galactose transport defect
E. chronic nonspecific diarrhea of childhood

Suggested answer: C. This patient has evidence of fat malabsorption (wasting), including Vitamin K (bruising), Vitamin E (decreased deep tendon reflexes), and perhaps even Vitamin A (night blindness or retinitis pigmentosa). Abetalipoproteinemia (ABL) can cause such symptoms.

The body uses lipoproteins to shuttle cholesterol esters and triglycerides among organs. Lipoproteins have a core of cholesterol esters and triglycerides, surrounded by a monolayer of cholesterol, phospholipids, and dedicated lipoprotein peptides called apolipoproteins. There are many types of apolipoproteins, with beta-apolipoproteins being the largest. Furthermore, different lipoprotein particles have different apolipoproteins. For example, chylomicrons (a lipoprotein particle made in enterocytes) carry beta-apolipoprotein 48 (ApoB-48), whereas VLDL (a lipoprotein particle made in hepatocytes) carry beta-apoliprotein 100 (ApoB-100).

In ABL, enterocytes can absorb lipids properly but cannot exocytose the chylomicon particles from their basolateral membrane into the systemic circulation. The defect is caused by a mutation in microsomal triglyceride transfer protein (MTP). As a result, patients with ABL have lipids trapped in their enterocytes, leading to fat malabsorption, diarrhea, and severe malnutrition. Without chylomicrons to deliver ingested lipids, they have low levels of lipoprotein particles and their corresponding apolipoproteins. Perhaps the most serious consequence is Vitamin E malabsorption. By 2-6 years, infants show profound Vitamin E deficiency manifested by symptoms such as retinopathy and spinocellular degeneration. Treatment is a medium chain triglyceride diet and copious Vitamin E supplementation.

Gluten enteropathy (celiac disease) would have started only after exposure to gluten, not while the child was still exclusively breast feeding. Congenital lactase deficiency is rare and would have led to diarrhea and malnutrition, without the extra neurological signs. Similarly, glucose-galactose transporter defects are rare and lead to severe diarrhea and dehydration in infants. They are caused by defects in the sodium/glucose cotransporter (SGLT1), and can be treated with fructose-based formulas.

Question 19:
An 11-year-old girl presents with a history of epigastric abdominal pain for 2 months. The pain is worse after meals and has occasionally awakened her from sleep. She denies diarrhea or constipation, skin rash, fever, or mouth sores. Physical examination is completely normal. An upper gastrointestinal radiograph reveals a duodenal ulcer. Which one of the following is indicated at this time?

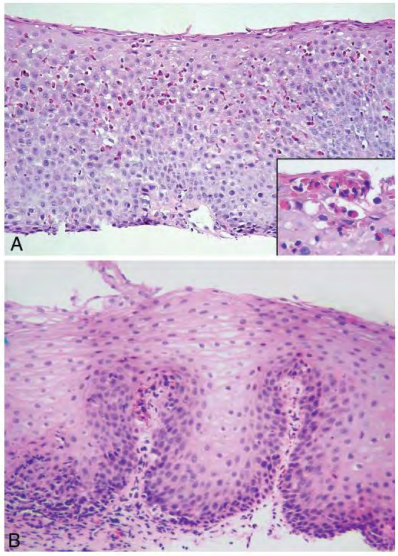
A. upper endoscopy with biopsy
B. Helicobacter pylori antibody titers
C. fasting serum gastrin level

D. colonoscopy with biopsy
E. cytomegalovirus antibody titer

Suggested answer: A. This patient has a duodenal ulcer. Endoscopy is the gold-standard for diagnosing ulcers, because radiography depends on patient compliance/flexibility and can miss up to 50% of duodenal ulcers. Endoscopy in this case has many advantages: i) allows for therapeutics in cases where the ulcer is bleeding/at risk for bleeding; ii) allows for visualization of other ulcers as in hypersecretory disorders; and iii) allows for diagnosis of H. pylori.

H. pylori antibody titers are not used in pediatrics, in part because standards for IgG levels do not exist and infections are usually too chronic for abnormal IgM levels. A fasting serum gastrin level could be useful to diagnose Zollinger-Ellison syndrome; however, this disease usually is diagnosed in patients between 20-50 years old. A colonoscopy would be useful if the upper endoscopy showed signs of Crohn disease, but would not be an appropriate first test. CMV gastrointestinal disease is very rare in immunocompetent hosts. If present, upper endoscopy with viral studies on biopsy specimens would be a better test than measuring serum antibody titers.

Question 20:
A 9-month-old boy has irritability and regurgitation. Growth and development are normal, as is his physical examination. Upper gastrointestinal radiograph is normal with no gastroesophageal reflux, normal anatomy, and no obstructive lesions. Upper endoscopy is normal. The results of an esophageal biopsy are shown in the figure (Genevay et al. Archives of Pathology and Laboratory Medicine 2010, 134: 815-825). What is the most likely mechanism that explains these findings?



A. achalasia of infancy
B. inappropriate relaxation of the lower esophageal sphincter
C. protein intolerance
D. infection of the gastrointestinal tract
E. gluten enteropathy

Suggested answer: C or B (Note: No picture was included in the original question) Picture A shows esophageal findings that may be present in infants with protein intolerance. There are many eosinophils with superficial layering, basal cell hyperplasia (>50% of epithelial cell thickness), and dilated intercellular spaces. Eosinophilic abscesses are seen in the inset. Picture B shows reflux, or

inappropriate relaxation of the LES. Basal cell hyperplasia, papillary elongation, and fewer eosinophils are present.

Achalasia of infancy is very rare, would appear on UGI (dilated esophagus, distal taper), and usually does not have histological findings on routine upper endoscopy biopsy. Reflux may or may not be present on UGI, and endoscopy findings are nonspecific. Mild protein intolerance would be undetected by UGI or endoscopy, though severe cases in older children may be seen as narrowing on imaging and furrowing on endoscopy. Celiac disease has small intestinal, not esophageal, findings.

Question 21:
A 15-year-old girl with chronic ulcerative pancolitis complains of recent recurrence of diarrhea and bleeding while taking Azulfidine 4.0 gm/d. Although she had a difficult course during the first year of disease, she subsequently has not required corticosteroid therapy for over 9 years. Which one of the following endoscopic findings has the most ominous prognosis?

A. pancolitis
B. stricture in the ascending colon
C. pseudopolyps in the rectum and sigmoid colon
D. inflammatory infiltrates noted on endoscopic ileal biopsy
E. lack of haustra in the transverse colon

Suggested answer: B. Prognosis in UC relates to the extent of disease, with 20% of adults with proctitis/distal colitis resolving spontaneously in some studies. Pseudopolyps in the rectum and sigmoid colon suggest relatively distal disease, whereas lack of haustra (a sign of chronic UC) in the transverse colon identifies more proximal disease. Pancolitis is consitent with the entire colon being involved, with some inflammatory infiltrates spilling over to the terminal ileum in 10-15% of cases ("backwash ileitis").

Unlike in Crohn disease, in UC strictures are rare and concerning for neoplasm. UC patients most vulnerable are those with long-standing (>7 years), more extensive (beyond the splenic flexure) disease as in this case. Strictures should be sampled by endoscopy to rule out colon cancer. Benign strictures can also occur in UC, usually from repeated bouts of inflammation and muscle hypertrophy.

Question 22:
A 9-year-old presents with abdominal pain, nausea, and vomiting continuing for several weeks. Upper endoscopy reveals some erythema and a few superficial erosions in the antrum. Gastric biopsies reveal mild chronic inflammatory infiltrates and tight ~5-7Φm spiral-shaped bacteria in the mucosa. A ^{13}C-Urea breath test was negative. Which one of the following is the most appropriate next step in treating this child?

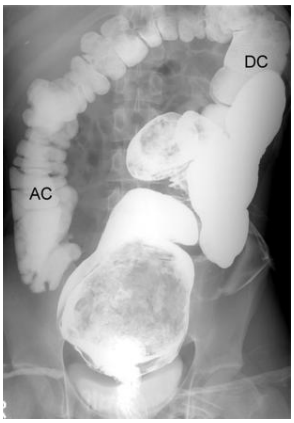
A. penicillin G, single intramuscular dose
B. omeprazole, amoxicillin, and metronidazole orally for 2 weeks
C. amoxicillin orally for 6 weeks
D. H-2 blocking agent for 8 weeks
E. amoxicillin and metronidazole for 1 week

Suggested answer: B. This patient has chronic gastritis caused by Helicobacter heilmanni. Both H. heilmanni and H. pylori are spiral-shaped; however, H. heilmanni gives a negative urea breath test. H. heilmanni compared to H. pylori usually produces a less severe gastritis, with fewer ulcers/erosions that are limited to the antrum. Intestinal metaplasia and MALT is less common with H. heilmanni as well. Treatment is similar to treatment for H. pylori, and consists of a PPI plus two antibiotics, usually

amoxicillin and clarithromycin or flagyl and clarithromycin for 2 weeks. Older regimens includes a PPI, amoxicillin, and flagyl for 2 weeks.

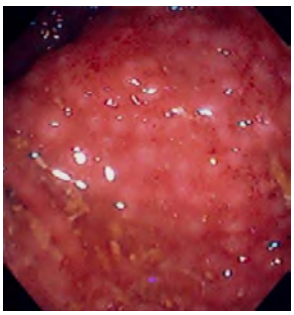
Question 23:
The barium enema shown in the figure (no figure included in original question) is obtained in a young infant with abdominal distention and vomiting. Which one of the following is the most likely diagnosis?

A. intussusception
B. Hirschsprung's disease
C. malrotation
D. distal intestinal obstruction syndrome
E. anal stenosis



Suggested answer: B. In Hirschsprung's disease, a barium enema can identify the aganglionic segment. The area usually shows a thin lumen and colonic dilation proximally. Barium enemas are no longer used when there is a risk for perforation, as in intussusception and distal intestinal obstruction syndrome (partial or complete obstruction of the ileocecal area by intestinal contents, commonly seen in CF patients with pancreatic insufficiency and/or dysmotility). Rather, water-soluble contrast materials are used to reduce the intussusception or diagnose DIOS/clear the obstruction. A barium swallow, not barium enema, makes the diagnosis of malrotation, whereas no imaging is needed to diagnose of anal stenosis.

Question 24:
A 4-month-old formula-fed girl presents for evaluation of rectal bleeding. The remainder of the history is unremarkable, and the physical examination is normal except for heme occult positive yellow stools. The figure (no figure included in the original question) is a photograph taken at sigmoidoscopy. Which one of the following is the appropriate next step?



A. remove all cow and soy protein from the infant's diet
B. begin sulfasalazine
C. obtain an abdominal CT scan
D. blood test for APC gene abnormalities
E. give reassurance only

Suggested answer: A. This patient likely has cow's milk protein allergy in response to cow's milk in formula. The condition leads to mild colitis with patches of erythema in the rectum, and histology shows eosinophils. Treatment is eliminating cow's milk protein from the diet and using semi-elemental formulas (soy formulas are discouraged because a number of infants will also be sensitive to proteins in soy milk). After switching formulas, bleeding may resolve as fast as 72 hours or as long as a few weeks. Finally, nearly all children will outgrow the condition by 1 year of age.

In cow's milk protein allergy, the histological findings resolve with diet change and there is no need for anti-inflammatory medication. Furthermore, the bleeding is usually mild and imaging, such as a CT scan, is not needed. Colonic polyps and cancer are extremely rare in infancy, and without a family history of colon cancer gene testing is not warranted. In a select group of patients – those thriving on breast milk without any signs of anemia, whose mothers have already eliminated dairy and insist on breast-feeding – reassurance may be appropriate next step.

Question 25:
A 5-year-old boy is referred for evaluation of liver disease after presenting to his primary physician with chronic pruritus. His evaluation reveals a small child (below the fifth percentile for height; weight for height tenth percentile) with excoriations on his trunk and extremities. He has no icterus. A grade 2/6 systolic murmur is heard at the left upper sternal border. His liver is soft, about 1 cm below the right costal margin and nontender. Spleen was not palpable. He has diminished but symmetric deep tendon reflexes in his lower extremities. Laboratory studies reveal:

Hemoglobin	12.8
Platelet count	239,000
AST	129
ALT	134
Alkaline phosphatase	678
GGTP	948
Total bilirubin	0.7
Prothrombin time	13.9
INR	1.2

Which one of the following is the most likely diagnosis?

A. progressive familial intrahepatic cholestasis (e.g., Byler's disease)
B. sclerosing cholangitis
C. Niemann-Pick disease, type A
D. Alagille syndrome

E. alpha-1-antitrypsin deficiency

Suggested answer: D. With pruritis and a heart defect, this patient likely has Alagille syndrome. Alagille syndrome is characterized by paucity of bile ducts, pulmonic stenosis, butterfly vertebrate, posterior embryotoxin, and dysmorphic facies (triangular-broad forehead with small pointed mandible). Patients often are malnourished secondary to fat malabsorption, and show signs of fat-soluble vitamin deficiency (including Vitamin E deficiencies causing diminished reflexes, as in this case). Some patients also experience extreme pruritis, which may require a biliary diversion or even liver transplantation. Alagille syndrome is most commonly caused by mutations in Jag1, which serves as a ligand for Notch receptors during cholangiocyte cell fate specification.

PFIC1, or Byler's disease, causes growth failure and pruritis. It is associated with diarrhea, and has coarse granular bile on EM. However, similar to PFIC2, GGT levels are usually normal. Sclerosing cholangitis is characterized by pruritis, can precede a diagnosis of IBD (especially UC), and is not associated with heart findings. Niemann-Pick disease type A is caused by pathological accumulation of the phospholipid sphingomyelin in the monocyte-macrophage system, leading to fatty accumulation in the liver, spleen, and CNS (leading to early neurodegeneration). The disease is caused by a mutation in the lysozymal enzyme sphingomyelinase encoded by the SMPD1 gene. Finally, A1AT deficiency has a variety of liver presentation, with some children showing mild increases in transaminases and others progressing quickly to cirrhosis and liver failure. Similar to PSC, A1AT is not associated with cardiac defects.

Question 1:
A 5-month-old infant who was bottle fed cow milk-based formula had severe watery diarrhea for 4 days. It resolved within 24 hours of beginning an oral rehydration solution. Efforts to restart the previous formula result in a return of severe diarrhea.

At this time, you are MOST likely to recommend a 5-day course of:

A. elemental formula
B. evaporated milk
C. goat milk
D. lactose-free formula
E. oral rehydration solution

Suggested answer: D. This patient suffers from secondary lactose malabsorption. One possible pathogenesis model is: a) viral infection blunts small intestine villi; b) without villi, there is insufficient lactase (lactase sits on the tips of villi); c) lactose from milk cannot be digested; and d) lactose is delivered to colonic bacteria, which ferment it into osmotically active substances, causing diarrhea. Temporarily switching to a lactose-free formula would address the lack of lactase.

One unexplained issue is why secondary lactose malabsorption can take many weeks to resolve, even if villi are reformed properly. Some have proposed that there is something special about the disaccharidase lactase. Others have suggested that other factors rather than lactase deficiency may be responsible, including chronic small intestinal infection after the initial insult.

Question 2:
In which of the following conditions is intermittent (bolus) feeding PREFERRED to continuous nasogastric feeding?

A. Congenital heart disease with failure to thrive
B. Gastroesophageal reflux with failure to thrive
C. Inflammatory bowel disease with bloody diarrhea
D. Malabsorption syndrome with severe villous atrophy
E. Oromotor discoordination due to birth asphyxia

Suggested answer: C. Continuous feeds are problematic because they require the patient to be attached to the pump constantly, and because they ignore normal physiological patterns of feeding and fasting. However, they are useful when the stomach cannot handle large volumes. For example, in congenital heart disease, large volumes may divert too much blood to the gut and away from other vital organs. In reflux, large volumes may promote more vomiting and, if there is oromotor dysfunction, may lead to aspiration pneumonia. In malabsorption syndromes, neither bolus nor continuous feeding would be expected to provide adequate nutrition, and parenteral nutrition would be needed. Patients with inflammatory bowel disease affecting the colon should have intact gastric tissue, and should be able to handle bolus feeds.

Question 3:
In the preterm infant, supplementation of human milk or use of formulas containing increased concentrations of fat and protein often is necessary for adequate nutrition.

Of the following, the BEST explanation for this need for supplementation is that:

A. amino acids are poorly absorbed in the preterm infant

B. bile acid production in the preterm infant is normal but pancreas activity is deficient
C. fat in human milk is of low caloric value
D. malabsorption of up to 20% of ingested fat is common in the preterm infant
E. medium-chain triglycerides are poorly absorbed in the preterm infant

Suggested answer: D. Premature infants need increased nutrients for a number of reasons: 1) they may have been malnourished in utero (prompting the early delivery); 2) they undergo a number of challenges post-natally, including respiratory problems, sepsis, and temperature control; and 3) they have an immature digestive system and impaired absorptive capacity. Premature infants have the most trouble digesting lipids, as both bile acid and pancreatic lipase secretion are reduced. Amino acids, on the other hand, should be absorbed well because intestinal amino acid/peptide transporters are intact.

Fat in human milk is the major calorie source. Furthermore, fat from human milk is better absorbed by premature infants, in part because human milk also contains lipase. Human milk fat only contains approximately 12% medium-chain triglycerides. However, because MCTs can be absorbed without bile salts and lipase, premature formulas have MCT concentrations as high as 40%. Importantly, in infants this increased MCT concentration in formulas has never been shown to improve absorption or growth.

Question 4:
A 6-month-old infant who has congenital heart disease has grown poorly due to insufficient caloric intake. You recommend nasogastric feeding to enhance weight gain.

Of the following, the MOST common complication of nasogastric feeding is:

A. allergic reaction to the nasogastric tube
B. dehydration due to diarrhea
C. gastric perforation
D. gastritis
E. gastroesophageal reflux

Suggested answer: E. Children with failure to thrive require supplemental feeds. When oral intake is not sufficient, nasogastric tube feeding can be used. NG feeds have a number of advantages, including controlling precisely how many calories are delivered and adjusting fluid volumes according to the patient's needs. Complications such as gastric perforation and allergic reaction to the tube are rare, whereas complications such as gastritis may occur but are not prohibitive. Diarrhea can occur when high-sugar or osmolarity formulas are delivered, but dehydration usually is prevented because total fluid intake is controlled. Reflux is a common complication, because (a) the LES is stented open by the feeding tube; and (b) infants are often fed larger volumes than they are accustomed to, in order to promote catch-up growth.

Question 5:
A 2-week-old boy is admitted to the hospital with sepsis due to Escherichia coli. He is being breastfed and has been vomiting frequently. Findings include failure to thrive, lethargy, hypotonia, jaundice, hepatomegaly, and positive nonglucose reducing substances in the urine.

Of the following, the MOST likely explanation for these findings is:

A. galactosemia
B. glycogen storage disease
C. lactose intolerance
D. maple syrup urine disease

E. urea cycle defect

Suggested answer: A. Galactosemia classically presents in the context of E. coli sepsis, and is associated with hypotonia, jaundice, hepatomegaly, and failure to thrive. Reducing substances (galactose) are present in the urine. Galactosemia results from misprocessing of galactose. Normally galactose and glucose are generated from lactose by lactase. Galactose enters the cells and is phosphorylated to galactose-1-phosphate by galactokinase (GALK), which is then converted to uridine diphosphate galactose by glactose-1-phosphate uridyl transferase (GALT). GALK deficiency, a mild form of galactosemia, only causes cataracts from galactose accumulation. GALT deficiency, the severe from of galactosemia, causes cataracts as well as the more severe symptoms present in this vignette, presumably from galactose-1-phosphate accumulation.

Glycogen storage disease usually causes hypoglycemia when feeding intervals are lengthened, and hepatomegaly from metabolite accumulation. Lactose intolerance causes diarrhea from malabsorbed sugars. Maple syrup urine disease is caused by a defect in branched-chain amino acid metabolism, leading to poor motor and feeding problems and urine with a maple syrup odor. Urea cycle defects cause defects in ammonia disposal, generating very high levels of ammonia in newborns.

Question 6:
A 3-month-old infant girl is admitted to the hospital for evaluation of recurrent episodes of hypoglycemia. Physical examination reveals hepatomegaly. After 2 hours of fasting, she develops hypoglycemia.

Measurement of which of the following would be MOST helpful in determining the etiology of this patient's hypoglycemia?

A. Ammonia in the serum and the arterial pH
B. Cortisol and growth hormone in the serum
C. Insulin and glucose in the serum
D. Ketones and reducing substances in the urine
E. Organic acids in the urine and lactate in the serum

Suggested answer: D. The case vignette is most characteristic of glycogen storage disease, with symptoms caused by impaired hepatic glycogenolysis during fasting. Glycogen remains in the liver (causing hepatomegaly), and glucose is not deposited in the serum (causing hypoglycemia). Typically patients will have urine ketones from fat breakdown but no reducing substances in the urine.

A number of other diseases also lead to hypoglycemia. Defects in sugar metabolism such as galactosemia and hereditary fructose intolerance impair gluconeogenesis from galactose and fructose, respectively, and lead to hypoglycemia after many hours of fasting. They are not associated with urine ketones, but do have positive urine reducing substances. Defects in amino acid metabolism may cause hypoglycemia because of concomitant liver disease resulting in poor gluconeogenesis, while defects in fatty acid metabolism can cause hypoglycemia because of liver disease resulting in poor gluconeogenesis, as well as because of overused and depleted sugar stores in the absence of being able to utilize fats. Fatty acid metabolism defects can be detected by examining urine for organic acids.

