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Pathophysiology of Some Signs of Digestive System Disorder

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Table 11.1 An Overview of some Signs of Digestive System Disorder and Relevant Pathologic Process

S.No.	SIGNS	DEGP	DIMP	DMPP	DYGP	INPP	ISPP	LYPP	NEPP	TRPP
1	Abdominal distension			x	x	x	x		x	x
2	Abdominal mass					x			x	x
3	Abdominal tenderness			x	x	x	x		x	x
4	Anal abscess					x				
5	Anal fissure		x	x		x	x		x	x
6	Anal fistula				x	x			x	x
7	Anal wart/condylomata acuminate					x				
8	Angular stomatitis		x	x		x				x
9	Ankyloglossia				x					
10	Aphthous ulcers		x	x		x				
11	Ascites			x		x			x	
12	Asterixis/flapping tremor			x		x				
13	Borborygmus			x	x	x			x	x

Contd...

	SIGNS	DEGP	DIMP	DMPP	DYGP	INPP	ISPP	LYPP	NEPP	TRPP
14	Caput medusa			x	x	x			x	
15	Cheilitis		x	x		x				x
16	Cleft lip/palate				x					
17	Dental caries		x	x		x				x
18	Enterocutaneous fistula			x		x			x	x
19	Epulis					x				x
20	Faecal incontinence					x				x
21	Gingivitis			x		x			x	
22	Glossitis		x	x		x				x
23	Guarding			x		x	x			x
24	Gynaecomastia			x						
25	Halitosis			x		x			x	
26	Haemorrhoid			x		x			x	
27	Hepatomegaly			x	x	x	x		x	
28	Hernia	x		x	x					x
29	Imperforate anus				x					
30	Jaundice		x	x	x	x			x	x
31	Leucoplakia			x	x	x				
32	Macroglossia		x		x				x	x
33	Oral thrush			x		x				
34	Pallor			x		x			x	
35	Palmar erythema			x		x				
36	Pneumo-peritoneum			x		x	x			x
37	Pruritus ani			x		x				
38	Rebound tenderness					x				x
39	Rectal prolapse/ Procedentia					x				x
40	Spider angiomata			x						
41	Splenomegaly					x	x		x	x
42	Striae			x						
43	Variceal haemorrhages					x	x			
44	Weight loss			x		x			x	x
45	Xanthoma/xanthelasma				x	x				
46	Xerostomia	x	x	x		x				x

DEGP	Degenerative pathologic process	DIMP	Deranged immunologic process
DMPP	Deranged metabolic pathologic process	DYGP	Dysgenetic pathologic process
INPP	Inflammatory pathologic process	ISPP	Ischaemic pathologic process
LYPP	Lytic pathologic process	NEPP	Neoplastic pathologic process
TRPP	Traumatic pathologic process		

1. ABDOMINAL DISTENSION

Definition: This is the enlargement of the abdomen either from diminished tone of the wall musculature or from increased content such as fluid, gas, or solid. Abdominal distension may be generalised or may be localised to a discrete mass or enlargement of an organ.

Pathophysiology: Accumulation of fluid or gas within the abdominal cavity or intestine or enlargement of intra-abdominal organs or abnormal growth within the abdomen will lead to outward expansion of the abdomen and result in abdominal distension. Also, diminished tone in abdominal wall or intestinal musculature will lead to outward expansion of the abdomen which will result in abdominal distention. Pathophysiological processes that can lead to abdominal distention include the following:

Deranged metabolism: Hypokalemia may result from severe episodes of acute or chronic diarrhoea from infectious or noninfectious causes (as seen in chronic inflammatory bowel disease-IBDs). This is because potassium-rich intestinal fluid is lost in the diarrheal stools. The ensuing hypokalaemia causes weakness and paralysis of the gastrointestinal smooth muscles (in severe cases) with subsequent distention of the bowel loops. These distended bowels then cause abdominal distension. Deposition of abnormal metabolites in the liver will lead to enlargement of the liver and result in abdominal distension.

In another instance, severe protein–energy malnutrition (PEM) as seen in Kwashiorkor causes fatty change in the liver resulting in increase in the liver size. The enlarging liver may cause abdominal distension.

Dysgenesis: Congenital strictures and congenital absence of the ganglions (Hirschsprung's disease) will lead to intestinal obstruction which will cause distension of the intestines and result in abdominal distension.

Inflammation: Inflammation occurring in the liver from a variety of causes, such as viral infections may result in enlargement of the liver, which then results in abdominal distention. Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis. The ensuing inflammation results in a thickened and stiff bowel wall. The mesentery, which is thickened, oedematous, and contracted, fixes the intestine in one position. Transmural inflammation may cause loops of intestine to be matted together causing small bowel obstruction and as such abdominal distension.

Ischaemia: Thrombosis or embolism in the superior or inferior mesenteric arteries will lead to reduced blood supply to the bowel loops and ischaemia which will cause reduced peristalsis, enlarged bowel loops and result in abdominal distension.

Neoplasm: Malignant transformation and proliferation of small intestinal cells result in tumors like adenocarcinomas, carcinoids, lymphomas, and leiomyomas. As tumour size increases, they may cause partial or complete mechanical intestinal obstruction from intussusception or volvulus. Intestinal obstruction in turn results in distention of the bowel and thus, abdomen.

Trauma: Obstruction of the intestine may be caused by scars or adhesion from previous abdominal or pelvic surgeries. These adhesions may form across intestinal loops strapping them down, thus, impairing or obstructing movement of bowel contents. When this occurs, there is accumulation of air and fluid above the level of obstruction which causes distention of the intestine, visible on examination as abdominal distension.

2. ABDOMINAL MASS

Definition: This is a discrete or vague abnormal structure felt within the abdominal cavity on palpation. The location may sometimes give a clue to its origin. An abdominal mass is an abnormal growth that occurs in the abdomen, which is felt on palpation and which may or may not cause visible swelling and change in the shape of the abdomen.

Pathophysiology: Enlargement of the intra-abdominal organs, including the lymph nodes or abnormal growth within the abdomen will result in abdominal mass which can be felt on abdominal palpation. Pathological processes resulting in abdominal mass include the following.

Inflammation: Infection by *Mycobacterium tuberculosis* bacilli may become disseminated and involves the gastrointestinal tract, liver and peritoneum. Chronic granulomatous inflammation in these tissues may spread to affect contiguous abdominal lymph nodes. As inflammation continues, the affected GI tract, peritoneum and lymph nodes

may become matted to form a vague abdominal mass. In addition, chronic inflammation in the liver may result in a palpable enlargement.

Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis. Transmural inflammation may cause loops of intestine to be matted together. The thickened bowel loops, thickened mesentery, or an abscess may cause a palpable abdominal mass, often in the right lower quadrant.

Infection with the protozoa *Entameba histolytica* occurs when its cysts are ingested and pass to the colon where vegetative trophozoites enter the intestinal mucosa, causing colonic ulcers. Amoebae then enter the portal vein and are carried to the liver. In the liver, the amoebae block small portal radicles, release enzymes, and cause focal inflammatory lesions resulting in the formation of single or multiple abscesses. Abscesses may also develop from focal areas of purulent bacterial infection within the hepatic parenchyma. As the inflammation continues, the liver enlarges and a hepatic mass may be felt in the area where abscesses have formed.

Neoplasm: Malignant transformation and proliferation of gastric or hepatic cells result in gastric carcinoma or hepatocellular carcinoma, respectively. As the tumuor mass increases, they form an intramural mass which when large is palpable as an upper abdominal mass. Benign gastric tumours like leiomyomas, lipoma, neurofibroma, lymphangioma, ganglioneuroma, and hamartoma can also grow into the gastric lumen to form a palpable abdominal mass.

Trauma: Traumatic injury to the abdomen can lead to damage to the intra-abdominal organs and cause bleeding into the abdominal organs or into the peritoneal cavity. The haematoma that forms will result in abdominal mass.

3. ABDOMINAL TENDERNESS

Definition: Abdominal tenderness is the objective elicitation of pain on palpation of the abdomen. The patient usually will wince when affected abdominal areas are palpated.

Pathophysiology: Irritation of the peritoneum, or stretching of the coverings of the intestinal organs as a result of distension of the intestine or intestinal organs or reduced blood supply to the intestine will lead to stimulation of the nocireceptors, which will result in pain and tenderness on palpation. Also, contraction of the intestinal muscles or hyper-sensitivity to normal intestinal activities will also result in abdominal tenderness. Pathological processes that lead to abdominal tenderness include the following.

Deranged metabolism: Chronic ingestion of steroids or iron tablets or ingestion of a strong acid or alkali will lead to perforation of the intestine. Seepage of intestinal contents will cause inflammation of the peritoneum and result in generalized abdominal tenderness. Also, perforation of a peptic ulcer will lead to spillage of acid gastric contents which causes an intense peritoneal reaction and abdominal tenderness.

Dysgenesis: Congenital intestinal obstruction will lead to distension of the intestine with stretching of the intestinal wall which will cause stimulation of the norciceptors and result in abdominal tenderness.

Inflammation: Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD) (such as Crohn's disease and ulcerative colitis). The ensuing inflammation results in a thickened and stiff bowel wall. In both conditions abdominal tenderness is elicited over areas of disease activity.

Inflammation of the appendix may result from a fecalith obstructing the appendix lumen causing appendicitis. The inflammation causes a colicky abdominal pain initially poorly localised at the peri-umbilical area, but later becomes localised at the right iliac fossa. This pain may be elicited as abdominal tenderness in the right iliac region at McBurney's point and corresponds to the location of the inflamed appendix.

Colonic diverticula are mucosal out-pouchings occurring where arteries penetrate the muscularis to reach the submucosa and mucosa. Because these areas are inherently weak and under stress, prolapse of mucosa and submucosa may sometimes occur. Inflammation of a diverticulum (diverticulitis) results when a fecalith becomes impacted in a diverticulum, with erosion through the serosa sometimes resulting in perforation. This causes tenderness located in the left lower quadrant of the abdomen.