Hypoglycemia may also be caused by too much sugar utilization, as in the case of hyperinsulin states. Finally, low cortisol (Addison's disease, congenital adrenal hyperplasia) and low growth hormone cause hypoglycemia, presumably from poor gluconeogensis. For these children, hormone replacement is the treatment of choice.

Question 7:

The mother of a 3-month-old infant reports that the boy is demanding frequent feedings and has a noticeably protuberant abdomen. Physical examination reveals doll-like facies and marked hepatomegaly. Laboratory findings include a serum glucose level of 20 mg/dL and an elevated venous lactate level of 44 mg/dL (normal, <18 mg/dL).

Of the following, the most appropriate INITIAL management of this infant is:

A. administration of a formula that has high concentrations of fructose and galactose
B. daily injections of glucagon
C. insertion of a portacaval shunt
D. nocturnal infusion of glucose via a nasogastric tube
E. referral for liver transplantation

Suggested answer: D. This patient has glycogen storage disease type 1, or Von Gierke disease. It is caused by a deficiency is glucose-6-phosphatase, the last step in glycogenolysis (and the final step in gluconeogenesis). Patients have doll-like facies and hepatomegaly, and laboratory results are significant for marked hypoglycemia and lactic acidosis. Patients usually present when they begin to sleep through the night and have longer periods without feeds. Treatment includes frequent glucose feeds during the day and continuous feeds at night, usually with uncooked starch that releases glucose slowly. Efforts to increase glycogenolysis (via glucagon) or gluconeogenesis (via fructose, galactose, or amino acid formulas) do not help. There is no evidence of portal hypertension, so a shunt is not needed, and diet modification – not liver transplant – is the standard treatment.

Question 8:
A 5-year-old girl was treated with amoxicillin for otitis media. One week after antibiotic therapy was completed, she developed crampy abdominal pain and has been passing six stools daily that contain both bright red blood and mucus. Physical examination reveals a temperature of 38.5°C (101°F), abdominal distension, and diffuse abdominal tenderness.

Among the following, the most appropriate INITIAL diagnostic study to perform is a(n):

A. barium enema
B. colonoscopy
C. culture of stool for Clostridium difficile
D. evaluation of stool for ova and parasites
E. evaluation of stool for rotavirus

Suggested answer: C. C. difficile infection typically occurs during or shortly after antibiotic use, and presents with watery stools, abdominal pain, and leukocytosis. In more severe cases, fever, bloody stools, and (in the most severe forms) toxic megacolon is present. Diagnosis can be made by anaerobic cultures. However, because cultures take time to grow, various toxin assays – including cytotoxin assays, immunoassays, and PCR tests – have been developed. Colonoscopy can also be used to make the diagnosis, which may show a spectrum of findings from erythema to ulcers to pseudomembranes (ulcers filled with inflammatory material). First line treatment is flagyl, with oral vancomycin used for reoccurring cases.

Question 9:
A previously healthy 2-year-old boy presents with irritability, drooling, and refusal to eat. Results of physical examination include: drooling; symmetric aeration with normal breath sounds; and absence of wheezes, retractions, or rhonchi. You suspect a foreign body was ingested.

The MOST likely location of the foreign body is the:

A. esophagus
B. oral cavity
C. right main stem bronchus
D. stomach
E. trachea

Suggested answer: A. Foreign body ingestion is a common problem in the 6 month to 3 year old age group, occurring approximately 80,000 times each year in the US. The most important initial step is to rule out airway involvement. Drooling in this case suggests the object has lodged in the esophagus. Imaging can confirm the diagnosis, with most esophageal objects trapped at physiological areas of narrowing (UES, aortic arch, LES) or areas of stricture (usually mid-esophagus). Treatment depends on the object and symptoms. If the object is sharp, a battery, causing complete obstruction, or causing other systemic symptoms (fever, pain), the object should be removed immediately. If the object is blunt and not causing any other symptoms, the object may be allowed to pass into the stomach on its own. However, waiting beyond 24 hours for the object to pass is not advised, because the object may cause local trauma after long periods of time.

Question 10:
A 6-week-old previously well girl is brought to the emergency department because she is irritable, jaundiced, and feeds poorly.

Of the following, the most appropriate INITIAL laboratory investigation to determine the etiology of this child's illness is:

A. an upper gastrointestinal series
B. cultures of the blood, cerebrospinal fluid, and urine
C. complete blood count and reticulocyte count
D. determination of serum electrolyte levels
E. measurement of serum acetaminophen level

Suggested answer: B. The differential diagnosis for this patient is sepsis vs. toxin ingestion vs. metabolic disease. After taking a history negative for toxin ingestion, a sepsis work-up is an appropriate first step. This patient likely has galactosemia, which presents with poor feeding, jaundice, and hepatomegaly. Galactosemia also commonly occurs alongside E. coli sepsis, explaining the irritability and sepsis-like presentation. In addition to blood work, a urinalysis showing reducing substances would also help establish the diagnosis.

Question 11:
Vitamins and minerals are incorporated into infant formulas in the United States to provide an essentially complete diet.

Which of the following minerals or trace minerals must be SUPPLEMENTED in ready-to-feed infant formulas to meet the recommended daily allowances?

A. Calcium
B. Fluoride
C. Iron
D. Magnesium
E. Selenium

Suggested answer: B. Ready-to-feed infant formulas are pre-mixed, compared to powdered formulas that must be mixed by the parent before feeding. Ready-to-feed formulas have certain advantages, including avoiding mixing mistakes and preventing infectious diseases from dirty water. However, ready-to-feed formulas are made without fluorinated water. As a result, infants drinking ready-to-feed formulas (or living in areas with fluorinated water) should receive fluoride supplementation after 6 months of age.

Formulas (whether pre-mixed or powdered) contain many supplements. Formulas are supplemented with calcium (milk-based ~50-55 mg/100ml and soy-based ~70 mg/100ml vs. breast milk ~33 mg/100ml). Formulas is also supplemented with Vitamin D, while breast milk contains very little Vitamin D. As a result, all breast fed infants, and formula fed infants drinking less than 1 liter of formula, require supplementation to achieve 400 IU.

Iron is also supplemented in formula, because iron deficiency is the most common nutrient deficiency in children. Children require 0.5-0.8 mg/day of iron. Breast milk provides approximately 0.3-1 mg/L of iron and is 50% bioavailable; unsupplemented formula, on the other hand, provides 1-2 mg/L but is only 4-6% bioavailable. Supplemented formula, in contrast, contains 12 mg of iron per liter of formula. With a 4-6% bioavailability, this gives the infant 0.48-7.2 mg absorbed iron per liter of formula consumed.

Magnesium in breast milk and formula is abundant and readily bioavailable. Magnesium is present at 4-5 mg/100ml in routine formula, 5-8 mg/100ml in soy formula, and ~3.4 mg/100ml in breast milk. Finally, selenium is present in higher quantities in breast milk, and selenium supplementation of formula has been shown to improve infants' selenium status. Formula selenium supplementation may be a change seen in the future.

Question 12:
You suspect the cause of abdominal pain in a 17-year-old child is Helicobacter pylori-associated gastroduodenitis.

Of the following, the most appropriate INITIAL step in management is to:

A. begin an empiric 2 week course of amoxicillin therapy
B. begin a trial of omeprazole therapy
C. obtain serologic testing for anti-Helicobacter antibodies
D. obtain upper gastrointestinal series to exclude gastric adenocarcinoma
E. refer for endoscopy and gastric biopsy

Suggested answer: E. Even though H. pylori is the most common cause of uncomplicated gastric/duodenal ulcers in patients not taking NSAIDs, other causes do exist. As a result, establishing the diagnosis is important before starting treatment. H. pylori can be diagnosed with endoscopy, urease breath tests, and stool antigen tests. Serological testing for anti-pylori IgG was common (most infections are chronic, so IgM serologies are less useful), but has since fallen out of favor because of its high false positive rate and low positive predictive value. A negative serology test, however, does suggest no infection.

Stool antigen tests are preferred over serology, and are especially useful for pediatric population in which serological ranges are not available. Stool antigen tests may produce false-negative results in the setting of PPI use.

Question 13:
An 8-year-old boy recently was diagnosed as having severe ulcerative colitis.

Of the following, the best INITIAL management is:

A. bowel resection
B. continuous nasogastric feedings
C. intravenous corticosteroids
D. oral azathioprine
E. oral 5-aminosalicylates

Suggested answer: C. This patient is having a flare, and short-term IV steroids are the treatment of choice to reduce inflammation acutely. Bowel resection is too aggressive as a first step, though may be needed if the disease is steroid-resistant. NG feeds are used to treat mild-to-moderate IBD in some places such as Canada, but more severe disease requires extra therapy. Similarly, oral 5-ASAs may be effective for mild-to-moderate disease but alone would be inadequate for a severe flare. Finally, oral azathioprine would be an appropriate maintenance medication. However, it takes weeks to have full effect, and would be inadequate in the short-run to improve symptoms.

Question 14:
In a child who has chronic diarrhea and weight loss, the PREFERRED method for providing nutritional support is:

A. continuous nasogastric feedings
B. intermittent (bolus) nasogastric feedings
C. nasoduodenal feedings
D. oral feedings
E. parenteral nutrition

Suggested answer: D. For ill patients needing supplemental nutrition, the first decision is whether to feed enterally or parenterally. Those that can absorb nutrients (i.e. no small bowel disease) should be tried on enteral feeds first. Enteral feeds provide trophic support to the gut, and can be given by mouth (as in this case), by NG tube (if the oropharynx or esophagus is diseased), or by ND tube (if the stomach empties poorly). On the other hand, those with small bowel disease (Crohn disease, celiac disease, tufting enteropathy) have poor absorptive function and may require parenteral nutrition. Parenteral nutrition has many disadvantages including a high rate of complications such as line infections.

Question 15:
A 16-month-old boy who has leukemia is receiving prednisone, vincristine, L-asparaginase, and intrathecal methotrexate. On the seventh day of chemotherapy, broad-spectrum antibiotics were administered for fever. All cultures were negative, and antibiotics were stopped after 14 days. Over the past 2 weeks, abdominal distension and pain have developed. Hematologic findings are normal.

The MOST likely etiology of the abdominal findings is:

A. candidal mucositis
B. chemotherapy-induced mucositis
C. chemotherapy-induced neurotoxicity
D. Clostridium difficile infection
E. leukemic infiltration of the bowel wall

Suggested answer: D. The most common possibilities for this case are C. difficile versus teflitis. Teflitis is a necrotizing enterocolitis that develops after induction chemotherapy, thought to be due to a combination of damaged mucosa from chemotherapeutics and microorganism invasion from neutropenia. It typically

presents in neutropenic patients with RLQ abdominal pain and fever. Given the normal neutrophil count and recent antibiotic use, C. difficile infection is the more likely. Chemotherapy-induced neurotoxicity usually affects peripheral nerves, and damage of the enteral nervous system causing ileus would take longer to develop. Leukemic infiltration of the bowel wall – especially after starting chemotherapy – would be rare. Pancreatitis with ileus is another possibility, given that L-asparaginase often induces pancreatitis.

Question 16:
Among the following, the MOST specific clinical manifestation of an antral web in an infant is:

A. diarrhea
B. distension of the lower abdomen
C. extreme irritability
D. hematemesis
E. nonbilious vomiting

Suggested answer: E. Antral webs are rare, as are all non-pyloric stenosis causes of gastric outlet obstruction in the neonate. The incidence is thought to be 1 in 100,000, and they are commonly associated with other GI or cardiac abnormalities. Antral webs usually are located 1-2 cm proximal to the pylorus and are 1-4 mm thick. Webs with apertures greater than 1 cm are rarely asymptomatic, whereas those with near complete closure cause nonbilious vomiting in the first feeds after birth. The diagnosis can be made by UGI showing two compartments to the stomach, and the definitive treatment is surgical removal. Lower GI symptoms (diarrhea, distension of the lower quadrants) would not occur. Hematemesis could occur but nonbloody vomiting would be more common. Finally, although patients with antral webs may be hungry and irritable, irritability is a general sign and not specific to any particular disease.

Question 17:
An 18-month-old infant who has intestinal atresia has been maintained on total parenteral nutrition via a central venous catheter since birth. He is brought to your office with a 1-day history of lethargy, fever, and jaundice.

Of the following, the MOST likely cause of this infant's findings is:

A. cholelithiasis
B. fulminant hepatic failure
C. infection of the central venous catheter
D. intrahepatic cholestasis
E. viral hepatitis

Suggested answer: C. Parenteral nutrition, though life-saving, has a number of acute and chronic disadvantages. Acutely, patients commonly develop central line infections. Infected children may have mild symptoms initially, that rapidly progress to shock requiring resuscitation. Chronically, patients develop TPN-associated cholestasis, likely from compounds present in the intralipid formulation. The cholestasis leads to bile salt back-up into the liver and liver damage, which ultimately could lead to liver failure. Cholelithiasis, secondary to poor bile flow, is another chronic complication of TPN. It could lead to cholecystitis and produce similar symptoms, though abdominal pain would be a more prominent finding. Finally, fulminant hepatic failure and viral hepatitis are both acute and would not be more likely to occur in a patient on parenteral nutrition.

Question 18:
A 1-week-old boy has a seizure. Significant findings on physical examination include a "cherubic" face, protuberant abdomen, and profound hepatomegaly. Glycogen storage disease is suspected.

The MOST important issue in the initial management of this patient is to:

A. decrease serum lactate
B. prevent hypoglycemia
C. reduce hypercholesterolemia
D. reduce serum free fatty acids
E. treat hyperuricemia

Suggested answer: B. This patient is having hypoglycemic seizures, which can be managed by administering sugars to return the infant to a euglycemic state. Patients with glycogen storage have a number of other serum findings (particularly those with GSD 1/von Gierke disease, or glucose-1-phosphatase deficiency, as in this case). They may have elevated lactate levels from massive amounts of glucose-1-phosphate, created from the breakdown of glycogen during fasting but trapped in the liver, undergoes glycolysis. Furthermore, in the absence of usable glucose, de novo triglyceride production increases dramatically and leads to elevated cholesterol concentrations. This hyperlipidemia is associated with xanthomas but not premature atherosclerosis, and, as a result, cholesterol-lowering drugs are not recommended. Finally, the excessive glycolysis creates large amounts of phosphorylated intermediate compounds, which inhibits re-phosphorylation of adenine nucleotides. This causes nucleic acid degradation and produces excessive uric acid, which may lead to nephrolithiasis.

Question 19:
A 5-month-old boy with frequent vomiting is switched from human milk to formula. His symptoms immediately worsen, and he becomes highly irritable. Shortly afterward, he becomes comatose. Physical examination reveals a small, hypotonic child responsive only to pain. Laboratory studies reveal: increased anion gap; metabolic acidosis; serum ammonia concentration, 150 mg/dL; and serum glucose level, 85 mg/dL.

Which of the following classes of inborn errors of metabolism is MOST likely in this patient?

A. Disorder of fatty acid oxidation
B. Glycogen storage disease
C. Lysosomal disease
D. Organic acidemia
E. Urea cycle defect

Suggested answer: Urea cycle defects should be considered in patients with an anion gap, high ammonia, and normal glucose. Urea cycle defects lead to high ammonia, because there is a defect in converting ammonia to the secreted product urea. High ammonia causes neurological deficits through mechanisms incompletely understood. High ammonia also causes an anion gap, possibly by impairing brain mitochondria, forcing anaerobic metabolism of sugar, and producing lactic acid as a by-product. This patient showed mild symptoms with human milk (i.e. frequent vomiting), because human milk has low protein levels (2.3 g/dL protein at birth and decreasing to 1.5-1.8 g/dL after 2-4 weeks). The symptoms increased with formula, because formula has more protein (approximately 2.1-2.2 g/dL) which led to an increased accumulation of ammonia.

Question 20:
Of the following, the inborn error of metabolism that exists MOST frequently in a vitamin-dependent form is:

A. argininosuccinase deficiency

B. branched-chain ketoaciduria
C. cytochrome C oxidase deficiency
D. homocystinuria
E. phenylketonuria

Suggested answer: D. Homocystinuria occurs with a defect in the conversion of methionine to cysteine, leading to accumulation of the intermediate product homocysteine. Normally cystathionine beta synthase (CBS) uses B6 to transsulfurate homocysteine to cysteine. However, in CBS deficiency, homocysteine accumulates and causes developmental delay, osteoporosis, ocular abnormalities, thromboembolic disease, homocystinuria, and premature atherosclerosis.. Treating with excessive B6 can drive the reaction forward and reduce symptoms in some cases. Homocysteine can also be remethylated to methionine, using methyl donors such as folate and B12.

Argininosuccinate synthetase/lyase deficiencies are responsible for urea cycle defects. Branched-chain alpha-ketoacid dehydrogenase complex (BCKD) deficiency causes branched chain ketoaciduria (maple syrup urine disease), a disease characterized by improper metabolism of branched chain amino acids. This results in a shortage of substrates for gluconeogenesis, energy production, and fatty acid/cholesterol synthesis. Cytochrome C oxidase deficiency is the most common respiratory chain defect causing myopathy in newborns, resulting in poor energy production. Finally, phenylalanine hydroxylase causes phenylketonuria because of an inability to convert phenylalanine to tyrosine. Excessive phenylalanine accumulates and causes mental retardation.

Question 21:
A previously healthy 20-month-old boy develops gastroenteritis with anorexia, vomiting, and diarrhea; 24 hours later he develops seizures and has a decreased level of consciousness. The serum glucose level is 25 mg/dL, electrolyte concentrations are normal, and urinalysis reveals no ketones.

Among the following, the MOST likely diagnosis for this patient is

A. alcohol ingestion
B. glycogen storage disease type I
C. hereditary fructose intolerance
D. insulinoma
E. medium-chain acyl-CoA dehydrogenase deficiency

Suggested answer: E. For patients with hypoglycemia and no ketones, a disorder in fatty acid metabolism should be suspected. Normally, with fasting or illness, the liver creates energy for the brain by beta-oxidizing fatty acids from adipose tissue into ketones. However, in fatty acid oxidation defects such as medium-chain acyl-CoA dehydrogenase deficiency (MCAD), the liver cannot produce ketones and the brain is left without an energy source. Without ketones, sugars are rapidly used as the sole energy source by all tissues, eventually creating hypoglycemia and further depriving the brain of energy.

Alcohol ingestion can create hypoglycemia, but is inconsistent with the clinical history. Glycogen storage disease produces ketones, as fatty acids must be mobilized because glucose is limiting. Hereditary fructose intolerance results in hypoglycemia and low ketones, but presents at the onset of fructose ingestion with vomiting and failure to thrive. Finally, insulinomas also have hypoglycemia and low ketones (insulin prevents fatty acid mobilization), but insulinomas are very rare in infants.

Question 22:

The mother of a 3-month-old boy reports that he has a poor appetite and constipation. Findings on physical examination, when compared to those 2 months ago, include poor interim growth, increased lethargy, hoarse cry, decreased tone, large fontanelles, and a more pronounced umbilical hernia.

Of the following, the MOST likely cause of this infant's problem is

A. agenesis of the thyroid gland
B. endemic goitrous hypothyroidism
C. end-organ unresponsiveness to thyroid hormone
D. inborn error of thyroxine synthesis
E. thyroid gland unresponsiveness to thyrotropin

Suggested answer: A. Congenital hypothyroidism occurs in 1:2000-4:000 births and is the leading reason for preventable mental retardation. Congenital hypothyroidism is most commonly caused by thyroid gland dysgenesis (agenesis, hypoplasia, ectopy). Other causes include defects in thyroid hormone synthesis, secretion, transport, metabolism, and/or responsiveness. Most infants appear normal at birth because of maternal contributions of T4; hence, screening tests to measure free T4 and TSH are administered to identify hypothyroid infants before symptoms described in the vignette develop.

Question 23:
A 3-month-old infant who has a history of gastroesophageal reflux has had increasing vomiting for 2 days. This morning she developed rapid, deep, labored breathing; lethargy; and shock. Findings include: serum sodium, 144 mEq/L; potassium, 4.5 mEq/L; chloride, 89 mEq/L; bicarbonate, 5 mEq/L; pH, 7.16; glucose, 48 mg/dL; ammonia, 128 mcmol/L; and ketonuria.

The MOST likely explanation for these findings is:

A. aminoacidopathy
B. ethylene glycol poisoning
C. metoclopramide toxicity
D. organic acidemia
E. urea cycle defect

Suggested answer: D. This patient has organic academia. These diseases are usually caused by defects in enzymes that metabolize amino acids, and can also be caused by defects in fat and carbohydrate metabolism. Infants present with poor feeing, vomiting, and lethargy in the first weeks of life, similar to infants with sepsis. Laboratory results show a profoundly high anion gap metabolic acidosis (in this case, the gap is 50), with increased ammonia, decreased glucose, and electrolytes consistent with dehydration. Organic acid analysis in urine is used to confirm the diagnosis. Acute management involves rehydration and glucose infusion; after stabilization, protein feeds can be reintroduced as long as the offending amino acid is omitted.

Aminoacidopathies refer only to defects in amino acid metabolism; however, the patient in this vignette could have problems with fat or sugar metabolism leading to organic acidemia. Ethylene glycol poisoning also causes a high anion gap metabolic acidosis, but gaps at 50 would only occur very acutely after ingestion. Metoclopramide toxicity usually causes tardive dyskinesia, which may or may not be reversible. Finally, urea cycle defects usually have higher ammonia levels and a less severe, lactic acid metabolic acidosis.