Acute inflammation of the peritoneum from bacterial infections or intestinal contents (including gastric acid, gastrointestinal luminal contents, bile, or pancreatic juice) in the peritoneal cavity results in

peritonitis. Secondary peritonitis may also result from any definable cause, such as perforation of a viscus (from acute appendicitis or diverticulitis), perforation of an ulcer (peptic ulcer, malignancy), and trauma, including iatrogenic intervention (e.g., surgery, needle biopsies). The peritoneal irritation and inflammation causes a generalised abdominal tenderness.

Ischaemia: Thrombosis or emboli within the superior mesenteric arterial vessels or twisting of the intestine in volvolus or intussusception will cause obstruction to the blood supply to the intestine. This will lead to ischaemia, infarction and abdominal tenderness. The infarcted intestine may also perforate and lead to leakage of intestinal content into the peritoneum, thereby causing inflammation and abdominal tenderness.

Neoplasm: Intraluminal intestinal tumour can lead to intestinal obstruction which will lead to distension, stretching of the intestine and result in abdominal tenderness. Also, intrabdominal tumours can also cause intestinal obstruction or erode the walls of the intestine and result in distention or leakage of intestinal content which will result in irritation of the peritoneum and abdominal tenderness.

Trauma: Penetrating or blunt abdominal trauma can lead to damage to intrabdominal organs and result in abdominal tenderness

ANAL ABSCESS

Definition: An abscess is a localized collection of pus surrounded by inflamed tissue. When this occurs in the anus, it is called anal abscess.

Pathophysiology: Patho-physiological processes that can lead to anal abscess include:

Inflammation: Infections arising in the anal glands at the dentate line may localize in the adjacent tissue spaces with exudation of purulent materials forming an abscess.

Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis. The ensuing inflammation results in a thickened and stiff bowel wall. The presence of peri-anal disease may be visible as fistulous openings, indurations and anal abscess.

5. ANAL FISSURES

Definition: Anal fissure is a small laceration of the muco-cutaneous junction of the anus just inside the anal verge. It may be acute or chronic. About 90% of anal fissures occur in the posterior midline, where skeletal muscle fibers that circle the anus are weakest.

Pathophysiology: Trauma or injury to the anal canal from passage of hard faecal mass and hypertonicity of the internal anal sphincter will lead to overstretching of the anal canal which will result in a tear in the anoderm at the dentate line mostly in its posterior midline.

Patho-physiologic processes that result in anal fissure include the following.

Deranged immunology: Antiendothelial antibodies activate the endothelium, generating vasoconstriction and procoagulant activity. This mechanism induces ischaemia of the anoderm and formation of anal fissure.

Deranged metabolism: Inadequate intake of water will lead to dehydration which will cause constipation. Passage of these hard stools will lead to excessive straining, stretching of the anal canal and damage to the anal canal which will result in tears and anal fissure.

Inflammation: Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occur in inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis. If this process occurs around the anus, the extension of the inflammatory process through the anal wall can result in anal fissure.

Ischaemia: Blood flow in the anoderm at the posterior midline, the site of most fissures, is less than one-half that in other quadrants in the anal canal. This reduced blood flow will lead to ischaemia, infarction and damage to the anal canal which will result in anal fissure. Hypertonicity of the internal anal sphincter will lead to increased resting anal pressure and cause spasm and reduced blood flow to the anus. This will result in ischaemia, infarction, and damage to the anal canal and anal fissure.

Neoplasm: Malignant transformation of dysplastic cells in the anus may result in carcinomas as seen in epidermoid carcinomas of the anus. The anal carcinoma may extend directly into the sphincters and

other surrounding perianal tissues and cause an anal fissure.

Trauma: Forceful passage of hard stool (constipation) may result in a tear of the anoderm during defecation causing acute anal fissure. Trauma to the anal canal resulting from digital insertion (as during a rectal examination), foreign body insertion, or anal intercourse will lead to a tear in the anal canal and result in anal fissure.

6. ANAL FISTULA (FISTULA-IN-ANO)

Definition: An anal fistula is an abnormal inflammatory tract connection between the epithelialized surface of the anal canal and the perianal skin. There are four categories of fistulas, based on the relationship of fistula to sphincter muscles and include intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric.

Pathophysiology: Most anal fistulas originate in anal crypts (anal glands), which get clogged and become infected, with ensuing abscess formation. When the abscess is opened or when it ruptures, a fistula is formed. Patho-physiologic processes that result in anal fistula include the following.

Dysgenesis: Anorectal malformations will lead to intestinal obstruction. If the outlet of the anal glands which are located between the two layers of the anal sphincters becomes blocked with impacted stool, this will lead to inflammation of the mucosa and formation of an abscess which will eventually point to the skin surface and cause formation of a tract between the anal canal and the skin which will result in an anal fistula.

Inflammation: Inflammatory bowel disease will lead to formation of anal abscesses which may rupture and cause a tract between the anal canal and the skin to form which will result in anal fistula.

Neoplasm: Malignancy involving the rectum will lead to inflammation of the rectum and anal canal. This may result in the formation of an inflammatory track between the anal canal and the skin and result in anal fistula.

Trauma: radiation or surgical injury to the rectum or anus will lead to formation of an inflammatory tract which will result in anal fistula.

7. ANAL WARTS / CONDYLOMATA ACUMINATA

Definition: Anal warts are small, discrete pearly white excrescences on the perianal skin and anoderm, caused by human papilloma viruses (usually types 6 and 11). They may also occur just above the dentate line where they appear as pink and velvety lesions.

Pathophysiology: The HPV has a high affinity for the transitional zones of the cervix and the pectinate line of the rectum at the squamous–columnar junction epithelium where the virus targets the basal membrane stem cells. This is where virus replication occurs. The genome of the HPV virus is composed of several early and late genes. The early genes promote the proliferation of epidermal cells; as a result, the superficial cell layer becomes thicker, forming the rough hills of condylomatous lesions. Pathophysiologic processes that result in anal warts include the following:

Inflammation: Infection by the human papilloma viruses (HPV) types 6 and 11 incites a chronic inflammatory reaction that leads to proliferation of epidermal cells, thickening of the superficial cell layer and ultimately results in the formation of the warts.

8. ANGULAR STOMATITIS

Definition: Angular stomatitis is irritation and fissuring in the corners of the lips.

Pathophysiology: Continuous moistness at the corners of the mouth will lead to breakdown of the skin around the corners of the mouth which can become infected to form cracks and fissures. Pathophysiolgic processes that result in angular stomatitis include the following.

Deranged immunology: Allergies to lipstick and toothpaste or adverse reactions to some types of medications can cause sores inside the mouth and at the corners of the lips and result in angular stomatitis.

Deranged metabolism: Iron is necessary for the up-regulation of transcriptional elements for cell replication and repair. Lack of iron can cause the genetic downregulation of these elements, leading to ineffective repair and regeneration of epithelial cells, especially in the mouth and lips leading to angular stomatitis. Deficiencies in B_2 (riboflavin), B_3 (niacin), B_6 (pyridoxine), B_9 (folic acid) or B_{12} (cobalamine) also cause angular stomatitis.

Inflammation: In individuals with "over-closed" jaws due to tooth wear or edentulousness, the jaws come close together and cause skin folds around the angle of the mouth to crack. Continuous moistness by saliva will in turn favour infection. Infection incites an inflammatory reaction at the angles of the mouth causing angular stomatitis.

Trauma: Ill-fitting dentures that do not fit correctly can cause the mouth to close in an unnatural way, which can create a fold in the corner of the lips. This fold can collect saliva and microorganisms which eventually cause those painful fissures. Frequent licking of the corners of the mouth is another factor that contributes to angular stomatitis.

9. ANKYLOGLOSSIA (TONGUE TIE)

Definition: Ankyloglossia (tongue-tie) is a condition in which the lingual frenulum is abnormally short thus hindering the tongue movement. The frenulum may lengthen as the child gets older. However, in severe cases, speech may be affected and surgical correction is indicated.

Pathophysiology: Shortness of the frenulum will lead to tethering of the tongue to the floor of the mouth and result in ankyloglossia. Patho-physiologic processes that result in ankyloglossia include the following.

Dysgenesis: A congenital malformation of the frenulum in-utero may result in shortening of its length causing ankyloglossia.

10. APHTHOUS ULCER

Definition: Aphthous ulcer or canker sore is a well-circumscribed, ulcerative oral lesion with a white necrotic base, surrounded by a red halo. Rarely, aphthous ulcers may occur in the esophagus, upper and lower GI tracts, and anorectal epithelium. The lesions last 10–14 days and heal without scarring but are prone to recurrence.

Pathophysiology: The pathophysiolgic processes resulting in aphthous ulcers include the following.

Deranged immunology: Immunodysregulation either from genetic predisposition or stress induced or allergies will lead to generation of interleukins and tumour necrosis factor which cause mucosal destruction and will result in aphthous ulcer.

Deranged metabolism: For yet unidentified reasons, stress or prolonged fever may precipitate eruptions of aphthous ulcers. Also, patients with severe nutritional deficiencies or anemia may also develop aphthous ulcer due to coexisting micronutrient deficiencies. Micronutrients are necessary for mucosal health, and their deficiencies result in mucosal compromise which may progress to erosion and aphthous ulcers which improves after treatment with iron, folate, or vitamin B_{12}.

Inflammation: Infections by herpes simplex virus and measles incite an inflammatory reaction in the oral mucosa which ulcerates causing aphthous ulcers.

11. ASCITES

Definition: Ascites is the accumulation of fluid in the peritoneal cavity. In large volumes, the ascitic fluid shifts with movement of the patient and conducts a percussion wave.

Pathophysiology: Sinusoidal portal hypertension and hepatic insufficiency are the initial factors that lead to a circulatory dysfunction characterized by arterial vasodilation in the splanchnic circulation (as a result of increased synthesis of local vasodilators). This results in a decrease in effective circulating blood volume. The arterial hypotension activates the plasma renin, aldosterone, and sympathetic nervous system, resulting in renal sodium and water retention, high cardiac output and hypervolemia. Splanchnic arterial vasodilation not only impairs systemic hemodynamics and renal function but also alters hemodynamics in the splanchnic microcirculation. The rapid and high inflow of arterial blood into the splanchnic microcirculation is the main factor increasing hydrostatic pressure in the splanchnic capillaries leading to an excessive production of splanchnic lymph over lymphatic return. Lymph leakage from the liver and other splanchnic organs is the mechanism of fluid accumulation in the abdominal cavity. Continuous renal sodium and water retention perpetuates ascites formation.

Pathophysiologic processes that result in ascites include the following.

Deranged: metabolism Multiple factors (alcohol, drugs, metabolites) may result in chronic liver injury which may eventually cause impairment in liver function. Since the liver is the main site of albumin production, impairment of its function eventually results in hypoalbuminaemia. Hypoalbuminaemia in turn causes a decrease in plasma oncotic pressure which then leads to transudation of fluid out of the blood vessels into the body tissues and the peritoneum causing ascites.

Inflammation: Infection of the liver with the hepatotrophic viruses such as hepatitis B and C incites an inflammatory response, which may become chronic and persistent. The damages caused by the continued inflammation may eventually lead to fibrosis, which may then progress to liver cirrhosis. The fibrosis causes portal hypertension because of increased outflow resistance in the liver from matrix deposition and possibly stellate cell contraction. Initially, albumin traverses the porous sinusoidal endothelium along with fluid; but as fibrosis progresses, only protein-free fluid can escape the sinusoid, from where it enters hepatic lymphatics. Continued accumulation of lymph overcomes the capacity for lymphatic drainage, and the excess fluid leaks into the peritoneal cavity forming ascites. Portal oncotic pressure is reduced in cirrhosis because of hypoalbuminemia, which is due to hepatic synthetic failure and further worsens the ascites.

In another instance, extrapulmonary tuberculous infection with peritoneal seeding incites an inflammatory response causing tuberculous peritonitis with exudation of fluid into the peritoneal space causing ascites.

Neoplasm: Neoplastic transformation and proliferation of hepatic cells result in carcinoma of the liver or hepatocellular carcinoma. Also, malignant cells can metastasise from other primary sites to the liver (secondary metastasis). Infiltration and encroachment of the neoplastic cells on the hepatocytes may obstruct outflow of normal lymphatics and the accumulation of lymph eventually exceeds the capacity for lymphatic drainage, and the excess fluid leaks into the peritoneal cavity forming ascites. In addition, where malignancy is extensive or metastasis becomes massive, portal hypertension may develop from the infiltration and distortion of the liver architecture. Portal hypertension causes increased outflow resistance and as such alters the Starlings forces in the portal circulation (increased portal venous hydrostatic pressure, reduced portal venous oncotic pressure) causing transudation of fluid into the interstitium from where they enter the lymphatic drainage system and eventually overflow into the peritoneum when the capacity is exceeded, forming ascites.

12. ASTERIXIS / FLAPPING TREMOR

Definition: Asterixis is a flapping tremor of the hand which develops late in the course of hepatic encephalopathy. To elicit asterixis, it is necessary to have the patient extend his or her hands against gravity and look for the release phenomenon that causes the flap. If the patient cannot follow this command, the patient can grasp two fingers of the examiner's hand and be asked to sustain the grasp; the release phenomenon might be thus elicited.

Pathophysiology: Focal, specific brain lesions or a generalised neurochemical imbalance in the ventrolateral thalamus will lead to damage to the brain cells in the diencephalon and episodic dysfunction of the diencephalic motor centers in the brain, which regulate the muscles involved in maintaining position and sustained or tonic muscle contraction. This will lead to involuntary contractions of antagonistic groups of muscles, thereby resulting in inability to actively maintain a position and jerking movements of the outstretched hands when bent upward at the wrist. The brief lapse of posture causes a sustained voluntary muscle contraction and arrhythmic interruptions of these sustained voluntary muscle contraction result in asterixis.

Pathophysiolgic processes resulting in asterixis and flapping tremor include the following.

Deranged metabolism: Ammonium ion (NH_4^+) is produced in abundance in the intestinal tract, especially the colon, by the bacterial degradation of luminal proteins and amino acids. It is also produced from endogenous urea (25% of the daily production of which diffuses into the intestinal lumen). The NH_4^+ thus produced diffuses into the portal circulation and is transported to the liver, where it is detoxified by its conversion to urea through the Krebs-Henseleit urea cycle. The urea thus formed is then excreted by the kidneys. Failure of this detoxification process occurs when the liver is damaged as seen in severe liver diseases such as fulminant hepatic failure; or when there is direct entry of portal blood into the peripheral circulation through spontaneous or surgically created porto-systemic shunts. The serum ammonia level rises and when circulated to the brain causes the neurologic signs of hepatic encephalopathy and asterixis. Acetaminophen is a dose-dependent hepatotoxin and toxic levels cause zonal necrosis and acute liver failure. The liver injury is caused by a toxic metabolite of acetaminophen formed by the cytochrome P-450-dependent drug-metabolizing system. Below threshold doses, this metabolite is efficiently detoxified by conjugation with glutathione. In the toxic dose range, glutathione stores are rapidly exhausted and the metabolite reacts with essential cellular constituents, leading to cell dysfunction with

rapid progression to acute hepatic failure with signs of hepatic encephalopathy and asterixis.

Inflammation: Infection of the liver with the hepatotrophic viruses such as hepatitis B and C incite an inflammatory response which may become chronic and persistent. The damages caused by the continued inflammation may eventually lead to chronic inflammation and fibrosis with progressive loss of functional liver cells. Chronic liver injury eventually results in the death of hepatocytes followed by the accumulation of fibrous tissue and cirrhosis. The fibrous tissue distorts the architecture of the organ, causing portal hypertension and the development of porto-systemic shunting. This shunt circumvents detoxification of the NH_4^+ produced in the gut by the liver (see above) which then circulates to the brain and leads to signs of hepatic encephalopathy and asterixis.

13. BORBORYGMUS

Definition: This is a rumbling sound made by the movement of gas in the intestines, which can be heard with or without the aid of a stethoscope.

Pathophysiology: Muscle contraction of the stomach and intestine will lead to movement of fluid and gas. As the wave of muscle contraction move the food and gas through the digestive system, the food is pushed against the intestinal wall. The process of this contraction (peristalsis) and the movement of the food and gas induce the rumbling or gurgling or growling noise which results in borborygmi. Pathophysiolgic processes resulting in Borborygmus include the following.

Deranged metabolism: Incomplete digestion of carbohydrate-containing foods, including milk and other dairy products (lactose intolerance or the use of α-glucosidase inhibitors by diabetics), gluten (protein in wheat, barley, and rye) (celiac disease), fruit, vegetables, beans, legumes, and high-fiber whole grains can lead to excess gas in the intestine which will result in excessive abdominal noise and borborygmi.

Dysgenesis: Congenital intestinal obstruction will lead to obstruction to the movement of food and gas. There is increased intestinal muscle contraction and peristalsis in an attempt to overcome the obstruction which will result in rumbling sound and borborygmi.

Inflammation: Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis. Transmural inflammation may cause loops of intestine to be matted together and cause small bowel obstruction. Intestinal obstruction in turn causes increased and visible peristaltic wave as they try to propel gut content through the obstruction. These increased peristaltic waves give rise to loud borborygmi.

Neoplasm: Malignant transformation and proliferation of small intestinal cells result in tumours like adenocarcinomas, carcinoids, lymphomas, and leiomyosarcomas. As tumour size increases, they may cause partial or complete mechanical intestinal obstruction from intussusception or volvulus. Intestinal obstruction in turn causes increased and visible peristaltic wave as they try to propel gut content through the obstruction. These increased peristaltic waves give rise to loud borborygmi.

Trauma: Obstruction of the intestine may be caused by scars or adhesions from previous abdominal or pelvic surgeries. These adhesions may form across intestinal loops strapping them down, thus, impairing or obstructing movement of bowel contents. Intestinal obstruction in turn causes increased and visible peristaltic wave as they try to propel gut contents through the obstruction. These increased peristaltic waves give rise to loud borborygmi.

14. CAPUT MEDUSA

Definition: This is a pattern of distended veins radiating from the umbilicus. It results from collateral circulation in the para-umbilical vessels which develops in the presence of portal hypertension causing increased flow resistance within the liver. The restriction of hepatic blood flow leads to diversion or shunting of blood through alternative circulations that by-pass the liver (Fig. 11.1).

Fig. 11.1 Caput medusa

Pathophysiology: The umbilical vein carries oxygenated blood from the mother to fetus *in utero* and normally closes within one week of birth. In portal hypertension, there is increased liver pressure which causes the umbilical vein to become recanalised. Blood is forced to shunt from the liver circulation to the systemic circulation via the collateral umbilical and paraumbilical veins. Because these paraumbilical veins are not naturally equipped to receive such high volumes of blood, they become distended and engorged forming a sunburst pattern of vessels radiating around the umbilicus and thus result in caput medusa. Pathophysiolgic mechanisms that result in caput medusa include the following.

Deranged metabolism: Alcohol, drugs and toxins can lead to acute damage to the hepatocytes. Healing by fibrosis will cause distortion of the channels that carry blood within it. As it becomes more difficult for blood to flow through the liver, pressure builds up in the portal circulation and the body attempts to bypass it by opening up alternative networks of veins. These networks connect the portal system with the systemic circulation and results in caput medusa.

Dysgenesis: In biliary atresia there is obliteration of the biliary tract which results in hepatic inflammation. Hepatocellular injury leads to cell death or necrosis. In response to such injury, hepatocytes and their supportive cells deposit an abnormally thick and dense extracellular connective tissue matrix leading to fibrosis. Fibrosis distorts liver architecture and shunts blood flow. This decompression of the high venous pressure and shunting of portal blood flow through the para-umbilical vessel, portosystemic collateral, results in caput medusa formation.