Question 24:
Which of the following is the most common cause of pancreatitis in childhood?

A. viral
B. drug induced
C. idiopathic
D. familial
E. abdominal trauma

Suggested answer: A. Pancreatitis in childhood has a number of causes. Viral infections are the most common cause (up to 13-33%), including infections by mumps, rubella, coxsackie B virus, CMV, and HIV. Other causes include trauma, drug-induced, anatomical (pancreatic divisum, choledochal cyst), toxin-induced, gall-stone induced, and hereditary (defects in cationic trypsinogen, CF gene).

Question 25:
Which of the following is not part of the Currarino triad characterizing caudal regression syndrome which can present as infantile constipation?

a. dysplasic sacrum
b. anal abnormalities
c. tethered cord
d. pre-sacral mass

Suggested answer: C. Caudal regression syndrome refers to a constellation of diseases with poorly formed caudal (sacral and lower lumbar) vertebrate. They are more common in infants of diabetic mothers, and often is accompanied with a tethered cord. Three types of caudal regression syndromes are: VACTERL (Vertebral, Anorectal, Cardiac, Tracheal-Esophageal fistula, Renal, and Limb abnormalities); OEIS (Omphalocele, cloacal Exstrophy, Imperforate anus, Spinal malformation); and Currarino syndrome (partial sacral agenesis, a pre-sacral mass, and recto-anal abnormalities).

Question 1:
A TRUE statement regarding gastrointestinal functioning in the premature infant is:

A. Bile acid pools are elevated
B. Intestinal motility is normal
C. Lactose is digested effectively
D. Vegetable oils are digested poorly
E. Vitamins are absorbed adequately

Suggested answer: D. *Premature infants have a decreased bile acid pool, for a combination of reasons: a) bile acid synthesis proteins are not fully expressed, b) the gall bladder does not concentrate well, thereby diluting bile acids in bile, c) the terminal ileum machinery to reabsorb bile acids is immature, and d) the liver machinery to re-uptake bile acids from the portal circulation is also immature (explaining why infants have high circulating bile acids for up to 6 months). All of these reasons, in combination with low pancreatic lipase and colipase secretion in infants, lead to poor absorption of vegetable oils and fat soluble vitamins.*

Premature infants have reduced lactase expression, which may be induced with early feeding. Premature infants also have altered motility, with poor antral contractions before 32 weeks in some studies. Other studies report altered migrating motor complex (MMC) patterns lacking the strong contractions of phase 3 in infants less than 32 weeks old.

Question 2:
Which of the following BEST explains why solutions containing 1.2 to 2.5% glucose, rather than 5% glucose, are used for oral rehydration?

A. Absorption of sodium and water in the gut is maximized
B. Glomerular filtration rate is enhanced
C. Hyperglycemia and glycosuria are less likely to occur
D. Potassium absorption is decreased
E. Stomach distention with vomiting is less likely to occur

Suggested answer: A. *Enterocytes on villi express Na-coupled glucose transporter-1 (SGLT-1). The transporter is located on the apical side of the cell, and uses a sodium concentration gradient to bring 2 molecules of sodium and 1 molecule of glucose into the cell. (The gradient is created by the basal Na/K pump, which pumps sodium out of the cell). Water follows the sodium, promoting rehydration. The glucose is either used by the enterocyte, or enters circulation via facilitated diffusion through the basal transporter Glut2.*

Excessive glucose can be harmful, because it may be unabsorbed in the small intestine. When it reaches the large intestine, it may be metabolized by gut bacteria to create osmotically active substances. Diarrhea, and further dehydration, could result.

Question 3:
A TRUE statement concerning a low protein diet in patients with renal insufficiency is:

A. Appetite will increase because the diet is more palatable
B. Cognitive capacity will decrease
C. Nutrient absorption will increase
D. Renal osteodystrophy will be easier to control
E. The progression of renal insufficiency will be slowed

Suggested answer: E. *In renal failure, the kidneys have trouble clearing toxins related to urea. As a result, a constellation of symptoms may develop, including decreased cognitive capacity, decreased taste/*

appetite, decreased growth, and further renal damage by increasing GFR. A low protein does lead to an improvement of symptoms, presumably from less uremic toxins. A low protein diet is associated not only with lower creatinine measurements, but also slower progression to renal failure. Hence, children with renal insufficiency should be given limited amounts of high-quality protein.

Neural function such as taste/appetite and cognitive capacity may increase with less uremic toxins (but not because the low-protein diet tastes better). Absorption will not change with a low-protein diet. Renal osteodystrophy is related more to renal 1-hydroxylation of 25-OH Vitamin D and less to uremic toxins.

Question 4:
A 6-week-old boy with known congestive cardiomyopathy weighs 4 kg. He takes only 12 oz of formula daily. Of the following, the MOST likely consequence of decreased intake in this infant is

A. hypocalcemia
B. hypoglycemia
C. hypokalemia
D. poor growth in length
E. poor weight gain

Suggested answer: E. *Children with congestive cardiomyopathy have increased metabolic needs. Nutritional support is complicated because these children also have strict fluid requirements. The patient in this question is only taking 72 kcal/kg/day (assuming a 24 kcal/oz formula), which is insufficient even for an infant without heart disease. As a result, he will have poor weight gain, and if persistent, poor growth in length later.*

Question 5:
The weight of an adolescent boy is twice ideal body weight for height. If he remains obese as an adult, he is likely to develop each of the following EXCEPT

A. infertility
B. learning disorder
C. pulmonary insufficiency
D. sleep disorder
E. thromboembolism

Suggested answer: B. *Obesity has not been shown to cause an adolescent to develop learning disorders as he transitions to adulthood. However, some cases of obesity are related to neurological disorders (i.e. Prader Willi Syndrome, Bardet-Biedl Syndrome), and obesity in an otherwise normal child may cause low self-esteem and poor school performance. Obesity is associated with a number of other co-morbidities, including infertility (possibly related to leptin abnormalities), pulmonary insufficiency, obstruction sleep apnea, and hypercoagulation.*

Question 6:
A 6-month-old infant has been fed only goat milk. Laboratory studies reveal: hemoglobin concentration, 9.5 gm/dL; mean corpuscular volume, 100; white blood cell count, 4,200/mm^3; and reticulocyte count, 0.4%. In addition to dietary counseling, you would MOST likely recommend initial supplementation with:

A. ascorbic acid
B. folic acid
C. iron
D. pyridoxine
E. vitamin B12

Suggested answer: B. *Goat milk is an alternative for infants with cow's milk protein allergy. However, goat milk lacks folate, which can lead to a megoblastic anemia as seen in this patient. Folate is absorbed in the small intestine, when the brush border enzyme folate conjugase hydrolyzes dietary polyglutamates into folic acid. Hence, severe mucosal disease can also lead to folate deficiency. Finally, sulfasalazine use can lead to folate deficiency, because sulfasalazine competes with enzymes of the folate absorption pathway.*

Question 7:
A 4-year-old girl who attends preschool has had diarrhea for 10 days. Several other children have had similar symptoms, including fever and vomiting that persisted for 3 to 5 days. This child, however, has continued to have abdominal discomfort, excessive gas with abdominal distention, and watery stools. Her appetite is good, and she is not acting ill. Which of the following laboratory tests is MOST likely to confirm the diagnosis?

A. Breath nitrogen test
B. Clostridium difficile toxin and antigen
C. Stool culture
D. Stool for ova and parasites
E. Stool for pH and reducing substance

Suggested answer: D. *This patient has several risk factors for giardia (in preschool, watery diarrhea, excessive gas, appears well) and sending stool for ova and parasites is appropriate. If available, sending stool for giardia antigen may have a higher yield. Giardia is commonly treated with Flagyl (metronidazole) or Alinia (nitozoxanide).*

This patient's symptoms are less concerning for acute gastritis, so a breath nitrogen test to detect H. pylori would not be warranted (and if H. pylori was a concern, a stool antigen test would be better). Clostridium difficile is less likely because there is no prior antibiotic use, stools are non-bloody, symptoms are both upper and lower, and the symptoms seem to be rapidly contagious. Bacterial stool cultures would be more useful to work-up acute bloody diarrhea. Finally, the patient has no evidence of sugar malabsorption, so stool for pH and reducing substances would not be helpful.

Question 8:
Of the following, the BEST reason for administering parenteral alimentation through a peripheral vein rather than through a central vein is:

A. inability to insert and maintain a catheter in a central vein
B. lower incidence of hyperglycemia
C. lower incidence of infection
D. need for parenteral alimentation after discharge from the hospital
E. need to deliver solutions of high osmotic load

Suggested answer: C. *Lines in peripheral veins (including PICCs) have a lower incidence of infection. Peripheral IVs, however, last only a few days and are can only deliver a limited osmotic load. PICC and central lines last for long periods and can deliver a high osmotic load. Central veins are placed surgically, and may be used when peripheral access is limited. Hyperglycemia is a risk with all forms of parenteral nutrition, and involves many factors including glucose infusion rate, the patient's insulin production, and the patient's insulin sensitivity.*

Question 9:

During a routine health supervision visit, a 16-year-old girl is noted to have a hemoglobin concentration of 10 gm/dL and mean corpuscular volume of 72. The MOST common cause for anemia in such a patient is:

A. chronic hemolysis
B. Crohn disease
C. folic acid deficiency
D. iron deficiency
E. parasitic infestation

Suggested answer: D. *For a menstruating female, the most common reason for microcytic anemia is low iron from blood loss. Chronic hemolysis can lead to anemia but is rare. Crohn disease can also cause microcytic anemia from poor duodenal iron absorption; however, in this patient without Crohn disease symptoms, iron loss is much more likely. Folic acid deficiency causes a megoblastic anemia. Finally, parasites can also cause Fe-deficiency anemia, and is more common in the developing world.*

Question 10:

The mother of a 4-year-old boy reports that he has developed hives within 1 hour after ingesting acetaminophen syrup, brompheniramine elixir, and hard candies. He also has developed hives and wheezing following injection of penicillin. He inadvertently was given an acetaminophen tablet but had no reaction. Of the following, the MOST likely cause of this boy's symptoms is

A. allergy to sucrose
B. idiopathic urticaria
C. idiosyncratic reaction to artificial coloring or preservatives
D. multiple drug allergies
E. penicillin contamination of the acetaminophen syrup and brompheniramine elixir

Suggested answer: D. *This patient has an allergy to penicillin. He also has an allergy to brompheniramine elixir, because he tolerates Tylenol alone and hard candies are generally hypoallergenic. Interestingly, brompheniramine is an anti-histamine, which in most children would be expected to improve allergic symptoms. However, in this child with multiple drug allergies, the brompheniramine actually induces more symptoms. The pathophysiology of multiple drug allergy syndrome remains unknown.*

Question 11:

A 33-year-old pregnant woman wishes to breastfeed her baby. She has had systemic lupus erythematosus for 2 years and takes prednisone and hydralazine. Among the following, your BEST advice to her regarding her current medication regimen and breastfeeding is:

A. Both prednisone and hydralazine usually are compatible with breastfeeding
B. Captopril should be substituted for hydralazine
C. Cyclophosphamide should be substituted for prednisone
D. Cyclosporine should be substituted for prednisone
E. High dose aspirin should be substituted for prednisone

Suggested answer: A. *Although prednisone and hydralazine can be passed in breast milk, the absolute amount in negligible and poses no risk to the infant. Captopril is not contraindicated during breastfeeding, though has been associated with birth defects if taken during pregnancy. Cyclophosphamide and cyclosporine are contraindicated in breastfeeding mothers, as they may cause pancytopenia and other problems in the child. High dose aspirin must be used with caution in*

breastfeeding mothers, because aspirin is passed in breast milk and may cause bleeding and platelet abnormalities in infants.

Question 12:
The daily caloric requirement in kcal/kg for a healthy full-term infant is approximately:

A. 40
B. 60
C. 80
D. 100

Suggested answer: D. *The dietary recommended intake for a newborn is 102 kcal/kg/day, or approximately 150 cc/kg/day of human milk (approximately 16.5 ounces/day for a 3.5 kg newborn). From 4 months to approximately 3 years, the DRI is in the 80 kcal/kg/day range. From age 5-8 years old the DRI is the 60 kcal/kg/day range, and post-pubertal adolescents generally have a DRI below 40 kcal/kg/day.*

Question 13:
The MAIN advantage of enteral nutrition over parenteral nutrition is that enteral nutrition:

A. facilitates monitoring caloric intake
B. has fewer complications
C. permits maintenance of longer periods of positive nitrogen balance
D. prevents toxins from accumulating in the colon
E. provides improved caloric intake in the outpatient setting

Suggested answer: B. *Enteral nutrition is favored over parenteral nutrition, because parenteral nutrition has major complications. These include line infections, cost, TPN associated cholestasis, and calculation errors on nutrients delivered. With enteral nutrition, it may be harder to calculate caloric intake because everything that is given may not be absorbed. Both enteral and parenteral nutrition can permit positive nitrogen balance, depending on how much protein is delivered. Enteral nutrition may be associated with more toxin accumulation in the colon, as bacteria metabolize unabsorbed foods and create short-chain fatty acids and other compounds. Finally, both enteral and parenteral nutrition can be used in the outpatient setting.*

Question 14:
A TRUE statement about the sugar content of infant formulas is:

A. All lactose-containing formulas are cow milk-based
B. All cow milk-based formulas contain only simple sugars
C. All soy-based formulas are corn syrup-free
D. All soy-based formulas contain lactose
E. Proprietary formulas do not contain sucrose

Suggested answer: A. *Most cow's milk-based infant formulas contain the disaccharide lactose and not the disaccharide sucrose (there are exceptions). Soy-based formulas contains a combination of corn syrup solids, sucrose, and malto-dextrin. Proprietary formulas (i.e. Alimentum, Isomil, and Alsoy) also contain sucrose. The sucrose content in formula becomes important, especially in the work-up of hereditary fructose intolerance. Infants consuming cow milk-based formulas generally will not be exposed to sucrose, which is made of fructose and glucose. However, infants on soy or specialty formulas will be exposed to sucrose and hence fructose.*

Question 15:

Continuous, rather than intermittent (bolus), tube feeding is the PREFERRED choice for providing nutrition to the patient with:

A. a transpyloric feeding tube
B. anorexia nervosa
C. coma following head injury
D. esophageal obstruction
E. multiple facial fractures

Suggested answer: A. *Bolus feedings are preferred to continuous feedings, because they a) more closely replicate normal eating, and b) allow the patient to be disconnected from the pump for many hours during the day. However, if feeds are administered directly to the intestine, a continuous rate is needed. The intestine does not have the storage capacity of the stomach, and large bolus feeds would lead to dumping syndrome.*

Question 16:

A full-term infant, who weighed 2,200 gm at birth, has been breastfed for 4 months. General growth and development appear normal. Physical examination reveals enlargement of the costochondral junctions and subtle thickening of the wrists and ankles. The disorder that is MOST consistent with these findings is:

A. cleidocranial dysostosis
B. rickets
C. Rubenstein-Taybi syndrome
D. Russell-Silver syndrome
E. Scurvy

Suggested answer: B. *This patient's clinical symptoms are characteristic of rickets. Vitamin-D deficiency rickets is common between 3 months and three years, because calcium needs are high for growth and sunlight exposure is limited. Furthermore, vitamin D in breast milk is scant. Infants may be protected for the first 3 months, because 25-OH Vitamin D (clacidiol) is transferred via placenta from mother to fetus. Calcidiol has a half life of 3 to 4 weeks; afterwards, serum 25-OH Vitamin D concentration will fall unless supplemented through multivitamins, formula, or sunlight exposure.*

Question 17:

A TRUE statement regarding introduction of solid foods before the age of 4 to 6 months is:

A. Delaying introduction of solid foods beyond this age increases the likelihood of food allergy later
B. Feeding of solid foods helps the infant sleep through the night
C. Feeding of solid foods improves maternal-infant bonding
D. Starches are poorly digested because of low levels of amylase in the gut
E. Supplementation with solid foods is necessary for adequate nutrition

Suggested answer: D. *Solid foods should be introduced between 4 to 6 months of age. This is the ideal time, as introducing foods may provide extra calories to support extra growth, satisfy hunger, and reduce the occurrence of allergies. Introducing foods before this time may interfere with adequate energy intake, overload the kidneys, promote food allergies, and place the child at risk for aspiration. In addition, pancreatic enzyme secretion (including amylase)is immature for the first months of life, making starches difficult to digest. When foods are introduced after 6 months, infants may suffer from decreased growth (from decreased calorie intake), iron-deficiency anemia in breastfed infants, delayed oral motor function, and solid food aversion.*

Question 18:

A 6-week-old infant born at term has a hemoglobin level of 11 gm/dL and is diagnosed with physiologic anemia of the newborn. The MOST likely cause is:

A. inadequate iron stores in the bone marrow
B. inadequate serum levels of vitamin E
C. increased excretion of iron in the stool
D. low levels of serum erythropoietin
E. persistent fetal hemoglobin

Suggested answer: D. *Physiologic anemia of the newborn occurs when fetal hemoglobin normally declines at 6 to 8 weeks. Because fetal hemoglobin has a higher affinity for oxygen, serum erythropoietin levels are initially low. Erythropoietin levels eventually rise again with time, correcting the anemia. Some have investigated whether Vitamin E mitigate the normal hemoglobin nadir, with equivocal results.*

Question 19:
Most authorities encourage the early introduction of human milk in the very-low-birthweight (VLBW) infant. However, mothers must be informed early in the feeding process that supplementation of their milk with protein and other nutrients may be necessary. The MOST likely explanation for why protein supplementation of human milk often is required in the VLBW infant is that

A. human milk contains less than half the protein of cow milk formula
B. the hepatic metabolism of protein is ineffective in most preterm infants
C. the protein in preterm human milk is of poor nutritional quality
D. VLBW infants have excessive gastrointestinal losses of ingested protein
E. VLBW infants require an increased protein intake because of their high catabolic rate

Suggested answer: E. *Though VLBW benefit most from human milk, VLBW infants require higher protein intake to sustain adequate growth. They also have higher protein turnover rates. As a result, for VLBW infants, human milk should be fortified with extra protein to meet these increased needs. VLBW infants fed human milk without protein fortification have slower growth rates, lower BUN, and lower serum albumin, demonstrating the importance of protein supplementation.*

Human milk and formula contain almost equivalent amounts of protein; however, human milk contains more whey protein (quickly digested) whereas many formulas contain more casein protein (more slowly digested). There is no evidence that VLBW have increased protein losses from their gut.

Question 20:
A 3-year-old boy underwent a hepatoportoenterostomy (Kasai procedure) for extrahepatic biliary atresia at 6 weeks of age. He has been receiving cholestyramine to treat severe pruritus for the past 2 months. Of the following, the nutrient MOST likely to be malabsorbed because of this patients underlying liver disease and its treatment is:

A. carbohydrate
B. fat
C. protein
D. trace elements
E. water-soluble vitamins

Suggested answer: B. *This patient will have low luminal bile acids for two reasons: 1) poor bile acid secretion into the gut, secondary to biliary atresia; and 2) poor bile acid activity in the gut, secondary to binding with cholestyramine. Bile acids, pancreatic lipase, and pancreatic colipase work together to digest fats efficiently. Without bile acids, fat malabsorption will occur. Neither BA nor cholestyramine impairs duodenal or pancreatic function, so protein and carbohydrate absorption should be intact.*

Question 21:
A 5-year-old girl who has severe developmental delay is fed exclusively through a gastrostomy tube. Within 1 day of a change in her tube feeding formula, she develops diarrhea, abdominal distress, and flatulence. The stool pH is less than 5.0. These findings are MOST consistent with malabsorption of:

A. carbohydrate
B. fiber
C. lipid
D. protein
E. vitamins

Suggested answer: A. *This child has signs of symptoms of excessive carbohydrates in her feeds. Sugars that are not absorbed in the small intestine are delivered to gut bacteria in the colon. Here bacteria metabolize sugars into short chain fatty acids. The byproduct of this reaction is gas (causing bloating) and an increased colonic osmotic load (causing diarrhea). Furthermore, the short-chain fatty acids cause the stool to be acidic.*

Question 22:
A 10-month-old African-American infant who was born at 30 weeks gestation weighed 1,400 g at birth. She has been breastfed exclusively and has received no supplemental vitamins. General growth velocity has been slow, but development has been normal. Physical examination reveals enlargement of the costochondral junctions and slight thickening of the wrists and ankles. This infant MOST likely has a deficiency of:

A. folic acid
B. vitamin A
C. vitamin C
D. vitamin D
E. vitamin E

Suggested answer: D. *This child has Vitamin D-deficiency rickets. Premature babies are at higher risk for developing rickets, possibly secondary to poor maternal transfer of calcidiol through the placenta, poor bile acid production to absorb fat-soluble vitamins, and lack of sunlight in the NICU. In addition, breastfed infants receive inadequate Vitamin D in milk, as breast milk only contains 12-60 IU/L (recommended dose for infants controversial, and spans 200-400 IU/day). Hence, breastfed infants must receive supplements. Formula fed infants do not need supplements, because formula contains adequate amounts of added Vitamin D.*

Question 23:
You have volunteered to work in a refugee camp in Rwanda. You are examining a 15-month-old infant whose diet has been a dilute carbohydrate gruel since he was weaned from the breast at 9 months of age. Physical examination reveals pallor; apathy; thin, pale hair; a desquamating skin rash; pitting edema of the lower extremities; and weight at the 80th percentile for age. Among the following, the MOST likely diagnosis is:

A. kwashiorkor
B. marasmus-kwashiorkor
C. marasmus
D. vitamin A deficiency
E. vitamin C deficiency

Suggested answer: A. *This patient has kwashiorkor. Marasmus occurs secondary to inadequate total calories, and is characterized by low muscle and fat mass. Children look wasted. Kwashiorkor occurs*

secondary to adequate total calories but inadequate protein, and is characterized by low muscle mass and normal fat mass. Children look edematous and may have a scaly dermatitis resembling flaky paint. In the mixed picture, patients start with marasmus but then develop a pro-inflammatory state (i.e. from infection), leading to an edematous appearance. Vitamin A deficiency causes corneal dryness (xerophthalmia) leading to scarring and night blindness, whereas Vitamin C deficiency causes impaired collagen synthesis and scurvy.