Inflammation: Infection of the liver with the hepatotrophic viruses, such as hepatitis B and C incites an inflammatory response which may become chronic and persistent. Continuing chronic inflammation with fibrous deposition eventually leads to loss of functional liver cells. Loss of more than 70% of functioning liver cells results in the covert redistribution of splanchnic blood flow, an energy-deficient state, and the failure of multiple secondary organs. Chronic liver injury eventually results in the death of hepatocytes followed by the accumulation of fibrous tissue and cirrhosis. The fibrous tissue distorts the architecture of the liver causing portal hypertension and the development of porto-systemic shunting via collateral para-umbilical vessels; visible on the abdomen as caput medusa.

Neoplasm: Malignant infiltration of the liver either from neoplastic transformation of hepatocytes (hepatocellular carcinoma) or from distant metastasis from other sites, results in parenchymal cell destruction with resultant fibrosis and portal vein obstruction. This results in portal hypertension consequent upon which shunting of blood from the portal vein to the peri-umbilical collateral vessels occur, which is visible as radiating vessels from the umbilicus or caput medusa.

15. CHEILITIS

Definition: This is inflammation and dryness of the lips especially the lower lip, followed by scaling and cracking and accompanied by a characteristic burning sensation. It is usually caused by sensitivity to contact substances (from toys and foods) plus photosensitivity to the sun's rays.

Pathophysiology: Pathophysiologic processes that result in cheilitis include the following.

Deranged metabolism: Oral administration of some drugs (protease inhibitors, vitamin A) and nutritional deficiency of pyridoxine (vitamin B_6) can lead to ulcers on the lips and cheilitis.

Deranged immunology: Atopy or allergy to contact to some substances like lipstick or toothpaste can lead to dryness, ulceration and inflammation of the lips and result in cheilitis.

Inflammation: Inflammation of the lips, which may occur either from excessive salivation or lip licking will result in disruption of the epidermal barrier which in turn leads to dryness, scaling and cracking of the lips causing cheilitis. Bacterial, viral or fungal infection of the mouth can lead to inflammation of the lips which will cause dryness, scaling and fissuring and result in cheilitis.

Trauma: Constant lip licking or biting or moving against a strong wind can lead to dryness and irritation of the lips which will cause inflammation, fissuring and cheilitis

16. CLEFT LIP / PALATE

Definition: This is a fissure or opening on the lip or the palate (Fig. 11.2).

A B

Fig. 11.2 Cleft palate (A) and bilateral cleft lip (B)

Pathophysiology: The pathologic process, which can affect the DS and result in cleft lip/palate is dysgenesis.

Dysgenesis: Maternal drug exposure *in utero*, a syndrome–malformation complex, or genetic factors will lead to hypoplasia of the mesenchymal layer, resulting in a failure of the medial nasal and maxillary processes to join, which will result in cleft lip. Cleft of the palate represents failure of the palatal shelves to approximate or fuse.

17. DENTAL CARIES

Definition: Dental caries results from tooth/teeth decay usually from poor oral hygiene with eventual formation of cavities.

Pathophysiology: Presence of microorganisms in the mouth will lead to production of acid by bacterial fermentation of food debris (fermentable carbohydrates like sucrose, glucose and fructose) and accumulation on the tooth surface which will cause demineralisation and destruction of the hard tissues of the teeth (enamel, dentin and cementum). If demineralisation exceeds saliva and other remineralisation factors, such as calcium and fluoridated toothpastes, these once hard tissues progressively break down, producing dental caries (cavities, holes in the teeth). Pathophysiolgic processes resulting in dental caries include the following.

Deranged immunology: Autoimmune disorders (Sjögren's syndrome) which cause destruction of the salivary glands will lead to reduced production of saliva. Since the buffering capability of saliva is not present to counterbalance the acidic environment created by certain foods, demineralisation of the teeth progresses and result in breakdown and dental caries.

Deranged metabolism: Acidic foods with pH of 5.5 or less will lead to demineralisation (even in the absence of infection) and will result in dental erosion and caries. Medications like antihistamines and antidepressants which reduce the production of saliva from salivary glands will lead to loss of buffering effect of saliva, progressive demineralisation and result in dental caries.

Inflammation: Microorganisms, particularly mutant streptococci, have the ability to adhere to the tooth enamel, produce abundant acid, and survive at low pH which results in inflammation and cavity formation. Once the enamel surface cavitates, other oral bacteria (lactobacilli) colonise the tooth, produce acid, and foster further tooth demineralisation. Demineralisation is worsened in the presence of cariogenic sugar such as sucrose and eventually results in dental caries.

Trauma: Radiation injury which destroys the salivary glands will lead to less production of saliva and since the buffering capability of saliva is not present to counterbalance the acidic environment created by certain foods, there is progressive demineralisation of the hard tissues of the teeth which will result in dental caries.

18. ENTEROCUTANEOUS SINUS

Definition: This is an abnormal communication between the small or large intestine and the skin. As a result, contents of the stomach or intestines leak through to the skin.

Pathophysiology: Damage to the mucosa or intestinal wall will lead to perforation. Leakage of intestinal content will lead to irritation and inflammation, which will lead to breakdown of more tissues, including the skin, thereby result in an abnormal connection between the intestine and the skin. Pathophysiologic processes that result in entero-cutaneous sinus include:

Deranged metabolism: Severe malnutrition will lead to loss of integrity of the intestinal mucosa and wall. This will lead to perforation, leakage of intestinal content and irritation. The ensuing inflammation will lead to breakdown of tissue and formation of an abnormal connection between the intestine and the skin. Also, perforation of a peptic or duodenal ulcer will lead to spillage of intestinal content which will cause inflammation, breakdown of tissue and abnormal connection between the skin and the intestine.

Inflammation: Inflammation of the gut with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD) such as Crohn's disease. The ensuing inflammation results in a thickened and stiff bowel wall. The inflammation extends through all layers of the intestinal wall and may result in abscess formation which may drain externally through the skin causing an entero-cutaneous fistula.

Neoplasm: Colonic cancer may erode the walls of the large intestine and lead to spillage of intestinal content. This causes irritation, inflammation, tissue breakdown and an abnormal connection between the intestine and the skin.

Trauma: Following bowel surgery, there may be anastomotic breakdown which leads to leakage of intestinal content. This causes irritation and inflammation leading to breakdown of tissue and an abnormal connection between the intestine and the skin. Also, abdominal trauma, such as a stabbing or gunshot will create a traumatic enterotomy which will cause an abnormal connection between the intestine and the skin and result in enterocutaneous sinus and fistula.

19. EPULIS

Definition: This is the localised enlargement of the gum. It is usually painless but can be bothersome because of the awareness of bumps in the mouth.

Pathophysiology: Pressure from the flange of a denture causes chronic mechanical irritation. This will lead to formation of a benign hyperplasia of fibrous connective tissue in the gums as a reactive response and result in epulis. Pathophysiolgic processes resulting in epulis include the following.

Inflammation: Inflammation of the oral cavity with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in Crohn's disease. Attempts at repairing tissue damage occur by replacement of nonregenerated parenchymal cells by connective tissue, which in time produces fibrosis. When excess fibrous tissue formation (fibrous hyperplasia) occurs, it causes localised enlargement of the gum or epulis.

Trauma: When the edges of a tooth denture do not fit well, it traumatises the gum causing an overgrowth of tissue around the alveolar vestibule. The excess tissue usually forms a firm and fibrous epulis.

20. FAECAL INCONTINENCE

Definition: This is the loss of control or abnormal control of stool of normal consistency. Partial incontinence is the occasional loss of flatus or loose stool. The anus may be deformed and gaping, and an obvious anatomic defect may be visible and palpable. In other instances the structures appear normal.

Pathophysiology: Bowel function is controlled by multiple factors, including anal sphincter pressure, anorectal sensation, rectal compliance, colonic transit time, and stool volume and consistency. In addition, adequate cognitive function with appropriate ability to access bathroom facilities is necessary for continence. If any of these factors are compromised, incontinence can occur.

The internal anal sphincter (IAS) provides most of the resting anal pressure and is reinforced during voluntary squeeze by the external anal sphincter (EAS), the anal mucosal folds, and the anal endovascular cushions. The ability of the rectum to perceive the presence of stool leads to the rectoanal contractile reflex response, an essential mechanism for maintaining continence. Disruption or weakness of the EAS can cause urge-related or diarrhoea-associated faecal incontinence. Damage to the endovascular cushions may produce a poor anal "seal" and an impaired anorectal sampling reflex. Pudendal nerve injury may also be a mechanism in faecal incontinence. The pudendal nerve innervates the external anal sphincter muscle, anal canal skin, and coordinates reflex pathways such that damage will lead to dysfunction of the external anal sphincter and result in incontinence.

Pathophysiolgic processes resulting in fecal incontinence include the following.

Inflammation: Inflammatory bowel disease may lead to decreased compliance of the rectum and may manifest as faecal urgency, frequency, soilage, or incontinence.

Trauma: Surgical trauma or radiation injury around the pelvis will lead to damage to the pudendal nerve. This will cause diminished rectal sensation and lead to excessive accumulation of stool, causing fecal impaction, megarectum, and faecal overflow. Anal surgery, such as haemorrhoidectomy and sphincterotomy, has been associated with internal sphincter injury and subsequent urgency and incontinence. Also, damage to the puborectalis muscle will lead to disruption of the anal sphincter which may

involve both the external and internal anal sphincters and will result in faecal incontinence.

21. GINGIVITIS

Definition: Gingivitis is a localized or generalised reddening and swelling of the gingiva with clusters of small vesicles. It occurs when poor oral hygiene results in the accumulation of a dental plaque at the tooth gingival interface activating an inflammatory response.

Pathophysiology: Accumulation of microbial plaques in persons with inadequate oral hygiene will lead to an acute exudative inflammatory response. Both gingival fluid and transmigration of neutrophils increase with deposition of fibrin and destruction of collagen. As chronic local inflammation progresses, pockets develop where the gingiva separates from the tooth. Pathophysiolgic processes resulting in gingivitis include the following.

Deranged metabolism: Vitamin C deficiency and some medications which affect oral health may cause abnormal growth of gum tissue and lead to accumulation of bacterial plaque between and around the teeth, which triggers an immune response, which in turn can eventually lead to the destruction of gingival tissue and result in gingivitis.

Inflammation: Bacteria and food deposits adherent to the teeth (plaque) may accumulate, eroding the area where the gum and teeth meet. Incomplete dental care over time may result in this margin becoming inflamed with loss of integrity of vascular membrane, increased bleeding and low grade infections giving rise to gingivitis.

Neoplasm: Cancers involving the oral mucosa will lead to accumulation of bacterial plaque between and around the teeth, which triggers an immune response, which in turn can eventually lead to the destruction of gingival tissue and result in gingivitis.

22. GLOSSITIS

Definition: This is the patchy or complete filiform depapilation of the tongue. The tongue becomes erythematous sometimes with erosive changes or may become completely smooth and atrophic. Affected patient may experience lingual pain and burning sensation.

Pathophysiology: Pathophysiological processes that result in glossitis include the following.

Deranged immunology: Allergic reactions to medications, food, and other potential irritants like toothpaste may aggravate the papillae and the muscle tissues of the tongue and result in inflammation of the tongue and glossitis.

Deranged metabolism: Nutritional deficiencies such as B-group vitamins, iron and folate deficiencies, as well as of protein–calorie malnutrition can lead to glossitis. Chemical irritants and drug reactions can result in erosion of the filiform papillae of the tongue causing glossitis. Iron regulates cell growth by helping the body make red blood cells. Red blood cells carry oxygen to organs, tissues, and muscles. Low iron in the blood may result in low levels of myoglobin, a protein in red blood cells that is important for muscle health, including the tongue's muscle tissue, which can trigger inflammation with depapillation of the dorsal surface of the tongue and result in glossitis.

Inflammation: Infections (especially candidiasis), vesiculo–erosive diseases and some systemic infections can result in depapilation of the tongue. Oral herpes simplex, a virus that causes blisters, may contribute to swelling and pain in the tongue and result in glossitis.

Trauma: Mouth trauma may be caused by burns on the tongue leading to inflammation and glossitis.

23. GUARDING

Definition: This is an involuntary spasm of abdominal muscles on palpation commonly resulting from underlying inflammation of the peritoneum.

Pathophysiology: Inflammation of any abdominal organ will lead to inflammation of the inner abdominal (peritoneal) surface. This will lead to the tensing of the abdominal wall muscles to guard inflamed organs within the abdomen from the pain of pressure upon them. The tensed muscles of the abdominal wall which automatically go into spasm to keep the tender underlying tissues from being disturbed results in guarding. Pathophysiolgic processes resulting in guarding include the following.

Deranged metabolism: Insect toxins from black widow spider and tetanotoxins can lead to spasm of abdominal wall muscles which will result in guarding. Perforation of a peptic ulcer disease will lead to leakage of intestinal content which will cause inflammation of the peritoneum and result in guarding.

Inflammation: Acute inflammation of the peritoneum from bacterial infections or intestinal

contents (including gastric acid, gastrointestinal luminal contents, bile, or pancreatic juice) in the peritoneal cavity results in peritonitis. Secondary peritonitis may also result from any definable cause, such as perforation of a viscus (from acute appendicitis or diverticulitis), perforation of an ulcer (peptic ulcer, Crohn's disease, malignancy), and trauma, including iatrogenic interventions (e.g. surgery, needle biopsies). The peritoneal irritation and inflammation cause abdominal tenderness and eventually abdominal rigidity which is seen as guarding.

Ischaemia: Obstruction of the superior mesenteric vessels will lead to reduced blood supply and mesenteric ischaemia. This will lead to inflammation of the intestine and the peritoneum and will result in guarding. Also, vasospasm of mesenteric vessels in abdominal migraine will lead to an acute abdomen and guarding.

Trauma: Blunt or penetrating abdominal trauma will lead to rupture of abdominal vessels or organs and collection of blood within the abdominal cavity (haemoperitoneum). This will cause irritation and inflammation of the peritoneum and result in guarding. Intestinal surgery with anastomotic leakage will lead to inflammation of the peritoneum and result in guarding.

24. GYNAECOMASTIA

Definition: This is the development of excessive breast tissue in males.

Pathophysiology: Increased oestrogen activity or decreased testosterone activity or the use of numerous medications that alter the functions of these hormones in the males will lead to a benign proliferation of male breast glandular tissue and result in gynecomastia. Pathophysiologic processes that result in gynaecomastia include the following.

Deranged metabolism: The liver is the major site of chemical modification of a wide variety of exogenous drugs and toxins as well as endogenous substances, such as hormones (i.e. biotransformation). The reactions potentially involve numerous pathways and the cytochrome P-450-dependent microsomal mixed function oxidase system. Usually, biotransformation of an endogenous or exogenous substance inactivates it or renders it more suitable for urinary or biliary excretion. Liver diseases, especially if chronic may seriously impair the biotransformation of exogenous substances thus potentiating their actions; or it may enhance the biologic effect of endogenous hormones like oestrogen thus contributing to the feminising effects like excessive breast tissue seen as gynaecomastia. Chronic liver disease results in increased concentration of SHBG. Oestrogens are known to bind less avidly to sex hormone-binding globulin (SHBG) than androgens, such as testosterone. As a result, there is alteration of the oestrogen/testosterone equilibrium in the body in favour of oestrogens. This will lead to decreased bioavailable testosterone relative to free oestrogens and will result in gynaecomastia.

25. HALITOSIS

Definition: This is a malodorous emission from the mouth.

Pathophysiology: The mouth is home to hundreds of bacterial species with various nutritional preferences. Microbial metabolism of protein leads to production of foetid substances like volatile sulphur compounds in the mouth which cause halitosis (bad breath). Pathophysiolgic processes resulting in halitosis include the following.

Deranged metabolism: Liver cirrhosis is the end result of chronic injury to hepatocytes from a variety of causes (haemochromatosis, Wilson's disease, etc.). It occurs when injured hepatocytes and their supportive cells, such as the stellate cells deposit an abnormally thick and dense extracellular connective tissue matrix leading to fibrosis. Fibrosis in turn distorts the liver architecture. As the damage continues, compensatory overgrowth of liver tissue occurs to form regenerative nodules. The fibrosis and regenerative nodules impedes hepatic blood flow eventually resulting in portal hypertension and shunting of blood via collateral abdominal circulation. The capacity of the liver to detoxify or metabolise substances, such as ammonia is also reduced and ammonia and thiols accumulate and pass directly into the systemic circulation due to the portosystemic shunts. In the pulmonary circulation, the ammonia emits malodorous breath.

Inflammation: Infection of the upper respiratory tract inclusive of the oropharynx by bacteria results in the production of fatty acids and malodsterous compounds. Production of these compounds is from anaerobic respiration of such bacteria and can yield either the putrescent smell of indoles and polyamines or the "rotten egg" smell of volatile sulphur compounds such as hydrogen sulphides.

Neoplasm: Primary malignant transformation of cells of the oral cavity or local infiltration of malignant cells from contiguous structures will result in tumour formation. With progression, the rapidly enlarging cells out strips their blood supply resulting in ulceration and cell necrosis. With necrosis, there is production of dimethyl trisulphide which causes malodorous emissions from the mouth.

26. HEMORRHOIDS

Definition: Haemorrhoids are varicosities in the superior or inferior haemorrhoidal venous plexus, which results from increased intravenous pressure, causing distension and engorgement of the veins. Dilation and enlargement of the superior plexus of the superior haemorrhoidal veins above the dentate line cause internal haemorrhoids. Enlargement of the plexus of the inferior haemorrhoidal veins below the dentate line causes external haemorrhoids, which may protrude from the rectum.

Pathophysiology: Haemorrhoid cushions are sinusoids which lack muscle tissue in their walls. Any condition which increases intra-abdominal pressure like bearing down during daefecation will lead to increase in venous pressure and distension of the haemorrhoid cushions. This leads to stretching of the suspensory muscles which cause the haemorrhoid cushions to slide downwards with eventual prolapse of rectal tissue through the anal canal and result in haemorrhoids. Pathologic processes that result in hemorrhoids include the following.

Deranged metabolism: Diets low in fibre can result in constipation or passage of hard stool. If the condition is not remedied, the recurrent strain necessary to defaecate hard stools may eventually result in increase in intravenous pressure of the hemorrhoidal venous plexus causing them to distend and eventually prolapse as haemorrhoids.

Inflammation: Infections involving the liver will lead to damage to the hepatic cells which heal by fibrosis. This will lead to disruption of the hepatic architecture, blockage of blood flow and portal hypertension. The increased venous pressure will lead to engorgement of the haemorrhoid cushion which can prolapse and result in hemorrhoid.

Neoplasm: Colon malignancy will lead to increase intraluminal pressure which will reduce venous return leading to increased venous pressure. This will lead to distension of the haemorrhoid cushion which can prolapse and form haemorrhoids.

27. HEPATOMEGALY

Definition: This is an increase in the liver span that may be detected clinically as a palpable enlargement of the liver below the right costal margin.

Pathophysiology: Accumulation of substances within the liver which leads to swelling of the liver beyond its normal size will result in hepatomegaly. Pathophysiolgic processes resulting in hepatomegaly include the following.

Deranged metabolism: Certain metabolic conditions, such as obesity, protein–energy malnutrition, corticosteroid therapy, diabetes mellitus, and ethanol ingestion may cause an imbalance between the rate of triglyceride biosynthesis and secretion into the plasma, leading to excess accumulation of triglyceride in the liver (fatty liver). The deposition of fat if persistent will eventually result in enlargement of the liver or hepatomegaly.