Question 24:
A 3-week-old boy who was born at 28 weeks gestation is being fed 100 kcal/kg per day of fortified (24 kcal/oz) breast milk by gavage. He also is receiving aminophylline for apnea and low-flow oxygen and diuretic therapy for chronic lung disease. He is gaining weight at a rate of 5 g/day. Of the following, the MOST likely explanation for this child's slow weight gain is that:

A. administration of a loop diuretic causes excessive loss of glucose and protein
B. aminophylline therapy impairs fat absorption in the upper small intestine
C. multiple episodes of apnea/bradycardia increase the basal metabolic rate
D. the daily caloric intake is less than the recommended range for preterm infants
E. the metabolic rate of a growing preterm infant is twice that of a term infant

Suggested answer: D. *Preterm infants have increased energy needs, in part because they have lower body stores of fat and glycogen, expend more energy controlling their temperature, and have to support high rates of growth relative to their body size. Their metabolic rate is more than that of a term infant (but not twice as much), and hence they need more calories that the standard 100 kcal/kg/day needed by a term infant.*

Infants are commonly given theophylline/aminophylline (caffeine) for apnea and bradycardia, which also increases energy expenditure and may impair growth but does not impair fat absorption. Loop diuretics should not cause protein or glucose loss. Finally, apnea/bradycardia episodes may increase energy expenditure but would not affect the basal metabolic rate.

Question 25:
A 6-week-old boy who was born at home and who has been exclusively breastfed has had diarrhea for 5 days. His parents bring him to the emergency department because he has multiple deep ecchymoses and bloody stools. Until the results of laboratory studies become available, the best INITIAL management of this patient is to administer intravenous?

A. cryoprecipitate
B. factor VIII concentrate
C. fresh frozen plasma
D. platelets
E. vitamin K

Suggested answer: E. *Newborns receive Vitamin K supplementation at birth because many are vitamin K deficient. There are many reasons for this deficiency: 1) low vitamin K stores at birth, 2) poor placental transfer of vitamin K, 3) low levels of vitamin K in breast milk (but adequate amounts in formula), and 4) low colonic bacteria that normally generate vitamin K. Without adequate vitamin K, infants can develop bleeding at the umbilicus, in the mucous membranes, in the GI tract, at circumcision sites, and at IV sites. They can also have hematomas at sites of trauma, as well as life-threatening intracranial bleeding.*

Vitamin K administration is the first treatment of choice. For active bleeding, fresh frozen plasma should be administered. Prothrombin complex concentrates (PCC) can be given in life-threatening situations.

Question 1:
Shortly after birth, a 3,500 g term newborn is found to be jittery and to have a high-pitched cry. Physical examination reveals tachypnea and a liver edge that is palpable several centimeters below the umbilicus. Blood glucose concentration is 14 mg/dL.

Among the following, the MOST likely cause of the hypoglycemia in this newborn is:

A. galactokinase deficiency
B. glycogen storage disease
C. insulinoma
D. maternal diabetes mellitus
E. prolonged maternal labor

Suggested answer: B. Hypoglycemia in an infant suggests either too much insulin (insulinoma, maternal DM) or too little glucose release into the bloodstream in non-feeding states (GSD). MDM is much more common than insulinomas, and neither are associated with hepatomegaly,. On the other hand, GSD is associated with a large liver secondary to glycogen entrapment. Other signs include lactic acidosis, slight ketosis, and hyperuricemia.

Galatosemia is caused by defects in one of two enzymes. Classic galactosemia occurs from defects in galactose-1-phosphate uridyltransferase (GALT), which results in accumulation of galactose-1-phosphate, galactose, and oxidative and reductive products galactitol and galactonate. Patients develop hepatosplenomegaly and mental retardation, in addition to cataracts and galactosuria. The other mutation is in galactokinase, which works one step ahead of GALT and is used to create galactose-1-phosphate. Infants with mutations in this gene have cataracts and galactosuria, but do not have hepatosplenomegaly or mental retardation (presumably because galactose-1-phosphate is not produced so does not accumulate). Cataracts cccur in both types of galactosemia, when excessive galactose is converted to the osmotically active galactitol in the lens/eye.

Question 2:
A breastfed infant who appeared healthy at birth develops chronic diarrhea, failure to thrive, and hepatomegaly during the first few weeks of life. Ultrasonography reveals adrenal enlargement and calcification.

Of the following, the MOST likely explanation for these findings is:

A. cystic fibrosis
B. glucose-galactose malabsorption
C. glycogen storage disease
D. Niemann-Pick disease
E. Wolman disease

Suggested answer: E. Wolman disease results from recessive mutations in lysosomal acid lipase. This enzyme acts on endocytosed lipoproteins, hydrolyzing cholesteryl esters and triacylglycerols. Without the enzyme, patients accumulate cholesteryl esters and triacylglycerols in various tissues. Patients have severe diarrhea (presumably from intestinal involvement), malnutrition, abdominal distension, hepatosplenomegaly, and calcification of the adrenal glands. Patients do not survive past infancy.

Niemann-Pick Types A, B, and C disease are associated with neurological changes rather than diarrhea. Types A and B are caused by defects in acid sphingomyelinase activity. Sphingomyelin accumulates intracellularly, producing hepatosplenomegaly, "foam cells," and, in Type A, severe neurodegenerative

disease and death by 3 years. Type C disease, caused by mutations in NPC1 or NPC2, involves defects in cholesterol trafficking from lysosomes to other compartments. As a result, excessive lipids are found in lysosomes.

Glucose-galactose malabsorption causes life-threatening diarrhea and dehydration in the first few weeks, associated with renal (not adrenal) calcium deposits. The disease is caused by recessive mutations in the sodium/glucose cotransporter SGLT1, which is the main transporter involved in transporting glucose and galactose into enterocytes. As a result, glucose and galactose remain in the gut lumen and act as an osmotic drive causing diarrhea. SGLT1 is also found in the kidney, and mutations can also lead to glucosuria. Treatment involves fructose-based formulas that do not contain glucose or galactose.

Question 3:
A 4-week-old infant is jaundiced. Findings include weight and length at the 75th percentile for age; icterus; hepatosplenomegaly; total bilirubin, 6.3 mg/dL; direct bilirubin, 5.5 mg/dL; alanine aminotransferase activity, 130 U/L; aspartate aminotransferase activity, 143 U/L; and gamma-glutamyl transpeptidase activity, 950 U/L.

Of the following, the BEST study to evaluate the excretion of bile from the liver is:

A. computed tomography of the liver
B. hepatic ultrasonography
C. hepatobiliary scintigraphy
D. measurement of galactose-1-phosphate uridyltransferase activity
E. measurement of the serum alpha1-antitrypsin level

Suggested answer: C. Bile excretion can be documented with the HIDA (hepatobiliary iminodiacetic acid) scan. The procedure is based on monitoring a radiolabeled compound as it travels from the hepatocyte, into the cannalicular space, through the biliary tree, and into the intestine. HIDA scans have been shown to be more sensitive than specific for biliary atresia; another better, yet more invasive test, to demonstrate patent bile ducts is the intraoperative cholangiogram.

The other choices do not measure excretion. CT is not needed in this case, whereas US is useful to demonstrate presence of a choledochal cyst, polysplenia (found in approximately 10% of BA cases), the triangular cord sign (thickening of left branch of portal vein in BA), and absence of gall bladder. GALT activity is useful if classic galactosemia is suspected. Finally, low A1AT levels may hint at A1AT deficiency, though PI (protease inhibitor) typing is a better test.

Question 4:
A 14-year-old boy has a 36-hour history of severe, continuous midepigastric pain radiating to the back, persistent vomiting, and fever. Physical examination reveals: blood pressure, 70/40 mm Hg; temperature, 39.5ºC (103.1ºF); marked midepigastric tenderness, guarding, and rebound; absent bowel sounds; and abdominal distention. You suspect acute pancreatitis.

The test or procedure that will be MOST specific in confirming the diagnosis is a(n):

A. abdominal ultrasonogram
B. endoscopic retrograde cholangiopancreatogram
C. serum alanine aminotransferase activity
D. serum amylase activity
E. white blood cell count

Suggested answer: D. Amylase can be used to make the diagnosis of acute pancreatitis; however, lipase has been shown to be sensitive and more specific. Amylase elevations can also occur in salivary disease, intestinal disease, gynecological disease, and neoplasms. Abdominal ultrasound may or may not show changes, and may be hampered in this case by air from abdominal distension. ERCP outlines the pancreatic duct to identify stones or strictures, but does not outline the pancreatic parenchyma. ALT/AST would be useful to identify gall-stone related common bile duct obstruction, leading to pancreatitis and hepatitis. Finally, WBC counts could be high in a number of infectious or inflammatory diseases.

Question 5:
Enteric diseases commonly occur in young children who attend out-of-home child care facilities.

Of the following, the enteropathogen most likely to cause CHRONIC diarrhea in an immunocompetent child is:

A. adenovirus
B. Cryptosporidium
C. Escherichia coli 0157:H7
D. rotavirus
E. Shigella

Suggested answer: D. Chronic diarrhea is diarrhea that occurs for more than 4 weeks. Viruses such as rotavirus and adenovirus can cause "post-enteritis syndrome," a form of chronic diarrhea thought to be secondary to the acute infection. Post-enteritis syndrome may be caused by a number of factors: a) disaccharide deficiency because of blunted villi, b) leaky mucosa leading to protein translocation and sensitivity/allergy, and c) repeated enteric infections following the initial insult. Cryptosporidium causes chronic diarrhea in immunocompromised hosts. E. coli and Shigella usually cause acute symptoms.

Question 6:
Among the following, the gastrointestinal disease MOST likely to respond to treatment with anti-cholinergic medications is:

A. constipation
B. dysentery
C. gastroesophageal reflux
D. irritable bowel syndrome
E. peptic ulcer disease

Suggested answer: D. Cholinergic agonists are used to stimulate the parasympathetic nervous system, thereby activating motility. Anti-cholinergic agents, then, would be expected to make dysmotility problems such as constipation and reflux worse. Anti-cholinergics can be used to treat IBS patients suffering from too much motility. Theoretically, they can also be used in peptic ulcer disease (acetylcholine is one input to parietal cells), but more often proton-pump inhibitors or histamine receptor agonists are chosen. Finally, dysentery should be treated by targeting the offending agent rather than by altering motility though anti-cholinergic medications.

Question 7:
For the past 6 weeks, a 4-year-old boy has had painless, bright red rectal bleeding associated with bowel movements. Examination of the abdomen and anus reveals normal findings. The rectal vault is empty, and no blood is noted on gross inspection.

Of the following, the MOST likely cause for the hematochezia is

A. hemolytic-uremic syndrome
B. Henoch-Schönlein purpura
C. intussusception
D. juvenile polyposis
E. Meckel diverticulum

Suggested answer: D. Juvenile polyposis is characterized by painless bright red blood associated with bowel movements. Histology usually shows hamartomatous changes. Meckel's diverticulum presents with melena (if slow bleeding) or bright red rectal bleeding not associated with bowel movements (if fast bleeding). HUS (a coagulopathy), HSP (a vasculitis), and intussusception (an anatomical defect) all present with abdominal pain.

Question 8:
A 2-year-old boy has had bilious vomiting and bloody stools since last night. Physical examination reveals a moderately ill, dehydrated child who has a scaphoid abdomen and absent bowel sounds. Stools are maroon-colored and strongly positive for blood.

After stabilizing the patient, the INITIAL diagnostic study that should be performed is a(n)

A. acute abdominal radiographic series
B. barium swallow
C. computed tomogram of the abdomen
D. Meckel scan
E. upper endoscopic examination

Suggested answer: A. This patient has signs of symptoms of an acute abdomen, likely secondary to volvulus causing bilious vomiting and ischemic gut. To confirm the diagnosis, radiographic films can be used to document ileus and presence of free air. A barium swallow would be poorly tolerated because of the intestinal obstruction, and may cause harm if perforation is present. CT of the abdomen would better outline the patient's anatomy, though may be more than what is needed before surgery. A Meckel's diverticulum would not cause upper GI symptoms, and an EGD would provide no diagnostic or therapeutic benefit.

Question 9:
A 13-year-old girl is being evaluated for diarrhea, abdominal pain, and weight loss.

Of the following, the feature that BEST distinguishes Crohn disease from ulcerative colitis is:

A. development of crypt abscesses
B. hepatic involvement
C. mucosal ulcerations on endoscopy
D. noncaseating granulomas on mucosal biopsy
E. poor growth

Suggested answer: D. Although the treatments overlap, the type of IBD does play a role in diagnostic tests and prognosis. Generally, UC is a mucosal disease which starts in the rectum. As the disease progresses, it involves continuous parts of the colon but does not extend into the ileum. Crypt abscesses are common, and hepatic involvement can be seen in the form of primary sclerosing cholangitis or autoimmune hepatitis. Crohn disease, on the other hand, extends throughout the thickness of the bowel

and can be present in skip lesions throughout the GI tract. Liver involvement is less common, though can be present. The most characteristic pathological finding is the noncaseating granuloma, comprised of macrophages coordinating an autoimmune reaction in the mucosa. Both UC and Crohn disease can be associated with ulcers on endoscopy and poor growth.

Question 10:
A 6-month-old boy has chronic diarrhea. Findings include: weight less than the 5th percentile and length at the 25th percentile for age; marked cachexia with protuberant abdomen; sodium, 125 mEq/L; chloride, 90 mEq/L; albumin, 2.5 g/dL; and total protein, 4.3 g/dL. Stool is negative for reducing sugars but positive for neutral fats; a 72-hour fecal fat collection shows a coefficient of absorption of 45% (normal, >93%).

These findings are MOST consistent with:

A. celiac sprue
B. cow milk-soy protein allergy
C. Crohn disease
D. cystic fibrosis
E. giardiasis

Suggested answer: C. Cystic fibrosis is associated with pancreatic insufficiency, secondary to inspissation of pancreatic secretions and poor secretion. As a result, patients develop fat malabsorption, protein malabsorption, chronic diarrhea, and malnutrition. Celiac disease starts when children consume gluten-containing foods, so would not be present as a chronic disease in a 6 month old. Cow milk-soy protein allergy presents as bloody stools, rectal eosinophilia, and possibly constipation, but does not lead to failure to thrive. Crohn disease is less common in a 6 month old, and does not necessarily lead to fat malabsorption. Finally, giardiasis can cause chronic diarrhea but would not be expected to cause steatosis.

Question 11:
The clinical manifestations of cholecystitis differ depending on the age of the patient.

Which of the following findings is MORE likely to occur in an affected child than in an affected adult?

A. Fat intolerance
B. Fever
C. Jaundice
D. Pain radiating to the right scapula
E. Palpable mass in the right upper quadrant

Suggested answer: C. Cholecystitis is defined as inflammation of the gall bladder, usually secondary to bile stasis and bacterial growth. It can be acute (from stone obstruction) or chronic (from stone obstruction or poor gall bladder motility). Symptoms include fever and pain in the RUQ and radiating to the right scapula. Pain intensifies with fatty meals that stimulate gall bladder contraction. Children more commonly present with jaundice, even if a stone is not identified. This jaundice is presumably from edema of the bile duct walls, preventing bile outflow and bilirubin back-up into the circulation.

Question 12:
A febrile 1-month-old infant has a generalized seizure. Findings include healthy appearance; weight and length, 90th percentile; liver span, 11 cm; serum glucose, 20 mg/dL; alanine aminotransferase activity,

123 U/L; aspartate aminotransferase activity, 153 U/L; total bilirubin, 2.0 mg/dL; and lactic acid, 4.7 mmol/L.

These findings are MOST suggestive of:

A. alpha1-antitrypsin deficiency
B. congenital hepatic fibrosis
C. galactosemia
D. glycogen storage disease
E. perinatal cytomegalovirus infection

Suggested answer: D. This patient is having a hypoglycemic seizure, likely from a glycogen storage disease. In type Ia GSD, there is a deficiency of glucose-6-phosphatase. In the liver, glucose-6-phosphatase converts glucose-1-phosphate (generated from stored glycogen) into glucose to be released in the circulation during times of fasting. In addition to hypoglycemia and related seizures, patients with GSD type I have hepatomegaly and hepatocyte damage from excessive stored glycogen.

A1AT could cause jaundice, elevated AST/ALT, and hepatomegaly; however, it is not associated with hypoglycemia at diagnosis. Similarly, congenital hepatic fibrosis and CMV infection involve the liver but would not lead to hypoglycemia so early. Galactosemia causes hepatosplenomegaly from galactose-1-phosphate accumulation; however, it is not characteristically associated with hypoglycemia.

Question 13:
A 6-year-old boy who has chronic constipation has been treated with cathartic medications for 1 week. You decide to place him on maintenance therapy with a lubricating laxative.

Among the following, the agent you are MOST likely to recommend is:

A. bisacodyl
B. docusate sodium
C. magnesium hydroxide
D. malt soup extract
E. mineral oil

Suggested answer: E. Mineral oil is a lubricating laxative, which coats the mucosa allowing stools to slide easily and preventing colonocytes from reabsorbing water. Docusate sodium acts like a soap, reducing the surface tension of stool and allowing more fat and water to enter. Magnesium hydroxide (along with polyethylene glycol and lactulose) are common osmotic laxatives, whereas bisacodyl is a stimulant laxative that increases persistalsis by irritating mucosal smooth muscle. Malt soup extract is a bulk forming fiber laxative. Its cellulose content absorbs water from the intestine and causes stool to become bulky and soft.

Question 14:
A 4-month-old boy regurgitates after all feedings. His weight has remained at the 10th percentile for age. Normal findings on an upper gastrointestinal barium study have excluded anatomic abnormalities. You suspect gastroesophageal reflux.

The best INITIAL management of this child would be:

A. administration of cisapride
B. administration of ranitidine

C. administration of small, thickened oral feedings
D. change to an elemental formula
E. referral for fundoplication

Suggested answer: C. This patient has uncomplicated GER with no pain, arching, or failure to thrive. The first intervention is to thicken oral feeds. The next intervention would be to try a hypoallergenic (not elemental) formula, because cow's milk allergy presents with symptoms similar to GER. Cisapride, a pro-motility agent, is not available due to associations with heart arrhythmias. Ranitidine or a proton-pump inhibitor may be good choice if the patient showed symptoms of pain, such as back-arching; however, without these symptoms, acid suppression is not warranted. Finally, a fundoplication is excessive for uncomplicated GER.

Question 15:
Examination of a developmentally normal 7-month-old boy reveals moderately enlarged cervical lymph nodes; a hemorrhagic seborrhea-like rash on the forehead, scalp, and trunk; and hepatosplenomegaly. Laboratory findings include: hemoglobin, 12.0 g/dL; mean corpuscular volume, 82 fL; white blood cell count 10,700/mm^3, with 40% neutrophils and 60% lymphocytes; and platelet count 260,000/mm^3.

These findings are MOST consistent with:

A. acute lymphoblastic leukemia
B. aplastic anemia
C. Langerhans cell histiocytosis
D. neuroblastoma
E. Niemann-Pick disease

Suggested answer: C. Langerhans cell histocytosis results from abnormal proliferation of the Langerhan cell, a dendritic cell subtype. Multisystem LCH involves the skin (rash), lymph nodes, liver (liver dysfunction, primary sclerosing cholangitis), spleen, and various other organs. LCH is treated with chemotherapy. In this scenario, ALL and aplastic anemia are unlikely because there is no anemia. Neuroblastoma can present with an abdominal mass. Niemann-Pick disease involves cholesterol trafficking, and leads to neurodegenerative changes.

Question 16:
A previously healthy 12-year-old boy presents with an upper gastrointestinal tract hemorrhage. Findings include: hepatosplenomegaly, ascites, a prominent vascular pattern on the abdomen, thrombocytopenia, mildly elevated aminotransferase activity, markedly elevated gammaglutamyl transpeptidase activity, and a prolonged partial thromboplastin time.

Which of the following laboratory studies is MOST likely to provide a diagnosis?

A. Alpha1-antitrypsin level
B. Fasting blood glucose level
C. Galactose-1-phosphate uridyltransferase activity
D. Hepatobiliary scintigraphy
E. Sweat test

Suggested answer: E. This patient has chronic liver disease (as demonstrated by the many signs of portal hypertension) caused by a biliary etiology (as suggested by high GGT levels). The most likely diagnosis is cystic fibrosis-related liver disease. CFTR is present in biliary epithelium and promotes proper bile flow. Without it, bile backs up and leads to liver cirrhosis. In addition, as in this case, children with CF-

related liver disease may have minimal lung disease and no growth problems. Biliary atesia causes similar symptoms and uses hepatobiliary scans in its work-up. BA, however, presents in infancy.