Dysgenesis: Mutations in the alpha-1-antitrypsin gene (A1 AT gene) can lead either to single amino acid substitutions or more extensive frame shifts or deletions. This causes a deficiency in alpha1-antitrypsin glycoprotein whose primary function is to inhibit neutrophil elastase. The mechanism of liver injury in this disease is unknown but eventually results in cholestasis and cirrhosis with palpable hepatomegaly.

Several different mutations in the Wilson's disease gene (WND) gene on chromosome 13 causes Wilson's disease, an autosomal recessive disorder characterised by accumulation of copper in the liver and other organs. WND encodes a copper-transporting adenosine triphosphatase that is expressed predominantly in liver and kidney; when a mutation occurs, there is impaired biliary excretion of copper leading to accumulation of copper in the liver. The accumulating copper results in postnecrotic cirrhosis with hepatic dysfunction and portal hypertension and palpable haepatomegaly. Autosomal recessive inheritance of a mutation in the HFE C282Y gene on chromosome 6 results in hereditary hemochromatosis. The mutation causes absorption of excessive amounts of iron from the gut which is subsequently deposited in the liver and many other body organs. In the liver, it results in iron overload and injury to hepatocytes. Iron accumulation in the liver is progressive from birth and eventually result in hepatomegaly. Glycogen storage diseases are inherited disorders of glycogen metabolism due

to various enzyme deficiencies. Because glycogen is stored in the liver, there is excessive accumulation of hepatic glycogen leading to hepatomegaly.

Inflammation: Infection of the liver with the hepato-trophic viruses, such as hepatitis B, D and C incites an inflammatory response, which may become chronic and persistent. The damages caused by the continued inflammation may eventually lead to chronic inflammation, followed by the accumulation of fibrous tissue and cirrhosis. The inflammatory reaction and fibrous deposition eventually leads to hepatomegaly.

Focal areas of bacterial infection within the hepatic parenchyma can result in inflammation with purulent discharge and may result in the formation of pyogenic liver abscesses. The underlying inflammation will result in a tender hepatomegaly on palpation.

Ischaemia: Hepatic vein thrombosis or blockage of the small veins in the liver will lead to pooling of blood within the liver parenchyma and result in hepatomegaly.

Neoplasm: Malignant transformation of hepatocytes may result in hepatocellular carcinoma (or hepatoma). As the tumor mass increases, it causes an increase in liver size which is detectable as hepatomegaly.

28. HERNIA

Definition: A hernia is a protrusion of an organ or structure into an opening or pouch. Abdominal wall hernias protrude through the retaining walls of the abdomen and have two parts: the orifice or defect in the aponeurotic wall of the abdomen, and the hernia sac, which consists of peritoneum and abdominal contents. Hernias are reducible when the protruding organ can be returned back to the abdomen and irreducible or incarcerated when it cannot. A hernia is strangulated when the vascular supply of the protruding organ is compromised and the organ becomes ischaemic or necrotic as a consequence

Pathophysiology: Defects or weakness in fascia or muscle or persistence of the process vaginalis in the inguinal canal will lead to protrusion of part of the intestine when intra-abdominal pressure is increased and will result in hernia. Pathologic processes that result in hernia include the following.

Degeneration: Chronic muscle weakness and deterioration of connective tissue (due to ageing, systemic disease, malnutrition, or smoking) may lead to herniation of abdominal content through the weakened abdominal muscles causing hernia.

Deranged metabolism: Chronically increased intra-abdominal pressure may result from obesity and ascites. Eventually, the sustained increased abdominal pressure may result in umbilical hernia.

Dysgenesis: Congenital areas of weakness or defects in the abdominal wall will result in hernias. These areas of weakness of the abdominal wall occur in areas where the fascia is devoid of the protective support of muscle. In the groin, there is such an area bounded by the rectus abdominal muscle medially, the ileo psoas muscle laterally, the pubic ramus inferiorly, and the aponeurosis of the transverse abdominal muscle superiorly. In this area, the external and internal oblique muscles thin to a fascial aponeurosis only, so that there is no muscular support of the transverse abdominal fascia and the peritoneum. Upright posture causes intra-abdominal pressure to be directed to this area and cause hernia development.

During embryologic development, the spermatic cord and testis in men (the round ligament in women) migrate from the retroperitoneum through the anterior abdominal wall to the inguinal canal along with a projection of peritoneum (called processus vaginalis). The defect in the abdominal wall (internal inguinal ring) associated with this process represents an area of potential weakness through which abdominal content like omentum, small bowel and colon may pass through to form an indirect inguinal hernia. The Hesselbach's triangle is an area of defect bounded by the rectus abdominis muscle, the inferior epigastric artery, and the inguinal ligament. Protrusion of abdominal content, such as the omentum, colon, small bowel, and bladder through this defect results in the formation of a direct inguinal hernia (which does not pass through the internal inguinal ring). Abdominal contents like omentum, colon and small bowel may protrude through the opening associated with the femoral artery and vein, forming a femoral hernia. They present inferior to the inguinal ligament and medial to the femoral artery. Congenital umbilical hernias may also occur in some infants.

Trauma: Incisional hernias may develop after surgeries, such as laparotomies producing post laparotomy hernias. Most cases arise when surgical wounds are complicated by infections or dehiscence.

29. IMPEFORATE ANUS

Definition: Imperforate anus is a defect that is present from birth in which the opening to the anus is missing or blocked.

Pathophysiology: The pathologic process, which can affect the "DS" and result in imperforate anus is dysgenesis.

Dysgenesis: The anus develops by a fusion of the anal tubercles and an external invagination, known as the proctodeum, which deepens toward the rectum but is separated from it by the anal membrane. This separating membrane should disintegrate at 8 weeks' gestation. Interference with anorectal structure development at varying stages leads to various anomalies, ranging from anal stenosis, incomplete rupture of the anal membrane, or anal agenesis to complete failure of the upper portion of the cloaca to descend and failure of the proctodeum to invaginate, which will result in imperforate anus.

30. JAUNDICE

Definition: This is the yellowish pigmentation of the skin and sclera caused by an excess accumulation of bilirubin in the blood. Jaundice occurs when bilirubin levels exceed 34–43 mmol/l.

Pathophysiology: Bilirubin is a product of red blood cell breakdown and accumulates when production exceeds metabolism and excretion, either due to excessive release of bilirubin precursors into the bloodstream or from impairment of its hepatic uptake, metabolism, or excretion. Pathophysiologic processes that result in jaundice include the following.

Deranged immunology: Immune-mediated disorder of unknown cause may result in chronic hepatic inflammation and end stage liver disease (autoimmune liver diseases). With disease progression, there is damage to hepatocytes and biliary system which will result in impaired metabolism of bilirubin and the development of jaundice.

Dysgenesis: A mutation in the promoter region of UGT-1 gene causes a reduction in the transcription rate of the gene and as such deficient quantities of bilirubin–uridine glucuronyl transferase enzyme, and its activity (Gilbert's syndrome). This enzyme is required for conjugation of bilirubin, as such its deficiency leads to unconjugated hyperbilirubinaemia and jaundice. Other mutations in the coding region of HUG-Br1 result in complete absence of UGT-1 activity (Crigler-Najjar syndrome). These result in the inability to conjugate bilirubin and severe hyperbilirubinemia, which is seen clinically as jaundice. A delay in the developmental expression of bilirubin UGT-1 causes a transient impairment of bilirubin metabolism with accumulation of bilirubin in the blood leading to physiologic jaundice.

The absence of canalicular expression of a multi-specific organic anion transporter results in decrease in bilirubin secretion into the bile canaliculus and may produce conjugated or mixed hyperbilirubinaemia and jaundice (Dubin-Johnson syndrome). In Rotor's syndrome, there is also a decrease in bilirubin secretion into the biliary canaliculus but the molecular basis of this is unknown. The direct bilirubin level is elevated and causes jaundice. Mutations in the alpha-1-antitrypsin gene (A1 AT gene) can lead either to single amino acid substitutions or more extensive frame shifts or deletions. This causes a deficiency in alpha1-antitrypsin glycoprotein whose primary function is to inhibit neutrophil elastase. In the liver, there is injury to hepatocytes, which eventually results in cholestasis and cirrhosis. The cholestasis is manifested clinically as jaundice. Several different mutations in the Wilson's disease (WND) gene on chromosome 13 cause Wilson's disease–an autosomal recessive disorder characterised by accumulation of copper in the liver and other organs. WND encodes a copper-transporting adenosine triphosphatase that is expressed predominantly in liver and kidney; when a mutation occurs, there is impaired biliary excretion of copper leading to accumulation of copper in the liver, which ultimately results in postnecrotic cirrhosis, with hepatic dysfunction and impaired ability to metabolise bilirubin causing jaundice. Autosomal recessive inheritance of a mutation in the HFE C282Y gene on chromosome 6 results in hereditary haemochromatosis. The mutation causes absorption of excessive amounts of iron from the gut which is subsequently deposited in the liver and many other body organs. In the liver, it results in iron overload and injury to hepatocytes, impairment in bilirubin metabolism and as such, jaundice. Glycogen storage diseases are inherited disorders of glycogen metabolism due to various enzyme deficiencies. Because glycogen is stored in the liver, there is excessive accumulation of hepatic glycogen which impairs the ability of the liver to metabolise bilirubin leading to jaundice.

Deranged metabolism: Toxic levels of the analgesic and antipyretic drug like acetaminophen may occur from inadvertent therapeutic overdose, frequent

dosing with over-the-counter and prescription combination drugs that contain acetaminophen, and during suicide attempts. Acetaminophen is a dose-dependent hepatotoxin and toxic levels cause zonal necrosis and acute liver failure. The liver injury is caused by a toxic metabolite of acetaminophen formed by the cytochrome P-450-dependent drug-metabolising system. Below threshold doses, this metabolite is efficiently detoxified by conjugation with glutathione. In the toxic dose range, glutathione stores are rapidly exhausted and the metabolite reacts with essential cellular constituents, leading to cell dysfunction with rapid progression to acute hepatic failure and jaundice.

Inflammation: Infection of the liver with the hepatotrophic viruses, such as hepatitis B, D and C incites an inflammatory response which may become chronic and persistent. The damages caused by the continued inflammation may eventually lead to chronic inflammation and fibrosis with progressive loss of functional liver cells. Chronic liver injury eventually results in the death of hepatocytes with progressive impairment of hepatic synthetic and metabolising function, including impairment in bilirubin metabolism, hyperbilirubinaemia and jaundice.

Neoplasm: Hepatocellular carcinoma, or hepatoma, is an epithelial tumor arising from malignant transformation of the hepatocyte. As the tumour mass increases it encroaches or invades the hepatocytes and biliary tract leading to obstructive jaundice. Malignant transformation and proliferation of small intestinal cells result in tumours like adenocarcinomas, carcinoids, lymphomas, and leiomyosarcomas. As tumour size increases, they may cause partial or complete mechanical intestinal obstruction from intussusception or volvulus.

If the malignancy spreads to involve the peri-ampullary region, it may block the common bile duct and as such obstruct bile and bilirubin flow into the gut leading to obstructive jaundice.

Trauma: Traumatic damage to the liver will lead to impaired hepatic function which will lead to defective bilirubin uptake, metabolism and excretion and will result in accumulation of bilirubin and jaundice.

31. LEUCOPLAKIA

Definition: This is the formation of white firm smooth patches at the sides of the tongue. The mucosa is white and irregularly thickened but remains soft. Spread may occur occasionally to the ventral tongue surface, the floor of the mouth, the tonsillar pillars, and the pharynx.

Pathophysiology: Thickening of the keratin layer (hyperkeratosis) or thickening of the stratum spinosum (acanthosis) will lead to masking or hiding of normal pink-red color of mucosae (the result of underlying vasculature showing through the epithelium). This makes the abnormal keratin to appear white when it becomes hydrated by saliva, and light reflects off the surface evenly. Patho-physiologic processes that result in leucoplakia include the following.

Deranged metabolism: Iron deficiency, some vitamin deficiencies will lead to mucosal atrophy which will cause keratosis and result in leucoplakia.

Dysgenesis: The *DKC1, TERT, TERC, NOP10* genes encode proteins in the telomerase complex responsible for maintaining telomeres at the ends of chromosomes and helps stabilise the chromosomes. Telomerase dysfunction has been found to be associated with dyskeratosis congenital syndrome (DKC) and makes the tongue prone to irritation which results in the development of leukoplakia.

Inflammation: Infection of the basal epithelial cells of the oropharynx by Epstein-Barr virus (EBV), especially among immune suppressed hosts is usually followed by latent infection, where the virus enters B cells and persists indefinitely. Cytotoxic T lymphocytes cannot eliminate EBV from the body, but they are essential in maintaining the latent state of the infection which causes infection in the oropharynx with formation of leucoplakia patches.

32. MACROGLOSSIA

Definition: This is an abnormally large tongue.

Pathophysiology: Dilation of lymphatics, muscle hypertrophy or inflammation involving the tongue will lead to enlargement of the tongue, which will result in macroglossia. Pathophysiologic processes that result in macroglossia include the following.

Deranged immunology: Allergic reactions to drugs or toxins from insects will lead to release of histamine which can lead to increased vascular permeability, swelling and enlargement of the tongue which will result in macroglossia.

Dysgenesis: Genetic abnormalities of the distal region of chromosome arm 11p have been found to be associated with Beckwith-Wiedemann syndrome.

There is fetal hyperinsulinaemia and hyperglycaemia which result in increased hepatic glucose uptake and glycogen synthesis, accelerated lipogenesis, and augmented protein synthesis. The increased protein synthesis results in hypertrophy and hyperplasia of the foetal tissues and infant organs like the tongue causing macroglossia.

Neoplasm: Congenital tumours involving the tongue (haemangioma, lymphangioma) will lead to the enlargement of the tongue and result in macroglossia.

Trauma: Direct trauma to the tongue will lead to localized oedema and enlargement causing macroglossia.

33. ORAL THRUSH

Definition: Oral thrush is a whitish plaque covering all or part of the oropharyngeal mucosa and usually results from oro-pharyngeal infection with the fungus, *Candida albicans*. These plaques are removable from the underlying surface, which is characteristically inflamed with pinpoint haemorrhages. The diagnosis is confirmed by direct microscopic examination on potassium hydroxide smears and culture of scrapings from lesions (Fig. 11.3).

Fig. 11.3 Oral thrush

Pathophysiology: Disruption of the normal host immunity or normal host flora will lead to overgrowth of *Candida albicans* on the oral mucosa, which leads to desquamation of epithelial cells and accumulation of bacteria, keratin and necrotic tissue. This debris combines to form a pseudo-membrane, which may closely adhere to the underlying mucosa. Pathophysiologic processes that result in oral thrush include the following.

Deranged metabolism: Prolonged ingestion of antibiotics or steroids or severe malnutrition will lead to disruption of the normal host immunity or normal host flora. This will lead to overgrowth of yeast on the oral mucosa and result in oral thrush.

Inflammation: *Candida* invasion of the stratified squamous epithelium of the oral mucosa occurs when the fungus adheres to the tissues using its surface adherence molecules. It invades the tissue and eventually transits from yeast to hyphal forms which ultimately spear their way out of cells that engulf them. In time, this process results in considerate deposits of superficial white patches and oral thrush.

34. PALLOR

Definition: This is paleness (or whiteness) of the body commonly observed in the palms, soles of feet, palpebral conjunctiva and buccal mucosa. It is usually due to a reduction in red blood cells (RBC) and hemoglobin content of blood.

Pathophysiology: Reduction in red blood cells (RBC) and haemoglobin content of blood will lead to reduced amount of oxyhaemoglobin in the skin and mucous membrane and result in pallor. Pathological processes that result in pallor include the following.

Deranged metabolism: Deficiency of iron or vitamin C which is required for the formation of red blood cells will lead to a reduction in the RBC, reduced amount of oxyhaemoglobin in the skin and mucous membrane and result in pallor. Also lead poisoning will lead to defective erythropoiesis, reduced RBCs, reduced amount of oxyhaemoglobin in the skin and mucous membrane and result in pallor.

Inflammation: Infestations with hook worm will lead to chronic blood loss which will cause reduced haemoglobin concentration and pallor.

Neoplasm: Malignant transformation and proliferation of gastric cells result in gastric carcinoma. As the tumour mass increases, they form an intramural mass with central ulceration and bleeding into the GI tract causing chronic blood loss and anaemia which is observed as varying degrees of pallor. Other benign gastric tumours like Leiomyomas, lipoma, neurofibroma, lymphangioma, ganglioneuroma, and hamartoma can also grow into the lumen with secondary ulceration and bleeding leading to pallor.

Trauma: Traumatic injury to the abdomen will lead to bleeding into the intra-abdominal cavity or intra-abdominal organs. This will lead to reduced intravascular volume of blood and results in pallor.

35. PALMAR ERYTHEMA

Definition: This is the reddening of the skin on the palmar aspects of the hand, most noticeable over the thenar and hypothenar eminences and the tip of the fingers (Fig. 11.4).

Fig. 11.4 Palmar erythema over the thenar and hypothenar eminences

Pathophysiology: Palmar erythema can result from many pathophysiological mechanisms which include increased cardiac output, capillary dilatation in the palms, excessive production of red blood cells, localised inflammation, high circulating oestrogen and toxic dermatological reaction. Patho-physiologic processes that result in palmar erythema include the following.

Deranged metabolism: Damage to the hepatocyte from chronic liver injury occurs in chronic liver diseases. The damaged hepatic cells lose the ability to inactivate oestrogen. In addition, impaired hepatic removal of androstenedione in the circulation provides more substrate for its peripheral conversion to oestrogen. It is thought that excess oestrogen causes vasodilation and increased blood flow which in turn may cause palmar erythema.

Inflammation: Infection with coxsackie A virus that causes hand, foot and mouth disease will lead to capillary dilatation in the palms, localised inflammation and result in palmar erythema.

36. PNEUMOPERITONEUM

Definition: This is the presence of gas in the peritoneal cavity. It can be elicited by obtaining a tympanitic percussion note in the abdomen, even over solid organs such as the liver, and indicates a viscus perforation.

Pathophysiology: Perforation of an abdominal viscus or bowel will lead to escape of gas into the peritoneal cavity and result in pneumoperitoneum. Pathophysiologic processes that result in pneumo-peritoneum include the following.

Deranged metabolism: Gastric erosion from gastric juice may result in gastric perforation and pneumoperitoneum.

Inflammation: Various bacterial and viral agents, including *Escherichia coli*, *Klebsiella spp*, *Clostridium perfringens*, *Staphylococcus epidermidis*, and rotavirus may cause inflammation of the gastrointestinal tract. This results in superficial mucosal ulcerations and submucosal edema and haemorrhage leading to transmural coagulation necrosis and perforation. Intestinal perforation results in leakage of intestinal gas into the peritoneal cavity causing pneumo-peritoneum.

Ischaemia: Obstruction of the superior or inferior mesenteric arteries will lead to reduced blood supply to the intestines. Eventually, the ischaemia will result in infarction, necrosis and perforation of the intestine. This will result in gas in the peritoneal cavity.

Trauma: Trauma to any part of the gastrointestinal tract either by a blunt or penetrating injury may result in perforation of viscus (e.g. the bowels) and leakage of gas into the peritoneal cavity with resultant pneumo peritoneum.

37. PRURITUS ANI

Definition: Pruritus ani is perianal itching from a variety of causes. Examination finding may be normal, or there may be moist, macerated, excoriated perianal skin.

Pathophysiology: Moisture, pressure and rubbing caused by clothing and sitting and intestinal parasites or yeast cause irritation. Pathophysiologic processes that result in pruritus ani include the following.