Alpha-1-antitrypsin deficiency can present with cirrhosis in adolescents, but usually AST/ALT levels are higher secondary to misfolded A1AT protein accumulating in hepatocytes. Also, A1AT is best diagnosed with PI typing, because alpha-1-antitrypsin levels may be falsely elevated in times of inflammation. Fasting blood glucose may be low secondary to liver dysfunction, but would not identify the primary liver disease. GALT deficiency leads to classic galactosemia, which presents in infancy.

Question 17:
A 14-year-old boy is being evaluated for jaundice that was first noted 1 week ago following an upper respiratory tract infection. He reports not feeling very hungry for the past month. Physical examination reveals a firm liver, an enlarged spleen, and an intention tremor.

Among the following, the test that would be MOST helpful for making a definitive diagnosis in this patient is a:

A. liver biopsy for copper content
B. serum bilirubin concentration
C. serum ceruloplasmin level
D. serum transaminase activity
E. slit lamp examination of the cornea

Suggested answer: A. In an adolescent with liver disease and neurological findings, Wilson disease should be suspected. Wilson disease is caused by a mutation in the ATP7B copper transporter. Mutations result in abnormal copper trafficking at 2 levels: 1) impaired copper binding to apoceruloplasmin inside the hepatocyte, and 2) decreased secretion of copper into the biliary system. Copper accumulates in hepatocytes and other tissues (brain, kidneys, heart), leading to clinical symptoms.

Only 50% of patients have the classical findings of Kayser-Fleischer rings (detected by slit lamp examination) and low serum ceruloplasmin. Serum ceruloplasmin is especially tricky, because although it should be low secondary to low serum copper levels, it may be elevated as an acute phase reactant in the setting of chronic liver inflammation. Elevated serum transaminase activity or bilirubin concentration may initiate the work-up but are not specific to Wilson disease. The gold standard for diagnosing Wilson disease is hepatic copper content. 85% of patients have a hepatic copper concentration greater than 250mcg/g of liver tissue.

Question 18:
A 4-month-old infant has had diarrhea for 6 weeks. Findings include: weight less than the 5th percentile and length at the 10th percentile for age; cachexia; a protuberant abdomen; total protein, 4.3 g/dL; albumin, 2.8 g/dL; stool pH, 4.5; stool for reducing substances, 2+; stool culture, negative for enteric pathogens; and sweat chloride, 10 mEq/L.

The study that would be MOST helpful in determining the cause of this child's diarrhea is

A. D-xylose test
B. serum trypsinogen level
C. small bowel biopsy
D. stool alpha1-antitrypsin level
E. upper gastrointestinal barium study

Suggested answer: C. This patient has severe malnutrition, with poor weight compared to height, low serum proteins, and sugar malabsorption. The differential diagnosis for this child's condition is broad, and includes infection, pancreatic insufficiency, and villi disease (i.e. tufting enteropathy, microvillus inclusion disease). EGD to visualize the mucosa and collect samples for routine histology as well as electron microscopy will help distinguish between some of these possibilities.

It is already clear that the child has malabsorption, so a D-xylose test is unnecessary. (In the test, D-xylose, a substance absorbed in the SI, is given and then measured in blood and urine. Low values suggest malabsorption). Serum trypsinogen is used to detect pancreatitis, which is unlikely in this child. Elevated stool alpha-1-antitrypsin identifies protein loss in the gut, which in an infant raises the possibility of congenital intestinal lymphangiectasia. However, in congenital intestinal lymphangiectasia, lymphatics are blocked and drain backwards into the bowels, leading to fat – rather than sugar – malabsorption. Finally, an UGI barium swallow is used to detect malrotation when the primary symptom is vomiting.

Question 19:
Physical examination of a 13-year-old boy who is being evaluated for short stature reveals aphthoid lesions in the mouth and skin tags and fissures around the anus.

Of the following, these findings are MOST consistent with

A. Crohn disease
B. herpes simplex virus infection
C. immunoglobulin A deficiency
D. pseudomembranous colitis
E. ulcerative colitis

Suggested answer: A. Crohn disease is characterized by involvement of all parts of the GI tract, including mouth (aphthous ulcers), small intestine (poor growth), and perianal areas (skin tags and fissures, present in 1/3 of cases). Ulcerative colitis, on the other hand, usually presents sub-acutely with bloody diarrhea and symptoms restricted to the colon. HSV infection could cause mouth ulcers but would not cause chronic growth problems and anal findings. Those with IgA deficiency are usually asymptomatic. The 10% with symptoms may have diarrhea secondary to persistent Giardia infection. Pseudomembranous colitis occurs acutely in response to C. difficile infection. It can be seen endoscopically as membranes of host protein, mucus, and inflammatory cells over C. difficile-induced mucosal ulcers.

Question 20:
A 4-week-old boy who was born at 28 weeks' gestation and weighed 800 g at birth is gaining weight at a rate of only 5 g/day even though his caloric intake is 125 kcal/kg. The stool is poorly formed and bulky. The infant is receiving a lactose-free formula containing 24 kcal/oz.

Which of the following interventions is MOST likely to result in a decrease in steatorrhea and improved weight gain?

A. Increase the daily caloric intake to 150 kcal/kg
B. Increase the glucose polymers in the formula
C. Increase the protein intake
D. Increase vitamin A and vitamin E supplements
E. Substitute medium-chain triglycerides for long-chain triglycerides

Suggested answer: E. Premature infants absorb long-chain triglycerides poorly, because they have not yet developed the machinery to digest and absorb fats. They have poor pancreatic and bile excretion, leading to low amounts of lipase, colipase, and bile acids in the intestinal lumen. Without these enzymes, micelles do not form, lipids are not absorbed into the intestinal lymphatics, and, as a result, fats are passed into the stool. Medium chain triglycerides can circumvent this problem because they are absorbed directly into enterocytes without digestion by bile acids. Hence, changing the fat content of the formula should lead to better absorption and better weight gain.

Question 21:
A 14-year-old female adolescent who has severe juvenile rheumatoid arthritis presents to your office with epigastric abdominal pain. Six weeks earlier she began taking a nonsteroidal anti-inflammatory drug (NSAID) because of worsening joint complaints.

Of the following, the most appropriate INITIAL management of her symptoms would be

A. administration of an antibiotic effective against Helicobacter pylori
B. administration of an H2-receptor antagonist
C. dietary modification
D. substitution of salicylate for NSAID
E. upper endoscopy and gastric biopsy for gastric adenocarcinoma

Suggested answer: B. NSAIDs (and aspirin) cause gastric/duodenal damage by inhibiting COX enzymes and prostoglandin production. Prostoglandins have a number of protective roles in the upper GI tract, including decreasing acid secretion, stimulating mucus production, stimulating bicarbonate production, and promoting vasodilation of gastric vessels to increase oxygen delivery. To counter these effects, acid suppression therapy with H2-receptor antagonists and proton pump inhibitors can be used. Misoprostol, a prostaglandin E analog, seems to have even more gastroprotective effects, but also causes diarrhea and abdominal discomfort.

H. pylori may predispose patients taking NSAIDs to develop peptic ulcer disease, so testing and treating positive cases is appropriate. There is no evidence that this patient consumes foods likely to increase acid secretion, so dietary modification would not be the primary intervention. Upper endoscopy may be appropriate to confirm ulcers (not adenocarncinoma) caused by NSAID/aspirin use.

Question 22:
The essential difference between elemental formulas and casein hydrolysate formulas is that elemental formulas are MOST likely to include:

A. a hyperosmolar composition
B. an increased concentration of vitamins and minerals
C. lactose as the predominant carbohydrate source
D. medium-chain triglycerides
E. protein in the form of amino acids rather than oligopeptides

Suggested answer: E. Cow's milk and soy milk based formulas contain large protein epitopes which can trigger an allergic reaction. To address this, casein hydrolysate formulas are used, consisting of smaller peptides rather than full proteins. If the peptides still induce allergy, then elemental formulas consisting of individual amino acids are used. Individual amino acids do not produce allergic responses.

Elemental formulas have a slightly higher osmolarity than hydrolysate formulas, but this difference is not as important as their differing protein contents. The two formulas have equivalent vitamins and minerals, and use corn syrup solids, cornstarch, and in some cases sucrose (Similac Alimentum) as carbohydrate sources. The amount of MCT oils added is brand-dependent.

Question 23:
Among the following disorders, rickets is MOST likely to develop in patients who have:

A. acute pancreatitis
B. adrenal insufficiency
C. cirrhosis
D. congenital heart disease
E. lactose intolerance

Suggested answer: C. Patients with liver disease have two reasons to be Vitamin D deficient. First, if cholestatic, they have impaired absorption of fat soluble vitamins including Vitamin D2. (The skin can compensate to some extent, creating Vitamin D3). Second, the Vitamin D2/D3 is converted in the liver to 25-hydroxy-Vitamin D, which then passes to the kidneys and is converted to the active 1,25-dihydroxy-Vitamin D. Patient with cirrhosis have impaired 25-hydroxylation of Vitamin D2 and D3. Acute pancreatitis would not cause Vitamin D deficiency; however, chronic pancreatitis and pancreatic insufficiency would result in impaired lipase/colipase secretion, and would impact absorption of fat-soluble vitamins.

Question 24:
A 6-month-old boy developed a weepy, crusted dermatitis around the eyes, nose, mouth, diaper area, hands, and feet about 4 weeks after being weaned from human milk to formula. He is listless, recently developed diarrhea, and has stopped gaining weight. In addition to the dermatitis, he has sparse hair that is fine and lightly pigmented.

Of the following, this constellation of findings is MOST consistent with a deficiency in

A. copper
B. thiamine
C. vitamin A
D. vitamin C
E. zinc

Suggested answer: E. Acrodermatitis enteropathica, a recessive mutation in the zinc transporter SLC39A4, is responsible for this child's symptoms. Affected infants absorb zinc poorly, and have dermatitis (around orifices and the limbs), alopecia, diarrhea, growth retardation, frequent infections, neuropsychiatric problems, and delayed sexual maturation. Symptoms usually start when the infant is weaned from breast milk to formula, suggesting that breast milk has some compound that aids in zinc absorption. Treatment is with daily zinc supplementation.

Also on the differential in this case is Menkes syndrome. Menkes syndrome is caused by a mutation in the X-linked gene ATP7A, which is important in copper trafficking. In the small intestine, it is responsible for copper absorption. Symptoms arise when copper-dependent mitochondrial enzymes are impaired, and when copper abnormally accumulates in certain tissues. Infants present with "kinky" hair, growth failure, and neurological deterioration.

Poor nutrition can lead to deficiencies in many vitamins and minerals. Copper deficiency is associated with sideroblastic anemia, neutropenia, failure to thrive, and skeletal abnormalities. Thiamine deficiency (Vitamin B1) is associated with beriberi, consisting of cardiomyopathy and polyneuritis. Vitamin A deficiency causes night blindness, and Vitamin C deficiency causes scurvy. Zinc deficiency leads to dermatitis around perioral and perianal areas, poor appetite, diminished taste acuity, hypogonadism, and short stature.

Question 25:
Following an acute febrile illness, a 6-month-old infant has had diarrhea for 3 weeks. When the diarrhea began, the mother said she fed the infant an oral electrolyte solution exclusively. As the diarrhea slowed, the mother reintroduced cow milk infant formula, and the diarrhea recurred. The infant continues to receive oral electrolyte solution exclusively. She appears thin but is otherwise healthy.

The BEST management at this time is to administer:

A. a gluten-free diet
B. a hypoallergenic diet
C. a lactose-free diet
D. clindamycin
E. metronidazole

Suggested answer: C. Post-enteritis syndrome refers to chronic diarrhea persisting after an initial enteric infection. It was thought that such patients have lactose malabsorption secondary to villi damage and poor lactase production, which then leads to an osmotic diarrhea. Patients were instructed to avoid lactose and consume formulas with glucose polymers. If intolerance persisted, then protein hypersensitivity was thought to be the cause, presumably from damaged mucosa allowing translocation of large peptides. To treat this scenario, patients were put on hypo-allergenic formulas.

Recent work has shown that disaccharidase deficiency and protein sensitization are actually not that common. Rather, the mechanism of disease appears to be from repeated enteral infections following the initial infection. Some recommend treating with probiotics to hasten recovery times.

Question 1:
A 12 year old girl with cirrhosis due to alpha-1-antitrypsin deficiency presents for evaluation of a 6-month history of slowly progressive exertional dyspnea. Physical examination reveals multiple spider angiomas, clubbing, and acrocyanosis. Chest and cardiac examination are unremarkable and chest radiography and pulmonary function tests are normal. Arterial blood gas reveals a respiratory alkalosis with hypoxemia. Which one of the following is the best screening test to define the diagnosis?

A. Pulmonary angiography
B. Contrast echocardiography
C. Abdominal ultrasonography with Doppler examination of the hepatic vasculature
D. Bronchoscopy
E. Right heart catheterization to assess pulmonary arterial pressure

Suggested correct Answer: B. Alpha-1-antitrypsin deficiency is caused by mutations in the A1AT gene. The best diagnostic test is PI (protease inhibitor) typing, which is commonly mistaken as a genotyping test. PI typing is actually a phenotype test, in which different protein forms are identified by Western blot. There are 3 common protein variants: M (normal), S (somewhat abnormal), Z (abnormal). There is also a null variant, caused by a mutation that leads to no protein production.

A1AT deficiency leads to liver and lung disease. Lung disease happens in adults, from progressive damage of lung tissue from neutrophil serine proteases (there is no A1AT to counter these enzymes). The liver injury occurs earlier, because misfolded A1AT cannot leave the hepatocyte. It accumulates and causes damage. ZZ and SZ phenotypes are most likely to have accumulation and hepatocyte damage in children, whereas MZ may lead to liver issues later in life. Interestingly, the null phenotype will have no accumulation or liver damage but will have significant lung injury.

In this question, the child likely has a ZZ or SZ phenotype causing her liver symptoms. Her respiratory symptoms could be due to concomitant A1AT lung disease. However, lung disease in children is very rare, and would present as emphysema on exam and pulmonary function tests. In one study, adolescents with ZZ phenotype showed no significant abnormality in pulmonary function tests compared to age-matched controls. Another study showed a slight degree of hyperinflation in affected children, but no studies have conclusively shown major lung disease in the pediatric population.

The pulmonary findings of hypoxemia and alkalosis (presumably secondary to hyperventilation) are more likely from one of two processes related to any liver disease: hepatopulmonary syndrome vs. portopulmonary hypertension. Hepatopulmonary syndrome consists of hypoxemia, intrapulmonary vascular dilations, and liver disease. The vascular dilations lead to pulmonary R->L shunts detected on contrast (bubble) echocardiography or technetium 99m-labeled microalbumin study. Classic physical findings are clubbing, cyanosis, and spider nevi. Furthermore, because the shunts are more often found at the lung bases, symptoms usually worsen when standing.

Portopulmonary hypertension is the opposite of hepatopulmonary syndrome, because it involves pulmonary vasoconstriction (as opposed to dilation) and increased pulmonary pressures. It is not as well described in children. An echocardiogram showing increased tricuspid regurgitation would suggest this diagnosis, and right heart catherization would confirm it.

Question 2:
Hepatitis A occurs in cyclical outbreaks in the United States. These outbreaks spread largely because of:
A. HAV infection among injection drug users

B. Promiscuous sexual behavior
C. Infected food handlers
D. Widespread vaccination programs
E. Close personal contact with infected but asymptomatic individuals, particularly children

Suggested correct Answer: E. Hepatitis A is an RNA virus acquired by direct contact or through contaminated water/food. Most infections are asymptomatic, and nearly 100% of 18 year olds in developing countries (before the vaccine was available) had serological evidence of past infection. Children appear to be the reservoirs, making answer E the correct choice.

Infants and toddlers are less likely than older children or adults to develop jaundice, with one study showing that only 1 in 12 infants with Hepatitis A developing jaundice. Small children can present simply with diarrhea, and may be diagnosed as general acute viral gastroenteritis (whereas jaundice is more common in adults, diarrhea is more common in children). Finally, children may be completely asymptomatic with Hepatitis A ("anicteric hepatitis"). Despite these mild symptoms, vaccinations are warranted in children to prevent them from harboring the virus and ultimately spreading it to adults, in which the infection is more severe.

Question 3:
A previously healthy two year old boy is referred to you for elevation of liver function tests. When a liver profile was drawn during an episode of fever, his serum alkaline phosphatase concentration was elevated. He has no recent history of fractures. His growth and development have been normal. He did not have neonatal liver disease. Review of symptoms is negative for pruritis, chronic diarrhea, or acholic stools. His physical examination is normal. Laboratory studies at your institution confirm the biochemical findings. Serum 25-hydroxy vitamin D levels are within the normal range.

	Patient's results	Normal range
Calcium	9.2 mg/dL	8.8- 10.7 mg/dL
Phosphorus	4.2 mg/dL	3.0 -5.0 mg/dL
Blood urea nitrogen	8 mg/dL	5-20 mg/dL
SGOT	28 IU/L	20-60 IU/L
SGPT	18 IU/L	5-45 IU/L
GGT	12 IU/L	6-20 IU/L
Conjugated bilirubin	0.1 mg/ dL	< 0.3 mg/dL
Alkaline phosphatase	2800 IU/L	65-525 IU/L

Which of the following is the most appropriate next step to manage this child?
A. Abdominal ultrasound
B. Liver biopsy
C. Radiographs for rickets survey
D. 1,25 dihydroxy vitamin D level
E. No further laboratory tests

Suggested correct Answer: E. Some clinicians will further fractionate the alkaline phosphatase, to determine whether it came from bone, intestine, or liver. High bone alkaline phosphatase results from high osteoclast activity and bone turnover, such as with calcium or vitamin D deficiency. High intestinal alkaline phosphatase has been reported in intestinal disease, such as intestinal ulcers. High liver alkaline phosphatase comes from cholangiocyte injury and points to bile duct disease.

High alkaline phosphatase with no other clinical signs, however, often leads to a long course of lab work and other tests with little diagnostic yield (i.e. X-rays, CT scans, liver biopsies, endoscopies). A few case reports have been published on the issue, showing that alkaline phosphatase levels

eventually return to normal with time. Other names for this phenomenon are benign transient hyper-alkaline phosphatasia or benign transient hyperphosphatasemia. It is also known as "Ulysses syndrome," reflecting the long journey of diagnostic tests leading the clinician to no concrete diagnosis.

Question 4:
Mutations in the cystic fibrosis transmembrane regulator (CFTR) may cause cystic fibrosis. The protein is present on the apical surface of epithelial cells and regulates chloride secretion. Which of the following is the best evidence that the CFTR is a c-AMP dependent protein kinase A activated chloride channel?

A. Demonstration of c-AMP regulated chloride channels after transfection of the CFTR gene into cells lacking CFTR
B. The presence of mutations in the CFTR in patients with elevated sweat chloride concentrations
C. Structural similarity of the CFTR to other ATP Binding Cassette (ABC) membrane transporters known to regulate ion transport
D. Failure of heat stable enterotoxin to stimulate chloride secretion in cell with a mutation in the CFTR
E. Demonstration of message for the CFTR in lung, pancreas, and biliary epithelium

Suggested correct Answer: A. This is a basic science question about experimental method. One time-tested way to study a gene or protein is to introduce it into cells without it, and then study what changes occur in the cell. In this case, introducing CFTR into a cell line without CFTR will allow the scientist to manipulate the system to answer specific questions about CFTR.

One way to diagnose CF is the sweat test. This technique works because children with CF have high concentrations of sodium and chloride in their sweat. They have higher concentrations of chloride because the CFTR channel is used to reabsorb chloride from sweat as it passed through the ducts to the skin. In CF patients, the CFTR works improperly and chloride cannot be reabsorbed, leading to more chloride deposited in sweat.

Question 5:
A 2 year old boy with biliary atresia underwent liver transplantation for biliary atresia 6 weeks ago. He was CMV seronegative at transplantation and received a left lateral segment graft from his mother who was CMV seropositive. He has developed low-grade fever and vomiting. He is referred to you for evaluation. He is taking cyclosporine, prednisone 10 mg each day and no antiviral medications.

Based on the clinical picture, which of the following would be the most specific test to confirm the presence of active CMV disease?

A. Positive urine for CMV antigen
B. Blood sample which is CMV PCR positive
C. Rise in CMV IgG titers
D. Presence of increased CMV IgM titers
E. In situ hybridization positive for CMV in a gastric body biopsy

Suggested correct answer: E. CMV infection in normal hosts is usually inconsequential or consists of mononucleosis-like symptoms with mild hepatitis. On the other hand, CMV infection in immunosuppressed hosts (such as those status-post liver transplantation) can be devastating. CMV may come from the new organ, transfused blood, or reactivation of latent infection. It can lead to a clinical presentation similar to that of rejection, and if allowed to persist may progress to liver failure.

To diagnose CMV disease, the best test is to identify CMV in serum, urine, or biopsy tissues. In this case, the child has signs of CMV gastritis (vomiting), so identifying CMV is stomach tissue would confirm the diagnosis. Urine positive for CMV antigen and PCR positive serum documents infection somwhere in the body, but does not confirm or refute CMV causing GI symtpoms. Furthermore, PCR is more sensitive than specific, and may be positive in patients with latent CMV with no disease. Antibody tests can be confusing, because of maternal contributions (in <18 months) as well as antibodies transferred in transfusions. Treatment for CMV includes IV ganciclovir until the infection subsides, followed by PO valganciclovir.

Question 6:
Which of the following statements regarding transient lower esophageal sphincter relaxations (TLESRs) is false?
A. TLESRs represent the major mechanism by which acid reflux occurs.
B. TLESRs reduce or obliterate the resting pressure of the lower esophageal sphincter.
C. Gastric distension increases the frequency of TLESRs
D. TLESRs cannot be induced by pharyngeal stimulation.

Suggested correct Answer: D. The LES is tonically contracted at rest, a process mediated by vagal cholinergic and some sympathetic fibers. The LES relaxes with the esophageal peristaltic wave. The LES also relaxes with TLSERs which may be due to increased NO production from iNOS. TLSERs are thought to be the mechanism allowing GER to occur, and their frequency increases with gastric distension. Simulating the pharynx, as in swallowing, also promotes LES relaxation.

Question 7:
In a double-blinded placebo controlled trial involving 200 patients, investigators observed that drug A did not improve pulmonary function in children with cystic fibrosis. The change in pulmonary function was normally distributed for both groups. The investigator is concerned that that drug A improved pulmonary function but that the effect was not detected.

If the investigator is correct, which of the following is the most likely explanation for the observation:

A. Type 1 error
B. The analysts failed to use non-parametric analysis to compare the groups
C. Type II error
D. The patients in the study changed eating behavior while on drug A
E. The analysts failed to use Chi-square analysis to compare the groups

Suggested correct Answer: C. There are two types of common errors, type I and type II. Type I errors occur when an association is found that does not really exist (false positive), whereas type II errors occur when an association is not found when one really does exist (false negative). In epidemiological terms, if a null hypothesis is incorrectly rejected when it is in fact true then a type I error occurs. When a null hypothesis is not rejected despite it being false a type II error occurs. Alpha is used to denote type I errors, whereas Beta is used to denote type II errors.

Question 8:
A 17 year old young man presents with a 3 year history of dysphagia. There has been no weight loss, and the patient's nutrition is good. The findings of upper endoscopy and esophageal manometry are consistent with a diagnosis of achalasia. Which of the following statements is true?

A. The risk of esophageal perforation with pneumatic dilation is about 1 in 500.
B. Esophageal dilation must be repeated in fewer than 10% of patients.
C. Heller myotomy affords a good to excellent response in more than 80% of cases.

D. Acid reflux is more common after pneumatic dilation than after surgical myotomy.

Suggested correct Answer: C. Achalasia is a rare disorder in children, resulting in improper relaxation of the lower esophageal sphincter. One proposed mechanism is less NO formation, leading to tonic LES contraction. On physical exam, patients have trouble swallowing solids and eventually liquids. The classic manometry findings are: (1) poor esophageal peristalsis, and (2) no LES relaxation upon swallowing. The first finding is always present, whereas the second finding may be present to variable degrees. Other diagnostic modalities used are barium swallow study (proximal dilations present) and endoscopy (to rule out infection, carcinoma, and leiomyoma).

Therapies commonly used (with increasing success) include: (1) calcium channel blockers, (2) Botox injections, (3) pneumatic dilation, and (4) Heller myotomy. Pneumatic dilations can be done by a gastroenterologist, though they pose particular challenges. Technically they are difficult, because they require manipulations that cut the muscular layer but leave the mucosa intact. The incidence of perforation can be as much as 5%, and most patients require repeat dilation over time. Acid reflux is a common in all procedures that open the LES, and sometimes reflux control is attempted with fundoplication following myotomy.

Question 9:
Cytokines act as messengers to regulate immune responses. One of the mechanisms by which the calcineurin inhibitors, tacrolimus and cyclosporin, promote allograft survival following liver transplantation is inhibition of transcription of the cytokine, interleukin 2. Which of the following is the dominant mechanism by which interleukin 2 enhances the immune response to foreign tissue?

A. Promotes activation of macrophages
B. Promotes clonal expansion of activated T-cells
C. Promotes clonal expansion of plasma cells
D. Promotes activation of eosinophils
E. Promotes clonal expansion of B-cells

Suggested correct Answer: B. IL-2 binds to the IL-2 receptor and promotes T-cell expansion. IL-2 transcription is mediated by NF-AT (nuclear factor of activated T-cells), which moves into the nucleus and directs transcription only after it is dephosphorylated. Calcineurin is the molecule that accomplishes this dephosphorylation in the cytoplasm, and calcineurin activation occurs only through an increase in intracellular calcium secondary to T-cell receptor activation. Both tacrolimus and cyclosporine form complexes with different T-cell proteins. These complexes in turn bind to calcineurin and inhibit its dephosphorylation activity, even in the presence of high intracellular calcium levels.

Question 10:
A four year old boy presents to you with a history of bloody diarrhea. He was well until one week ago when he developed bloody diarrhea while on vacation with his family. His family had been traveling by car from California to Michigan and stopped at several fast-food restaurants. He was seen in a local emergency room and treated empirically with amoxicillin. His symptoms have persisted. Today, he appears pale and is listless. His serum hemoglobin is 7.8 and his white blood count is 14,000. His stool contains blood and mucus. Which of the following is the most appropriate next step in managing this child?

A. Stool culture and sensitivity
B. Treatment with Trimethoprim-Sulfa
C. Observation and reevaluation tomorrow
D. Colonoscopy

E. Complete blood count, renal group and urinalysis

Suggested correct answer: E. This patient has signs of hemolytic uremic syndrome (HUS), a vasculitis characterized by microangiopathic anemia, thrombocytopenia, and uremia. In children the majority of cases follow a diarrheal illness caused by Shiga-like toxin, usually from E. coli type O157:H37. The bacteria cause symptoms through 2 mechanisms: (1) local effacement of villi, leading to an early watery diarrhea, and (2) toxin secretion, producing damage in epithelial and microvascular endothelial cells throughout the body including the intestines and kidney, leading to renal damage and bloody diarrhea. Damage to endothelial cells results in localized clotting, which traps platelets and shears passing red blood cells. Coagulation times are normal in HUS.

Stool cultures should be done for public health reasons, especially in the cases of severe bloody diarrhea. However, the most appropriate immediate step is to confirm the diagnosis through a CBC and smear, and monitor for ongoing kidney damage (HUS is a leading pediatric cause of acute renal failure in many countries). Antibiotic treatment is considered a contraindication, because lysis of bacteria may release more Shiga-like toxin and worsen the vasculitis.

Question 11:
A 14 year old African-American young woman is referred for evaluation of asymptomatic elevation of serum transaminases. She has not received blood transfusions. She is not taking medications. Examination shows that her body mass index is 34. She is anicteric and has no signs of portal hypertension but has prominent acanthosis nigricans in her neck folds and axilla.

Laboratory evaluation

Hepatitis B surface Antigen	Negative
Hepatitis B surface antibody	Positive
Hepatitis C antibody	Negative
AST	100 IU/l
ALT	120 IU/l
Total serum bilirubin level	0.4 mg/dl
Serum immunoglobulin level	Normal

If a liver biopsy were performed, the most probable histologic findings would be:

A. Mixed portal infiltration with necrotic hepatocytes at the limiting plate
B. Macrovesicular hepatic steatosis with mild portal inflammation
C. Microvesicular hepatic steatosis
D. Cirrhosis with portal inflammation and Mallory bodies
E. Normal histology

Suggested correct answer: B. This patient likely has non-alcoholic fatty liver disease (NAFLD). The term encompasses a wide variety of liver pathology, from steatosis to steatohepatitis to cirrhosis. The pathophysiology of this disease centers around insulin resistance, which is probably present in this obese adolescent with acanthosis nigricans. The diagnosis of NAFLD is suggested by hyperglycemia, hyperlipidemia, elevated transaminases (ALT>AST), and increased echogenicity on liver ultrasound. A recent article on the topic concluded that normal ALT ranges at most children's hospitals are not sensitive for abnormal ALT levels, and that an ALT greater than 25 for boys and 23 girls should raise suspicion for liver disease.

The gold-standard diagnosis for NAFLD is (1) absence of other liver disease (i.e. infectious, autoimmune, toxin, or genetic causes, and (2) liver biopsy showing characteristic NAFLD findings.

The three most consistent biopsy findings are: i) macrovesicular > microvesicular steatosis, ii) lobular inflammation consisting of neutrophils and lymphocytes ("mixed"), and iii) hepatocyte ballooning. Fibrosis (portal > perisinusoidal in children) and glycogenated nuclei may also be present. In severe cases, extensive fibrosis leading to cirrhosis is present.

Treatment for NAFLD is evolving. Weight loss has proven to be beneficial. Other therapies being tested include insulin sensitizing agents (i.e. metformin), anti-oxidants to prevent oxidative damage (i.e. Vitamin E), and N-acetylcysteine, among many others. Liver transplant for patients with NAFLD-related cirrhosis has been performed, though fatty changes can reoccur in the transplanted organ. Bariatric surgery is also a potential new therapy, because it often improves insulin sensitivity which may in turn treat the pathophysiology underlying NAFLD.

Question 12 and 13:

A 19-month-old female infant came to the emergency room with a 5-day history of intermittent abdominal pain and diarrhea. She has been passing 8 to 10 brown, watery stools a day. There was no blood or mucus in her stools. She had vomited twice (once at the onset of the illness and on the day of presentation), and the vomitus was nonbloody and nonbilious. She had no fever or other systemic symptoms. There was no prior antibiotic use. Her mother had diarrhea for 2 days at the onset of her illness.

Physical examination results were within normal limits except for right lower quadrant tenderness. No masses were palpated. Rectal examination results were normal, but her stool was guaiac positive. Laboratory study results included a hemoglobin concentration of 11.9 g/dL and a leukocytosis of 17,400/mm ^{3} with a normal white blood cell differential count. Renal profile and urinalysis results were normal. Her stool was negative for leukocytes but positive for *Clostridium difficile* toxin and antigen. Abdominal radiographs were obtained (Fig 1), and when she continued to have significant abdominal pain, an abdominal computed tomography was requested (Fig 2).

Figure 1:

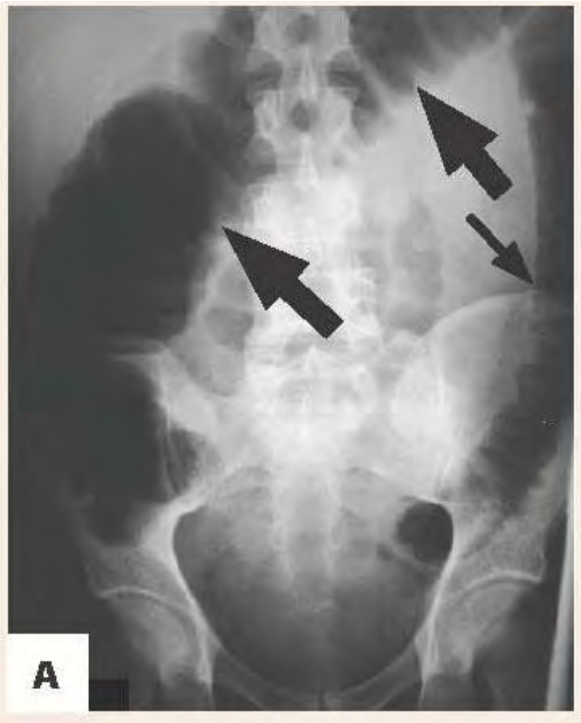
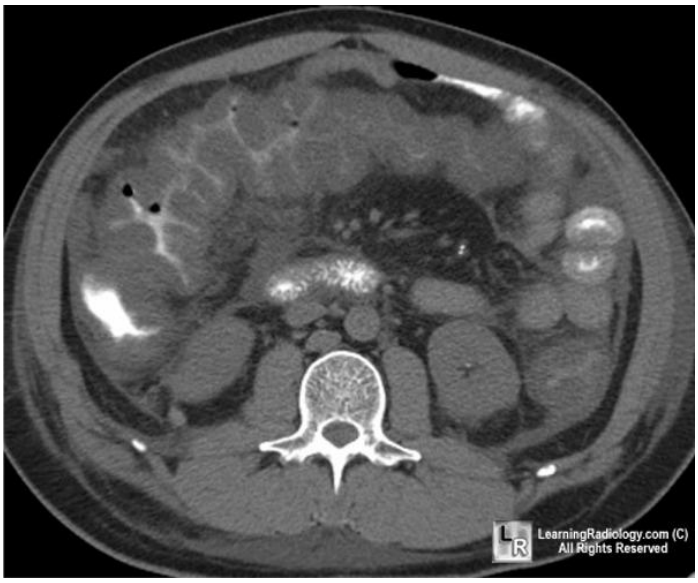


Figure 2:



12. Based on the findings on the imaging studies what is your diagnosis?

A. Pseudomembranous colitis
B. Ileocolonic intussusception
C. Lymphoma
D. Colonic polyp
E. Distal intestinal obstruction syndrome

13. What is the next appropriate step in the treatment of the patient?

A. Surgical resection
B. Colonoscopy
C. Air enema
D. Sweat chloride
E. Oral Flagyl

Suggested correct answers: A, E. Clostridium difficile is a gram-positive anaerobic bacillus that can produce an infectious colitis. This usually happens after antibiotics are administered, which allows C. difficile to flourish by clearing the bowels of normal flora. Infections are also commonly seen in patients receiving anti-neoplastic therapy. C. difficile elaborates Toxin A (disease causing) and Toxin B, which are identified in ELISA (protein) or PCR (gene) assays. C. difficile usually causes a mild limited watery diarrhea, but long-term diarrhea and/or bloody diarrhea can also occur. In pseudomembranous colitis, the most severe form of C. difficile infection, high fever, leukocytosis, and hypoalbuminemia are present. Imaging shows boggy, thickened areas of bowels.

Treatment consists of stopping causative antibiotics and/or starting anti-C. difficile antibiotics. Oral flagyl is the first line choice, followed by oral vancomycin. IV Flagyl is also acceptable, though IV vancomycin is thought to be ineffective because it does not penetrate into the gut lumen. Surgery may be needed in especially severe cases of pseudomembranous colitis.

Question 14:
The colon is able to absorb each of the following EXCEPT:
A. Monosaccharides
B. Acetate
C. Propionate
D. Butyrate

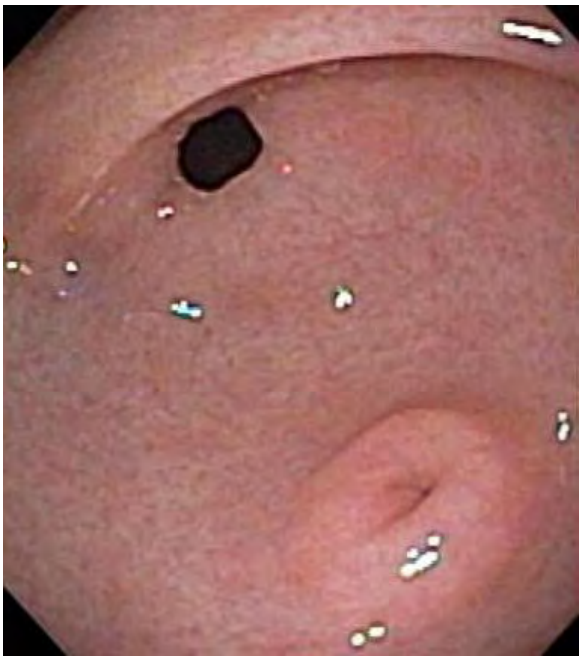
Suggested correct answer: A. The colon's best known functions are water absorption and fecal storage. However, the colon is also an enormous reservoir of gut bacteria. Bacteria metabolize carbohydrates that make it past the small intestine, including digestion-resistant starches, excess fructose and lactose, and poorly digestible monosaccharides such as lactulose, sorbitol, and sucrolose. Bacteria ferment these sugars, producing gas and short-chain fatty acids such as acetate, propionate, and butyrate as a by-product. These short-chain fatty acids in turn are absorbed by colonocytes and may have numerous benefits including trophic properties for enterocytes.

Monosaccharides are absorbed in the small intestine, and are the only form in which sugars can be absorbed. Salivary and pancreatic amylase digests starch into oligosaccharides, which are further digested by brush border enzymes into the monosaccharide glucose. The brush border enzyme lactase digests lactose into the monosaccharides glucose and galactose, whereas the brush border enzyme sucrase digests sucrose into the monosaccharides glucose and fructose. The monosaccharides then enter enterocytes through channels, because they are too big for passive diffusion. Glucose and galactose are co-transported with sodium driven by a sodium gradient. Fructose has its own channel that operates via diffusion from high fructose (lumen) to low fructose

(inside the cell) gradients. The Na-glucose transporter on villi is the bases for oral rehydration solution containing 2 molecules of sodium for every molecule of glucose. The diffusion-driven fructose channel explains why children who drink too much juice have excessive fructose that cannot enter enterocytes, leading to high fructose in the lumen and subsequent osmotic diarrhea (toddler's diarrhea).

Question 15:
A 2-year-old boy was referred to the Pediatric Gastroenterology Unit because of a short period of vomiting, dysphagia, and decreased appetite. He had been operated at birth for an esophageal atresia; the postoperative course and recovery had been uneventful. He remained healthy until the present episode of acute vomiting and dysphagia, which began 48 hours before referral to our unit. Physical examination was unremarkable. Complete blood count and sedimentation rate were normal. Contrast radiography of the upper gastrointestinal tract ruled out anastomotic esophageal stricture but strongly suggested the presence of a foreign body obstructing the lower esophagus. The child underwent esophagogastroscopy under general anesthesia. At esophagogastroscopy, no foreign body was present, but an ulcerative lesion of the lower esophageal region was noted, corresponding to the location of the presumed esophageal foreign body before spontaneous migration. Esophagoscopy was followed by a systematic examination of the stomach, pylorus, and duodenum. Surprisingly, a 10-mm diameter lesion was noted in the lumen of the prepyloric region (Fig 1); the surrounding mucosa was normal. Biopsies of this lesion were performed.

Figure 1



This lesion most likely represents:

A. Gastric leiomyoma
B. Heterotopic pancreas
C. Peptic ulcer
D. Gastric adenocarcinoma
E. Gastric hyperplastic polyp

Suggested correct answer: B. Heterotopic pancreas, also known as a pancreatic rest, is a congenital anomaly characterized by pancreatic tissue in ectopic locations. The defect results from abnormal migration of pancreatic tissue. The most common site of pancreatic rests is in prepyloric gastric antrum, though numerous other sites have been reported such as the duodenum, ileum, gallbladder, common bile duct, and splenic hilum. There are a few case reports of distal esophagus pancreatic rests in patients with isolated esophageal atresia.

Pancreatic rests are usually asymptomatic and found incidentally. They appear as a round, smooth submucosal mass with a central crater. They can be symptomatic when large (>1.5 cm), leading to abdominal pain, dyspepsia, and bleeding. Pancreatitis has also been described in pancreatic rests.

Neoplasms such as gastric adenocarcinoma usually do not occur in such young patients. Gastric polyps commonly come in two varieties: (1) parietal cell hyperplasia secondary to PPI use, and (2) hamartomas such as those in Peutz-Jehger syndrome. Reflux and strictures related to reflux may occur after repair of esophageal atresia, because an intact LES sphincter is not present. However, stomach protective mechanisms are functional and there is no increased incidence of peptic ulcers.

Question 16:
A one month old infant boy presents to you with complaints of persistent jaundice. The infant was a term product of an unremarkable pregnancy. Since going home, he has been breast fed and has nursed well. His mother has a prominent forehead with deep set eyes. Examination of the infant shows an icteric infant boy. He is afebrile. Heart examination shows an III/VI holosystolic murmur. His liver is palpable 2 centimeters below the right costal margin in the midclavicular line and he does not have ascites. An abdominal ultrasound showed a small gall bladder. Pertinent laboratory studies include:

Alkaline phosphatase	650 IU/L
Total serum bilirubin	7 mg/dl
Conjugated serum bilirubin	6.2 mg/dl
AST	95 IU/L
γ-glutamyl transpeptidase	650 IU/L
Serum albumin	3.6 mg/dL

Which of the following is the most likely diagnosis?

A. Biliary atresia
B. Alagille Syndrome
C. Galactosemia
D. Sclerosing cholangitis
E. Cystic fibrosis

Suggested correct answer: B. This patient has neonatal cholestasis. The differential of this condition is broad, and includes infectious, genetic, metabolic, and toxin causes. Biliary atresia must be ruled-out, because Kasai operations performed earlier (<45 days of life) may have the best outcome. Galactosemia, in which the child is unable to convert galactose to glucose secondary to deficiencies in one of 3 enzymes, leads to high serum galactose levels. It presents with weight loss, diarrhea, vomiting, lethargy, positive reducing substances (i.e. galactose) in the urine, and, commonly, E. coli sepsis. CF can present as neonatal cholestasis but cardiac findings are not characteristic. Neonatal sclerosing cholangitis is a rare entity that presents histologically like biliary atresia. It differs clinically because in sclerosing cholangitis the stools are pigmented. Sclerosing cholangitis is best diagnosed by ERCP.

In this patient, the combination of cardiac findings (usually pulmonary stenosis), cholestasis, and family history points to Alagille's syndrome. The disorder is characterized by paucity of intrahepatic/interlobular bile ducts. It is caused by defects in the Notch signaling pathway, which is critical for proper cholangiocyte differentiation. The most common mutation in Alagille's syndrome is in Jagged 1, the ligand for the Notch receptor. Because the Notch pathway is used in many developmental processes, Alagille's syndrome patients can have numerous extra-hepatic phenotypes. These include cardiac, skeletal (i.e. butterfly vertebrate), ocular (posterior embryotoxin), vascular (intracranial bleeding), and renal defects (in light of all these issues, pruritis from cholestasis is still the complaint most often made by patients). For still unclear reasons, the penetrance of Notch mutations varies, so that individuals in the same family with the same mutation may be affected to different degrees.

Question 17:
A 14 year old young man is referred for evaluation of abdominal pain. He had a history of gastroesophageal reflux disease that was refractory to medical therapy. He underwent a laparoscopic fundoplication 6 months ago. He now complains of postprandial abdominal pain and distension. The pain is not associated with vomiting, diarrhea, dysphagia or heartburn.

Which of the following is the most-likely cause for his symptoms?

A. Non-ulcer dyspepsia
B. Biliary tract dyskinesia
C. Recurrence of gastroesophageal reflux disease
D. Gas-bloat syndrome
E. Eosinophilic esophagitis

Suggested correct answer: D. The fundoplication operation takes proximal portions of the stomach and wraps it around the lower esophagus to recapitulate LES tone. In the past it was a mainstay for medication-resistant reflux. Subsequent studies, however, have shown that a sizeable number of children must return to PPI use within a few years of the surgery. Other complications include "gas bloat syndrome," which occurs when stomach gas cannot escape through the esophagus. Symptoms include abdominal distension, abdominal pain, wretching, and gagging.

Question 18:
All of the following statements regarding familial pancreatitis are true EXCEPT:

A. Pattern of inheritance is autosomal recessive
B. The mutated gene encodes cationic trypsinogen
C. Males and females are equally affected
D. Usually presents before 15 years of age
E. Patients with this disorder have a 50-fold increased risk of developing pancreatic cancer

Suggested correct answer: A. Familial pancreatitis involving the cationic trypsinogen gene (PRSS1) is autosomal dominant. Mutations cause trypsinogen to autoactivate in acinar cells, producing trypsin which in turn activates other pancreatic proenzymes. Together, the active enzymes collectively destroy pancreatic tissues (normally, trypsinogen is activated only in the intestinal lumen by enterokinase on the brush border). Other genetic causes of pancreatitis include mutations in the serine protease inhibitor Kazal type 1 (SPINK-1). Recessive mutations in the CFTR gene can also lead to chronic pancreatitis, by thickening the composition of secretions in the duct thus causing backflow into the pancreas. Cases of hereditary pancreatitis usually present before age 10, and patients with hereditary pancreas have a much higher risk for developing pancreatic cancer, presumably due to many years of chronic inflammation.

Question 19:
A 17-year-old girl is referred to you for evaluation of persistent episodic burning epigastric pain. An adult gastroenterologist previously saw her. She had a history of using non-steroidal anti-inflammatory drugs once each week for headaches. Serology for H. pylori was positive and esophagogastroduodenoscopy showed a duodenal ulcer. She was given a 14-day treatment of omeprazole and amoxicillin. Her symptoms have persisted. A stool antigen test for H. Pylori performed more than 4 weeks after treatment was positive.

Which of the following is the most likely cause for her persistent symptoms?
A. Unrecognized esophagitis
B. Failure to adhere to the medical regimen
C. Primary resistance of H.pylori to amoxicillin
D. Failure to use an effective treatment for H.pylori eradication
E. Peptic disease due to NSAID

Suggested correct answer: D. This patient's symptoms could be attributed to many causes, including H. pylori gastritis, peptic ulcer disease, and eosinophilic disease. Given the positive H. pylori test and duodenal ulcer, H. pylori disease is the most likely. H. pylori is a gram negative rod. Stool antigen testing is the noninvasive diagnostic test of choice (serology, as performed in this case, is not recommended, because standard values have never been established in children). Treatment consists of a PPI plus 2 antibiotics, such as amoxicillin and clarithromycin. Antibiotic resistance has been identified, and current guidelines recommend susceptibility testing only if the first round of treatment fails to eradicate the organism.

One important area of active research is determining when to test children for H. pylori. Many children are carriers (some populations have infection rates >50%), so results may return positive even if H. pylori is not responsible for the child's symptoms. H. pylori should be tested when ulcers are found endoscopically, in iron deficiency refractory to therapy, in patients with MALT lymphoma, in those with a family history of gastric cancer, and when checking the success of eradication therapy. H. pylori should not be checked in patients with recurrent abdominal pain/non-ulcer dyspepsia, GERD, and asymptomatic children. Practitioners who discover H. pylori incidentally (i.e. during foreign body removal, because a primary care physician ordered the test) must make a decision on whether or not to treat. Many practitioners will treat, given the H. pylori-associated long terms risks of MALT lymphoma and gastric cancer.

Question 20:
A 22-month-old boy is referred for evaluation of poor growth and chronic diarrhea since birth. His stools are large and foul-smelling. Stool cultures and examination of stool for ova and parasites has been negative. His past medical history is remarkable for recurrent otitis media. His physical examination shows that his weight and height are both below the 5th percentile for age. His abdomen is protuberant. A sweat chloride was normal. His serum trypsinogen is low. Abdominal ultrasound shows a large echogenic pancreas.

Which of the following laboratory abnormalities is most likely to be detected in this boy?

A. Increased stool alpha-1 antitrypsin levels
B. Elevated anti-endomysial antibody titers
C. Neutropenia
D. Peripheral eosinophilia
E. Macrocytic anemia

Suggested correct answer: C. This patient shows evidence of pancreatic insufficiency, including poor fat absorption, failure to thrive, low serum trypsinogen, and presumably low fecal elastase. The negative sweat test argues against CF, making Shwachman-Diamond syndrome the most likely diagnosis. Shwachman-Diamond syndrome leads to improper development of acinar cells (vs. pancreatic duct problems in CF). Pancreatic tissue is replaced with fatty tissue, and pancreatic lipomatosis produces an echogenic image on ultrasound. Treatment includes pancreatic enzyme and fat soluble vitamin replacement. With time, pancreatic function does appear, with half of the patients demonstrating pancreatic sufficiency by age 4.

Shwachman-Diamond syndrome also has bone marrow and skeletal abnormalities. Bone marrow problems include recurrent neutropenia, anemia, thrombocytopenia, and possible leukemia. Skeletal problems involve long bones and the thoracic cage. The inheritance is autosomal recessive, in an incompletely characterized gene names SBDS. The product of this gene is likely to play a fundamental role, because it is present in all archaea and eukaryotes. Another syndrome characterized by pancreatic insufficiency secondary to fatty replacement of the pancreas is Johanson-Blizzard syndrome. This syndrome comes with multiple congenital abnormalities (deafness, imperforate anus, urogenital malformations, dental anomalies, "beak-shaped" face) as well as significant endocrine involvement (hypothyroidism, panhypopituitarism, diabetes, growth hormone deficiency).

Question 21:
A two year old boy with biliary atresia presents with anemia and hematemesis. He underwent a hepatic portoenterostomy when he was 5 weeks old. Today, he is pale. His abdomen is non distended but he has prominent abdominal wall vessels and his spleen is palpable 5 cm below the left costal margin. After hemodynamic stabilization, you plan to perform upper endoscopy and sclerotherapy. Under which of the following conditions is antibiotic prophylaxis recommended?

A. The patient has aortic stenosis
B. The patient has a history of spontaneous bacterial peritonitis
C. The patient has a history of recurrent cholangitis
D. The patient has multiple dental caries
E. The patient has an nasojejunal feeding tube

Suggested correct answer: A. Prophylactic sclerotherapy therapy versus watchful waiting in patients with portal hypertension and esophageal varices is an active debate (banding is impractical in young children, because the equipment needed for banding is too large). Sclerotherapy has been shown to reduce to incidence of first-time variceal bleeds. However, these patients also had a higher incidence of gastric variceal bleeding if gastric varices were present, presumably secondary to congestive hypertensive gastropathy. Survival rate was not affected by prophylactic sclerotherapy.

Sclerotherapy can lead to transient bacteremia, so patients with heart disease are at increased risk. The patients that qualify for prophylactic antibiotics have recently been modified. High risk patients should receive antibiotics, including those with a prosthetic valve, history of endocarditis, complex cyanotic heart disease, and systemic-pulmonary shunts. Aortic stenosis does not fit into this category, so antibiotic therapy will be at the discretion of the endoscopist.

In cases of active bleeding, prophylactic antibiotics for all patients are warranted. Prophylactic antibiotics have numerous benefits: i) protects patient from bacteremia during the procedure, ii) may prevent infection from introducing endoscope, and iii) treats infections that may have caused increased portal pressures and promoted onset of the bleed.

Question 22:

A 22-month-old boy is referred for evaluation of chronic diarrhea. He has had persistent diarrhea following an episode of acute gastroenteritis 4 months ago. His stools are loose and watery and of large volume. He has never passed gross or occult blood per rectum. Despite his diarrhea, he has grown normally and remains active. Stool cultures and examination of stool for ova and parasites has been negative. Because of his diarrhea, his parents stopped giving him milk and he currently drinks more than 1 liter each day of juice or Kool-aid. His physical examination is normal. Which of the following is the cause for his chronic diarrhea?

A. Giardiasis
B. Excessive carbohydrate intake
C. Lactose intolerance
D. Celiac disease
E. Inflammatory bowel disease

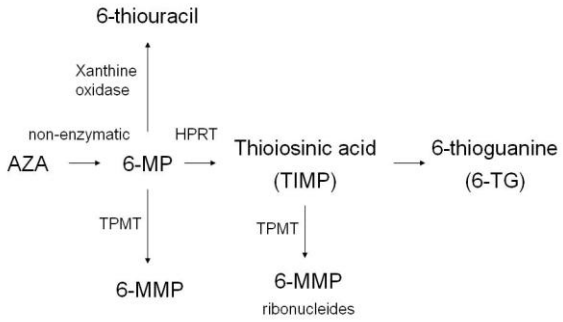
Suggested correct answer: B. This patient has "toddler's diarrhea," an osmotic diarrhea from excessive sugar intake. Clues to the diagnosis include normal growth and excessive juice intake. Toddler's diarrhea occurs with increased luminal sucrose. In the small intestine, sucrase digests sucrose into glucose and fructose. Glucose is readily absorbed through sodium-glucose channels, in a process that depends on sodium gradients. Fructose, on the other hand, is absorbed by diffusion through fructose channels. When intracellular fructose levels reach a certain point, more fructose cannot diffuse intracellularly and instead remains in the intestinal lumen. This excess fructose becomes an osmotic force, drawing water into the lumen and leading to a watery diarrhea. The patient's symptoms will improve once juice intake is returned to normal.

Question 23:
A 15-year-old girl with steroid-resistant Crohn's disease who is in remission has been started on mercaptopurine (dose 1.5 mg/kg/day). You find that she has decreased activity of the enzyme, thiopurine methyltransferase (TPMT) (the enzyme responsible for a major alternative catabolic pathway of mercaptopurine).

For which of the following is the patient at risk due to decreased TPMT activity

A. Relapse of Crohn's disease
B. pancytopenia
C. opportunistic infection
D. bacterial overgrowth
E. sclerosing cholangitis

Suggested correct answer: B. 6-MP is an antimetabolite initially developed to destroy immune cells in the setting of leukemia. It is converted to a purine analogue that disrupts DNA replication. At lower doses, it is used as immunosuppressive therapy in IBD. Azathioprine is converted to 6-MP non-enzymatically. 6-MP then has 3 fates: i) 6-thiouracil (inactive), ii) 6-MMP (hepatotoxic), and iii) 6-TG (active immunosuppressive compound). TPMT, or thiopurine methyltransferase, determines how much 6-MP is converted away from the active metabolite 6-TG to 6-MMP. Patients with low TPMT activity, or those with mutant alleles, produce excess amounts of 6-TG leading excessive immune suppression and bone marrow failure. For this reason, TMPT activity or genotype is often tested before administering 6-MP. Other important side effects of 6-MP include pancreatitis, hepatotoxicity (presumably in part from 6-MMP metabolites), and possible hematopoetic neoplasm.



Question 24:
A 16-month-old boy received a cadaveric liver transplant at age 10 months for biliary atresia. His immunosuppressive medications are tacrolimus and prednisone. He presents to you with complaints of diarrhea and intermittent fever. A colonoscopy shows findings consistent with post-transplant lymphoproliferative disease (PTLD) and biopsy of the lesions shows predominantly lymphocytic infiltrate. Which of the following is the best way to confirm the diagnosis (EBV associated PTLD)?

A. Quantitation of peripheral blood EBV viral load by polymerase chain reaction
B. Qualitative identification of peripheral blood EBV by polymerase chain reaction
C. Identification of B-cells in the biopsy by monoclonal antibody against CD20 (a specific marker for B-cell)
D. Flow cytometry of blood to identify activated B cells
E. In situ hybridization of biopsy with EBER-1 probe (labels EBV-encoded RNA in infected cells)

Suggested correct answer: E. PTLD is a post-transplant complication related to EBV infection and immunosuppression. When a child has been infected with EBV prior to transplant, he or she may do better on minimal post-transplant immunosuppression to prevent EBV reactivation while also preventing rejection. More often, children acquire EBV infection either i) during transplant from the donor or ii) after transplant while being heavily immunosuppressed. EBV titers can be accurately followed using serum EBV PCR measurements.

PTLD occurs when EBV-infected B cells proliferate excessively, usually (but not always) in the setting on increased EBV PCR titers. There are at least two broad steps to this process. First, viral genes overtake cellular machinery and promote polyclonal proliferation (ultimately, the fittest B cell clone is selected and the lesion becomes monoclonal). Second, immunosuppression impairs T cells, which normally check B cell proliferation. The final result is neoplastic proliferation of B cells, diagnosed through histology using two criteria: i) evidence of lymphoproliferation on tissue biopsy, and ii) presence of EBV (i.e. EBV RNA detected by in situ hybridization) in tissue.

Clinically, PTLD presents with mononucleosis-type symptoms, isolated lymph node involvement, and/or lymphocyte invasion of tissues (liver, gut, iris). Gut PTLD presents with diarrhea, GI bleeding, and weight loss. Treatment includes reduced immunosuppression (at the risk of inducing rejection), anti-virals, surgical excision of the lesion, localized radiation therapy, chemotherapy, monoclonal antibodies against the B cell antigen CD20, interferon therapy, and T-cell therapy.

Question 25:
A 6 year old boy is referred to you for post-prandial abdominal pain of 9-12 months duration. He has no associated vomiting, heartburn, dysphagia, or diarrhea. His appetite is decreased. Past medical history reveals that he found to have a Stage II Wilm's tumor at age 2 years. He was treated with

resection and received 3000 rads to his abdomen. Examination shows no evidence of malnutrition. He has mild epigastric and right lower quadrant tenderness to deep palpation.

Laboratory evaluation	
Hemoglobin	14 g/dL
Serum amylase	Normal

Which of the following would be the most appropriate next step?

A. CT scan of the abdomen
B. Esophagogastroduodenoscopy with small intestinal biopsy
C. Hydrogen breath test
D. Upper GI contrast study with small-bowel follow through
E. Colonoscopy with biopsy

Suggested correct answer: A. Radiation enteritis is common after radiation treatment to the intestines in pediatric patients. Radiation treatment creates free radicals from water, which in turn damage neoplastic and normal tissue. Acute changes include edema and inflammation, producing abdominal pain, diarrhea, and tenesmus. Chronic changes are due to obliterative arteritis that causes ischemia, leasing to fibrosis, stricture, and/or ulceration. Patients may have dysmotility, bacterial overgrowth, obstruction, altered absorption, in bleeding (with colonic involvement).

The first step in diagnosing the patient's GI problem is to obtain a CT image to look for signs of stricture/obstruction vs. tumor recurrence (though recurrence of stage I and II Wilm's tumor is uncommon). An UGI/SBFT may then be used to better evaluate the caliber of the small bowel and the presence of strictures. Colonoscopy would be performed if there were concerns for colonic disease, such as proctitis.

Question 1:
A 3-month-old boy has failure to thrive and chronic diarrhea. Stools are pale, foul-smelling, and greasy. Physical examination reveals a wasted, nonicteric boy who has coarse breath sounds and rhonchi. The abdomen is distended and tympanitic. The liver has normal texture and is palpable at the right costal margin.

Of the following, the MOST likely diagnosis is:

A. biliary atresia
B. celiac disease
C. congenital lactase deficiency
D. cystic fibrosis
E. Schwachman-Diamond syndrome

Suggested answer: D. Cystic fibrosis has a number of GI presentations. Meconium ileus at birth is pathognomonic for the disease. Most infants have some degree of pancreatic insufficiency, clinically leading to diarrhea (steatorrhea, secondary to fat malabsorption) and failure to thrive. Some infants also develop cholestasis from inspissated bile which progresses to chronic liver damage. Finally, older children and adults can develop intermittent small bowel obstruction, called distal intestinal obstructive syndrome (DIOS) or "meconium equivalent."

Biliary atresia would present with jaundice and pale stools. Celiac disease only presents after exposure to gluten, which occurs after the child starts taking foods. Congenital lactase deficiency is a rare cause of sugar malabsorption, which is not associated with steatorrhea or pulmonary problems. Schwachman-Diamond syndrome is a rare recessive condition characterized by: i) pancreatic insufficiency, leading to steatorrhea; ii) hypocellular bone marrow with some or all cell lines down, resulting in frequent infections; iii) skeletal abnormalities; and iv) poor growth.

Question 2:
A 15-year-old girl who is being evaluated for poor school performance and acting-out behaviors is noted to have a large, firm liver. Rings of brown pigment are seen in Descemet membrane on ophthalmologic examination.

Determination of which of the following is MOST likely to confirm the diagnosis in this patient?

A. Hepatic copper concentration
B. Hepatic iron concentration
C. Hepatitis B antibody titers
D. Serum alpha1-antitrypsin level
E. Sweat chloride level

Suggested answer: A. Wilson's disease should be considered in any teenager with new onset mental status changes. The disease is caused by mutations in ATP7B, which is involved in hepatocyte copper trafficking. Tests favoring the diagnosis of Wilson's disease include low serum ceruloplasmin (because the liver cannot incorporate copper into apo-ceruloplasmin to

create ceruloplasmin), high urinary copper excretion, and presence of corneal Kayser-Fleischer rings. Hepatic copper concentration is considered the gold standard test, with concentrations >250 mcg/g of tissue diagnostic (normal is <50mcg/g). However, because reports exist of patients with Wilson's disease and normal hepatic copper concentration, all factors must be considered when making the diagnosis.

Question 3:
A 17-year-old boy who has evidence of Crohn's disease in the terminal ileum develops severe inguinal pain.

The MOST likely visceral source for the referred pain in this patient is the:

A. appendix
B. diaphragm
C. gallbladder
D. small bowel
E. ureter

Suggested answer: E. Crohn disease patients, especially those with terminal ileum disease, are susceptible to renal calcium oxalate stone formation and resulting pain. Oxalate normally binds to calcium in the gut lumen to form an insoluble precipitate passed in stools. However, in the setting of fat malabsorption, calcium binds to free fatty acids instead and allows oxalate to bind sodium. Sodium oxalate is soluble and is absorbed into the circulation. The oxalate is then delivered to the renal system, where it binds calcium and precipitates out as stones.

Question 4:
Which of the following represents the MOST likely mechanism for peptic injury associated with chronic administration of nonsteroidal anti-inflammatory drugs (NSAIDS)?

A. Generalized ischemia of the gut
B. Genetic predisposition
C. Inhibition of prostaglandin
D. Promotion of growth of Helicobacter pylori
E. Topical caustic injury

Suggested answer: C. NSAIDs can cause gastrointestinal injury by two mechanisms. First, they can cause topical injury. NSAIDs are carboxylic acid derivates and are still protonated in the low pH stomach environment. As a result, they remain soluble, are absorbed, and within the more neutral gastric epithelial cells, deprotonate and cause injury. Second NSAIDs block cyclooxygenase (COX) activity, preventing conversion of arachidonic acid into prostaglandin precursors. Prostaglandins protect gastric mucosa from injury through various mechanisms, including stimulating mucin production and increasing bicarbonate excretion. Because both oral and IV NSAIDs cause peptic injury, the prostaglandin effect is thought to be more important than the topical effect.

NSAIDs that reach the distal small intestine and colon can cause intestinal damage and increased permeability through similar mechanisms. As a result, NSAIDs have been known to aggravate IBD.

Question 5:
A 7-year-old boy who has dysentery develops self-limited generalized seizures.

Of the following, the enteric pathogen MOST likely to cause these clinical findings is:

A. Campylobacter jejuni
B. Giardia lamblia
C. rotavirus
D. Salmonella typhimurium
E. Shigella dysenteriae

Suggested answer: E. Shigella species are resistant to stomach acid, multiply in the small intestine, and then invade colonic cells. They lead to a number of intestinal manifestations, including obstruction, perforation, toxic megacolon, and proctitis. They also have a number of systemic effects, including bacteremia, arthritis, and hemolytic-uremic syndrome. Shigella has also been associated with generalized seizures usually in the setting of high fevers in children <15 years old. A Shigella toxin is thought to cause the seizures, though the exact toxin has not been indentified.

Campylobacter jejuni is associated with Guillain-Barre syndrome, likely caused by antibodies made in response to C. jejuni antigens. Rotavirus infections have been associated with seizures, but less commonly that Shigella infections. Nontyphoidal Salmonella can lead to bacteremia and meningitis, usually in children <1 year old. Giardia manifestations are usually limited to the intestinal tract.

Question 6:
A 2-year-old girl is brought to the emergency department immediately after she swallowed some drain cleaner. Physical examination reveals a crying child who is drooling; there are no abnormal findings in the mouth.

Among the following, the BEST next step in the management of this child is to:

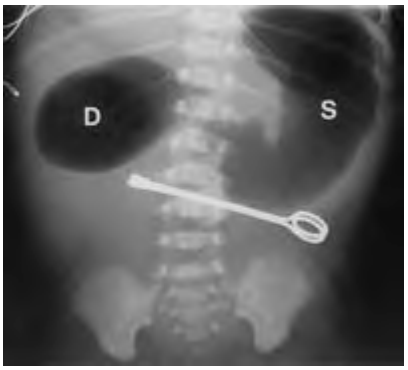
A. admit her for observation
B. arrange for follow-up in 1 week
C. encourage her to drink milk
D. obtain a consultation for upper endoscopy
E. order a barium swallow

Suggested answer: D. All patients with caustic ingestions should be evaluated with endoscopy, because esophageal/gastric injury can be present without oropharynx symptoms. Endoscopy is performed between 24-48 hours, because earlier endoscopy may not detect the full extent of damage and later endoscopy may cause perforation. Diluting the ingested substance with milk

or water is not recommended, because the amount of liquid required may induce vomiting and cause further caustic damage. Barium swallows are not useful in the acute setting, because they do not adequately detect injury or risk for stricture. However, in severe ingestions, they can be used 2 to 3 weeks post- ingestion to evaluate for strictures.

In severe esophageal injuries, a nasogastric tube is placed with endoscopy-assisted visual guidance to prevent perforation. The tube serves two purposes: i) allows a conduit for nutrition, and ii) prevents complete stricturing of the esophagus. Corticosteroids are not recommended, and they have shown no benefit in reducing strictures.

Question 7:
The physical features of a newborn girl suggest trisomy 21. She spits up the first feeding and develops bilious emesis with subsequent feedings. Findings include a scaphoid abdomen, no evidence of an abdominal mass, and quiet bowel sounds; the double-bubble sign is noted on a plain radiograph of the abdomen (see radiograph).



Among the following, the MOST likely cause for the findings in this patient is:

A. antral web
B. duodenal atresia
C. Hirschsprung disease
D. meconium ileus
E. tracheoesophageal fistula

Suggested answer: B. 5% of Down syndrome patients have congenital gastrointestinal abnormalities, including: i) duodenal atresia with our without annular pancreas, ii) imperforate anus, iii) esophageal atresia with tracheoesophageal fistula, iv) Hirschsprung disease, and v) celiac disease. Antral webs have been reported in Down syndrome patients but are not common. Meconium ileus is most often seen in cystic fibrosis. Duodenal atresia can be detected by KUB, which shows the "double bubble" sign (first bubble is stomach, second bubble is duodenum with atretic outlet distally).

Question 8:
An 18-month-old girl has had inconsolable screaming, abdominal distention, and nonbilious vomiting for the past 9 hours. Findings include irritability alternating with lethargy, quiet bowel

sounds, a palpable mass in the right upper quadrant, hemoccult-positive stool, and decreased bowel gas in the right lower quadrant.

The MOST appropriate next step is to obtain a(n):

A. air reduction enema
B. computed tomogram of the abdomen
C. laparotomy
D. ultrasonogram of the abdomen
E. upper gastrointestinal series

Suggested answer: A. Intussusception is the most common abdominal emergency in childhood, occurring most frequently in the ileo-cecal junction. When the diagnosis is uncertain, abdominal ultrasound or plain films may be useful. However, when the diagnosis is clear by the clinical symptoms (as in the case) and there are no clinical signs of perforation, non-operative reduction using air or water/saline is warranted. Surgical reduction is used if perforation is present, or if the intussusception is limited to the small intestine and is causing symptoms (most intussusceptions limited to the small bowel are asymptomatic and self-resolve).

Question 9:

For the past 3 months a 5-year-old girl has had intermittent, painless, bright red blood per rectum in association with bowel movements. Inspection of the anus reveals no fissures, but blood is present on the examiner's finger following digital examination of the rectum.

Of the following, the MOST likely cause of this patient's rectal bleeding is:

A. intussusception
B. juvenile polyp
C. Meckel diverticulum
D. peptic ulcer disease
E. ulcerative colitis

Suggested answer: B. Juvenile polyps and Meckel diverticulum – as opposed to intussusception, peptic ulcer disease, and ulcerative colitis – causes painless rectal bleeding. Juvenile polyps are benign hemartomas (non-neoplastic) usually found in the rectosigmoid region in children ages 2-8. They bleed when injured by stool in transit, and often present as bright red blood depending on how distal they are located. Meckel diverticulum is a remnant of the omphalomesenteric duct that persists in 2% of the general population. They consist of ectopic gastric mucosa, and bleeding results from acid-related ulceration of tissue. Only 4% of affected patients ultimately develop clinical symptoms, most before the age of 20 years.

Question 10:
A 6-year-old girl has had abdominal pain and nonbilious vomiting for 8 hours. History reveals cough and fever for the past 3 days. Findings on physical examination include temperature 39°C (102.2°F); tachypnea; toxic appearance; diffuse, voluntary guarding; and quiet bowel sounds.

Of the following, the examination MOST likely to establish the etiology of the abdominal pain and fever in this patient is a(n):

A. abdominal radiograph
B. chest radiograph
C. complete blood count
D. rectal examination
E. upper gastrointestinal series

Suggested answer: B. This patient likely has pneumonia and associated abdominal pain, which can best be diagnosed with a chest X-ray. A chest X-ray would also be able to detect air under the diaphragm, if perforation is a concern. Abdominal pain in the setting of pneumonia is referred, because the T9 dermatome distribution is shared by both the abdomen and lung. A CBC could indicate infection, but would not identify which part of the body is affected. A rectal examination would be useful if constipation causing abdominal pain is suspected. An UGI series is best used to define anatomy; however, given that this child has no history of previous emesis, malrotation is unlikely.

Question 11:
An 1800 g infant born at 34 weeks' gestation is being fed enterally with a 24 kcal/oz formula developed for preterm infants. The formula contains supplemental medium-chain triglycerides.

Among the following, the BEST explanation for using medium-chain triglycerides is to

A. decrease watery stools
B. enhance absorption of calcium
C. enhance absorption of iron
D. enhance absorption of vitamin C
E. prevent malabsorption of fat

Suggested answer: E. Premature infants have impaired bile and pancreatic lipase secretion, and, as a result, have fat malabsorption. Medium chain triglycerides can bypass these deficiencies, because they are digested and absorbed without the need of bile acids, pancreatic lipase, or co-lipase. In addition, MCTs enter the circulation directly from the enterocyte, without passing through the lymphatic system.

Despite the theoretical benefits of MCTs in preterm infants, their actual benefits remain controversial. In formulas with MCTs versus long chain triglycerides, there was no benefit in weight gain, lipid absorption, or mineral absorption. Furthermore, MCTs may be incompletely oxidized leading to increased urine dicarboxylic acid excretion and metabolic inefficiency.

Question 12:
A 10-year-old boy adopted from Romania has pruritus, mild icterus, and hematemesis. Physical examination reveals an anxious boy who has normal vital signs, ascites, hepatosplenomegaly,

and a prominent venous pattern over the abdomen. Stools are charcoal colored and guaiac positive.

Of the following, the MOST likely cause for the hematemesis is:

A. esophageal varices
B. gastric polyp
C. peptic ulcer disease
D. posterior nasal bleeding
E. thrombocytopenia

Suggested answer: A. This patient likely has liver disease and resulting portal hypertension, causing esophageal varices. Liver disease is suggested by pruritis (bile acid back-up into the circulation) and icterus. Portal hypertension is suggested by splenomegaly, ascites, and a prominent venous pattern on the abdomen. When esophageal varices bleed, they can result in hematemesis. Blood can also transit through the GI tract and appear as black, charcoal colored stool. Gastric lesions (such as a gastric polyp or peptic ulcer disease), posterior nasal bleeding, or thrombocytopenia would not give extra-intestinal symptoms such as ascites or splenomegaly.

Question 13:
A 17-year-old adolescent who is receiving nonsteroidal anti-inflammatory agents for juvenile rheumatoid arthritis has the acute onset of epigastric pain. He vomits "coffee ground" material containing flecks of blood that clears quickly with gastric lavage.

Among the following, the MOST likely cause for these clinical findings is

A. duodenal ulcer
B. gastritis
C. Helicobacter pylori infection
D. Mallory-Weiss tear
E. posterior nasal bleeding

Suggested answer: B. NSAIDs cause gastritis, by impairing prostaglandin production by gastric mucosa (see question 4 above). Prostaglandins exert their protective role by inducing mucin and bicarbonate secretion. NSAIDs and aspirin can also cause duodenal ulcers, though H. pylori infection is a more common cause. The mechanism by which NSAIDs cause duodenal ulcers is acid dependent and prevented by acid blockade. Mallory-Weiss tears are esophageal tears associated with vomiting, whereas posterior nasal bleeding should not cause epigastric pain.

Question 14:
A 9-year-old girl has the height age of a 7-year-old and the bone age of a 6-year-old.

Among the following, the MOST likely cause of her short stature is

A. achondroplasia

B. hypothyroidism
C. malnutrition
D. normal variant short stature
E. Silver-Russell syndrome

Suggested answer: B. This patient has short stature in the context of delayed bone age. Both hypothyroidism and growth hormone deficiency are associated with short stature and corresponding delay in bone maturation. As a result, when re-supplemented with either thyroid hormone or growth hormone, patients demonstrate good growth potential.

Achondroplasia, caused by a dominant mutation over-activating the Fgf3 receptor, leads to shortened bones that would produce a shorter stature than in this patient. At the growth plates, achondroplasia patients do demonstrate delayed bone age. Severe malnutrition will stunt growth but not affect bone age. Normal variant short stature by definition is short stature in the presence of normal bone age. Finally, Russell-Silver syndrome patients typically have a constellation of symptoms, including IUGR, prominent forehead, triangular face, and body asymmetry. They have delayed bone age early with fast advancement later.

Question 15:
A 15-month-old boy who is a recent immigrant from the Caribbean area has rectal prolapse. Stools sometimes contain mucus and blood. Physical examination reveals a child who appears well nourished, but short for age. The mucosal prolapse is easily reducible; other findings on rectal examination are normal.

Of the following, the MOST likely cause for this boy's rectal prolapse is:

A. celiac disease
B. chronic constipation
C. cystic fibrosis
D. rectal polyp
E. trichuriasis

Suggested answer: E. Rectal prolapse results from intussusception of the upper rectum and sigmoid colon. There are a number of predisposing factors, including: i) increased intra-abdominal pressure, from constipation, coughing, or vomiting; ii) diarrheal illnesses, from parasites such as Ascaris lumbricoides and Trichuris trichiura or from malabsorptive syndromes such as celiac disease; iii) malnutrition (hypoproteinemia leading to mucosal edema and smaller fat pads reducing perirectal support); iv) inflammatory lesions such as polyps producing lead points; and v) cystic fibrosis (may occur in 20% of CF patients under 3, from a combination of coughing, malabsorptive diarrhea, and malnutrition). The patient's clinical history is most consistent with parasitic infection.

Question 16:
An antral or pyloric web (diaphragm) is considered in the differential diagnosis of a 6-month-old girl with failure to thrive syndrome and nonbilious vomiting.

The MOST specific study for diagnosing this condition is

A. gastric emptying study
B. plain abdominal radiography
C. ultrasonography
D. upper gastrointestinal contrast study
E. upper gastrointestinal endoscopy

Suggested answer: E. An antral/pyloric web is a circumferential mucosal septum in the pyloric region, projecting into the lumen perpendicular to the long axis of the antrum. Antral webs may have a large aperature and be clinically insignificant; alternatively, they may be nearly complete and cause gastric outlet obstruction symptoms. Histologically, webs are made of gastric mucosa, submucosa, and muscularis mucosae. Plain abdominal radiography may show a dilated stomach, whereas an UGI study could show an extra compartment between the web and antrum reminiscent of a second duodenal bulb. The most specific study would be to directly visualize and sample the tissue through upper endoscopy.

Question 17:
A 10-year-old child has had intermittent diarrhea and weight loss over the past year.

A TRUE statement regarding testing with guaiac or orthotolidine for occult blood in this patient's stool is:

A. Microscopic examination of the stool is a better test for detecting occult blood
B. Negative results exclude lower gastrointestinal bleeding
C. Positive results confirm the presence of occult blood
D. These tests detect peroxidase activity in hemoglobin
E. These tests quantitate the amount of hemoglobin in the stool

Suggested answer: D. The guaiac-based fecal occult blood test (gFOBT) is a qualitative test that detects a peroxidase reaction (which turns guaiac-impregnated paper blue). Because heme from hemoglobin has peroxidase activity, gFOBT has been used to detect the presence of a GI bleed. However, gFOBTs can produce false positives and negatives. False positives occur because certain foods have peroxidase activity. These include animal meats with high heme content (beef, lamb) and raw peroxidase-rich fruits and vegetables (broccoli, cauliflower, radishes, turnips, and some melons). False negatives occur depending on sampling. As a result, in colorectal cancer screening, three to six gFOBTs are performed in sequence to establish a gFOBT negative result. Microscopic examination may miss blood depending on what part of the stool is studied.

Question 18:
An 18-year-old girl who is taking tolmetin for juvenile rheumatoid arthritis develops gastritis.

Which of the following medications would have been MOST likely to prevent the development of peptic disease in this patient?

A. Antacids
B. Corticosteroids
C. H2-blockers
D. Misoprostol
E. Sucralfate

Suggested answer: D. Tolmetin is an NSAID, which causes gastritis by inhibiting prostaglandin production. Prostaglandins in turn have a number of effects, including increasing bicarbonate secretion and mucin production. As a result, the prostaglandin E analog Misoprostol is the most appropriate prevention strategy. Though less effective than Misoprostol, PPIs have also been shown to be protective in preventing gastric ulcers or NSAID-related duodenal damage (NSAID-related duodenal damage, compared to gastric damage, is more closely related to NSAIDs ability to increase acid secretion). Antacids, H2-blockers, and sucralfate may all have some benefit because each replicates some aspect of the protective effects of prostaglandins. Corticosteroids promote gastritis.

Question 19:
A previously healthy 13-month-old boy has had two bloody stools in the past 6 hours. He has had no nausea, vomiting, or diarrhea. The child appears well and has good peripheral perfusion. The pulse is 130/min. Abdominal examination reveals normal findings except for hyperactive bowel sounds. Maroon-colored, guaiac-positive stool is found on rectal examination. Radiography of the abdomen shows a nonspecific bowel gas pattern.

Of the following, the MOST likely diagnosis is

A. anal fissure
B. Crohn disease
C. intussusception
D. Meckel diverticulum
E. peptic ulcer disease

Suggested answer: D. Four clinical aspects suggest a bleeding Meckel diverticulum: i) the bleeding is painless (vs. painful in intussusception and IBD); ii) the bleeding is copious (vs. not as much in anal fissures); iii) the patient is 13 months old and healthy (vs. usually older and malnourished for Crohn disease); and iv) the blood is maroon, suggesting a bleed in the proximal bowels. A Meckel scan may confirm the diagnosis, though false negatives are common. The scan uses intravenous 99m technetium pertechnetate which is taken up by gastric mucosa. Positive signal in the terminal ileum area indicates ectopic gastric mucosa and is consistent with a Meckel diverticulum.

Question 20:
A 2-year-old boy has just swallowed a quarter. Physical examination reveals a quiet child in no distress

The MOST appropriate first step in managing this patient is to

A. administer glucagon intramuscularly
B. administer papain
C. admit for observation
D. obtain radiographs
E. perform an upper endoscopy

Suggested answer: D. The most appropriate step is to obtain radiographs for two reasons. First, radiographs will confirm that the quarter in not in the trachea (if in the trachea, the side instead of the face of the coin would be seen on PA films). Second, radiographs will identify the quarter's location in the GI tract. Coins in the esophagus that cause symptoms should be removed immediately, whereas asymptomatic coins can be watched for 24 hours to allow passage in the stomach. Coins in the stomach can be left to pass in the stools; however, if the coin remains in the stomach after 4 weeks, it is unlikely to pass and should be removed endoscopically.

Coins lodged in the esophagus for more than 24 hours should be removed via upper endoscopy, because they may cause aspiration or other complications. There are 3 esophageal sites where coins/foreign objects become lodged: the cricopharyngeus, mid-esophagus, and above the LES. Glucagon, which lowers the LES, has been tried with little success in helping coins move to the stomach. Papain has also been tried in cases of food impaction, to digest the food. Papain is now contraindicated because it poses a risk for esophageal injury and possible perforation.

Question 21:
Of the following, the MOST common feature of chronic, nonspecific diarrhea of infancy and childhood (toddler's diarrhea) is:

A. guaiac-positive stools
B. intermittent fever
C. lactose intolerance
D. significant weight loss
E. unimpaired growth

Suggested answer: E. Nonspecific diarrhea of infancy (toddler's diarrhea) is defined as the passage of three or more large, unformed stools during waking hours (not at night) for four or more weeks. It begins in infancy or preschool years, does not cause failure to thrive, and does not have a specific definable cause. Toddler's diarrhea may be caused by rapid intestinal transit secondary to uninterrupted MMCs, because food particles are often seen in the stool. Other proposed mechanisms include dumping bile acids and hydoxyl fatty acids into the colon, as well as excessive sugar intake promoting an osmotic diarrhea. Symptoms usually improve with dietary modifications including increased fat and fiber intake, limited fluid intake, and avoidance of fruit juices (especially apple, prune, and pear juice which have a high osmotic load). Symptoms usually resolve by age 4.

Guaiac-positive stools, intermittent fever, and significant weight loss are associated with inflammatory or infectious causes of diarrhea. Primary lactose intolerance is rare in children and usually is accompanied by additional signs and symptoms including poor growth.

Secondary lactose malabsorption can occur in infants following temporary villi blunting from an infectious gastroenteritis.

Question 22:
Among the following, the LEAST important variable in the development of diarrhea is

A. gender
B. immunologic status
C. nutritional status
D. presence of chronic infection
E. presence of systemic disease

Suggested answer: A. Generally, diarrhea occurs when enterocytes are actively secreting solutes that draw water with them (secretory diarrhea) or when they are unable to absorb osmotically active solutes (osmotic diarrhea). There is a cyclic relationship between immunological and nutritional status in causing diarrhea, whereby poor immunological status leads to infection/diarrhea, which causes malnutrition, which in turn increases vulnerability to further infection/diarrhea. Systemic diseases can also cause malnutrition, which increases vulnerability to infection, which may in turn cause diarrhea. There is no evidence that gender is a direct variable correlating with the development of diarrhea.

Question 23:
A 5-year-old girl has had a recent onset of postprandial emesis and epigastric pain that awakens her at night. Physical examination reveals normal findings except for guaiac-positive stools. There is a strong family history of peptic ulcer disease.

Among the following, the MOST specific diagnostic study for peptic ulcer disease is

A. abdominal ultrasonography
B. plain abdominal radiography
C. technetium pertechnetate scanning
D. upper gastrointestinal contrast study
E. upper gastrointestinal endoscopy

Suggested answer: E. Peptic ulcer disease is most accurately diagnosed by visualizing the mucosa, via upper endoscopy with biopsies. UGI contrast studies have been used as a noninvasive test to detect mucosal abnormalities; however, they have high false positive and false negative rates. Technetium pertechnetate scanning (Meckel scan) is useful for detecting gastric tissue especially in ectopic places, not for detecting gastritis or ulcers. Abdominal ultrasonography and plain abdominal radiography are not used to diagnose peptic ulcer disease.

Question 24:
A 3-year-old boy with acute lymphoblastic leukemia in hematologic remission is receiving vincristine, methotrexate, and 6-mercaptopurine. He develops abdominal pain and distention and nausea without fever or diarrhea.

These findings are MOST likely caused by

A. Escherichia coli gastroenteritis due to granulocytopenia
B. intestinal candidiasis due to lymphopenia
C. intestinal mucosal ulcerations due to methotrexate toxicity
D. necrotizing enterocolitis due to 6-mercaptopurine toxicity
E. reduced intestinal motility due to vincristine toxicity

Suggested answer: E. In humans and animal models, vincristine reduces gastric motility presumably from its neuropathic side effects. The most common motility problem with vincristine is constipation, usually starting 3 days after the dose is given. However, other signs of dysmotility, including abdominal distension and vomiting, have been known to occur. The patient's lack of diarrhea is inconsistent with enteritis. Methotrexate commonly causes hepatotoxicity, vomiting, and mucositis, without abdominal distension. 6-MP commonly causes vomiting and may cause elevation in liver numbers. It is also associated with a severe hypersensitive reaction, with gastrointestinal symptoms of nausea, vomiting, diarrhea, and fever.

Question 25:
Of the following, the MOST likely cause of passage of bright red blood from the rectum in an otherwise healthy, asymptomatic 3-year-old child is

A. intussusception
B. juvenile polyp
C. Meckel diverticulum
D. peptic ulcer
E. ulcerative colitis

Suggested answer: B. The two most common causes of rectal bleeding in the 2-5 year age group are juvenile polyps (asymptomatic) and infectious colitis (symptomatic). A Meckel diverticulum is also possible, but classically the majority of cases (60%) occur before age 2. Intussusception causes pain and is accompanied by red "currant jelly" stool. Peptic ulcers usually present later and produce black, melanotic stools. Ulcerative colitis would likely be accompanied by other symptoms, including diarrhea.