Inflammation: Infestation with the eggs of the pin worm *Enterobius vermicularis* (usually from foeco-oral route) results in their hatching into larvae form within the human's stomach and duodenum. The larvae then migrate to the ileum and caecum where they mature into adult worms. After copulation in the caecum, the pregnant female pinworm migrates from the caecum to the anus and deposits her eggs on the perianal skin (at which point the female pinworm usually dies). The perianal egg deposition incites

a mucosal mastocytosis response, which causes itchiness around the anal region or pruritus ani.

Deranged metabolism: Oral antibiotics, systemic diseases (e.g. diabetes), poor or excessively zealous hygiene, warmth and moisture or dietary intolerance (coffee, cola, tomatoes, chocolate) can result in mucosal irritation or overgrowth of opportunistic fungi such as *Candida spp*, which causes itchiness around the anus (pruritus ani).

38. REBOUND TENDERNESS

Definition: This is abdominal pain detected during physical examination that is identified over an area of inflammation when pressure is released.

Pathophysiology: Stretching or moving will lead to the stimulation of the stretch receptors in the peritoneum. If there is irritation of the peritoneum in the anterior abdominal wall, the stretch will lead to aggravation of the inflamed parietal layer of the peritoneum and result in rebound tenderness. Pathophysiologic processes that result in rebound tenderness include the following.

Inflammation: Acute inflammation of the peritoneum from bacterial infections or intestinal contents (including gastric acid, gastrointestinal luminal contents, bile, or pancreatic juice) in the peritoneal cavity results in peritonitis. Secondary peritonitis may also result from any definable cause, such as perforation of a viscus (from acute appendicitis or diverticulitis), perforation of an ulcer (peptic ulcer, Crohn's disease, malignancy), and trauma, including iatrogenic intervention (e.g. surgery, needle biopsies). The peritoneal irritation and inflammation causes a generalised abdominal tenderness with rebound tenderness on releasing pressure on the examining hand.

Trauma: Abdominal injury will lead to bleeding into the peritoneum which will cause inflammation of the parietal layer of the peritoneum and result in rebound tenderness.

39. RECTAL PROLAPSE/PROCIDENTIA

Definition: Rectal prolapse is the exteriorisation of the rectal mucosa through the anus. When this extrusion includes all the layers of the rectal wall, it is called procidentia.

Pathophysiology: Defect in the pelvic fascia will lead to herniation of the rectal mucosa through the weak point and results in rectal prolapse. Loosening and stretching of the connective tissue attachments of the rectal mucosa will allow the tissue to prolapse through the anus. Also, invagination of the upper part of the rectum into the lower rectum will lead to protrusion of the rectum beyond the anal verge when intrabdominal pressure increases as occurs during straining. Pathophysiolgic processes that result in rectal prolapse/procedentia include the following.

Inflammation: Intestinal infections (bacterial, viral or parasitic) which leads to rapid intestinal transit time and straining will lead to stretching and weakness of the supportive connective tissue attachments which will result in rectal prolapse.

Trauma: Previous rectal surgery will lead to weakness of the connective tissue attachments which will result in rectal prolapse. Also previous pelvic trauma/lumbar disc trauma will lead to damage to the pudendal nerve, which will lead to weakness of the connective tissue attachments which will result in rectal prolapse.

40. SPIDER ANGIOMATA

Definition: This is a type of telangiectasia found slightly beneath the skin surface often containing a central red spot and reddish extensions, which radiates outwards like a spider's web. The central red spot is the dilated arteriole while the red "spider webs" are small veins carrying away the freely flowing blood. This occurs on the upper trunk and face, and except for the setting of pregnancy, may signal the presence of chronic liver disease (Fig. 11.5).

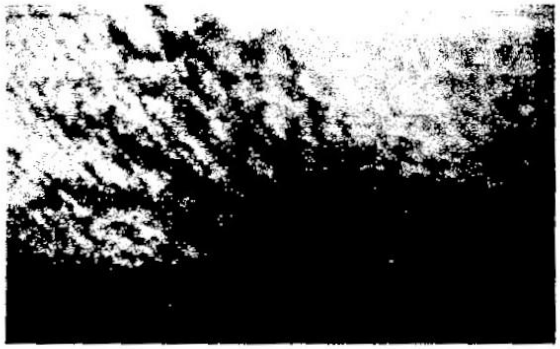

Fig. 11.5 Spider angiomata

Pathophysiology: Failure of the sphincteric muscle surrounding a cutaneous arteriole will lead to dilation of the arteriole (the central red spot) and development of small veins which carry away the freely flowing blood (red "spider legs"). Pathological processes resulting in spider angiomata include the following.

Deranged metabolism: Damage to the hepatocyte from chronic liver injury occurs in chronic liver diseases. The damaged hepatic cells lose the ability to inactivate oestrogen. In addition, impaired hepatic removal of androstenedione from the circulation provides more substrate for its peripheral conversion to oestrogen. It is thought that excess oestrogen causes vasodilation (the central red spot) and increased blood flow, which causes prominence of the venous drainage (the web) seen as spider angiomata in superficial skin.

41. SPLENOMEGALY

Definition: This is an increment in the size of the spleen, which is clinically detected as splenic enlargement below the left costal margin.

Pathophysiology: The spleen plays an active role in immunosurveillance and haematopoiesis. Exaggerations of the normal splenic function (increased haemolysis, excessive immune response) or accumulation of substances within the splenic parenchyma will lead to hypertrophy of the spleen, enlargement of the spleen and result in splenomegaly. Pathophysiologic processes that result in splenomegaly include the following.

Inflammation: Infection of the liver with the hepatotrophic viruses, such as hepatitis B and C incites an inflammatory response, which may become chronic and persistent. Chronic liver injury eventually results in the death of hepatocytes followed by the accumulation of fibrous tissue, cirrhosis and portal hypertension. Increased portal pressure in cirrhosis primarily results from increased resistance to blood flow through the shrunken, fibrotic liver, due to obstruction to flow by extracellular matrix as well as from dynamic organ and sinusoidal contraction by the activated stellate cells. Inability of venous flow within the liver results in back pressure within the portal venous system and damping of blood in the spleen with splenic congestion leading to splenomegaly.

Ischaemia: Splenic vein thrombosis will lead to ischaemia and congestion within the spleen and result in splenomegaly.

Neoplasm: infiltration of the spleen with cancer cells will lead to enlargement of the spleen and results in splenomegaly.

Trauma: Blunt abdominal injury will lead to bleeding into the splenic capsule and will result in slenomegaly.

42. STRIAE

Definition: These are linear wrinkled plaques on the skin, which result when gross stretching of the abdomen causes rupture of elastic fibre within the abdominal skin.

Pathophysiology: Rapid overstretching of the skin associated with rapid growth will lead to tearing of the dermis and the epidermis. Inability of the fibroblasts to form collagen and elastin fibres necessary to keep rapidly growing skin taut will create a lack of supportive material. As the skin is stretched and leads to dermal and epidermal tearing, it will result in reddish or purple lines, which gradually fade into lighter colours. Patho-physiologic processes that result in striae include the following.

Deranged metabolism: Prolonged exposure to high levels of exogenous steroid will result in excess circulating glucocorticoid hormones. Glucocorticoid hormones prevent fibroblasts from forming collagen and elastin fibres, necessary to keep rapidly growing skin taut. This results in skin distension, which in turn, leads to excessive mast cell degranulation with subsequent damage of collagen and elastin. This creates a lack of supportive material as the skin is stretched, leading to dermal and epidermal tearing and ultimately, formation of striae.

43. VARICEAL HEMORRHAGES

Definition: The portal circulation is a low-pressure system (<10 mm Hg) formed by the venous drainage from intra-peritoneal viscera, including the luminal gastrointestinal tract, spleen, gallbladder, and pancreas. Veins collecting from these sites form the splenic vein and superior and inferior mesenteric veins, which, in turn, merge to create the portal vein. Portal hypertension occurs when portal venous pressure exceeds the pressure in the nonportal abdominal veins (e.g. inferior vena cava) by at least 5 mmHg; portosystemic collateral vessels develop in an effort to equalise pressures between these two venous systems. These collateral vessels, or varices, most commonly develop in the oesophagus and proximal stomach and rectum, and can cause clinically significant bleeding or variceal hemorrhages. Oesophageal variceal haemorrhage typically occurs as painless, large-volume haematemesis or melaena with minimal abdominal pain and may be accompanied by signs of significant volume depletion, such as orthostasis and pallor.

Pathophysiology: Pathological processes that result in variceal haemorrhages include the following.

Inflammation: Infection of the liver with the hepatotrophic viruses, such as hepatitis B and C incites an inflammatory response, which may become chronic and persistent. Chronic liver injury eventually results in the death of hepatocytes followed by the accumulation of fibrous tissue, cirrhosis and portal hypertension. Increased portal pressure in cirrhosis primarily results from increased resistance to blood flow through the shrunken, fibrotic liver, due to obstruction to flow by extracellular matrix as well as from dynamic organ and sinusoidal contraction.by the activated stellate cells. When portal venous pressure exceeds the systemic venous pressure, porto-systemic collateral vessels develop in an effort to equalize pressures between these two venous systems and may cause variceal hemorrhages.

Ischaemia: Portal hypertension may arise from presinusoidal obstruction, either outside (e.g. portal vein thrombosis) or within the liver (e.g. schistosomiasis). When portal venous pressure exceeds the systemic venous pressure, portosystemic collateral vessels develop in an effort to equalize pressures between these two venous systems. These collateral vessels may result in variceal haemorrhages.

44. WEIGHT LOSS

Definition: This is the reduction in body mass below the normal for age and sex.

Pathophysiology: Pathophysiolgic processes resulting in weight loss include the following.

Deranged metabolism: inadequate food intake either from non-availability of food or from pain arising from sores in the mouth or from anorexia will lead to deficiency of macronutrients in the presence of continued catabolism. This will result in weight loss.

Inflammation: Inflammation of the intestine with infiltration of the lamina propria by lymphocytes, macrophages, and other cells of the immune system occurs in inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis. IBD is a relapsing and remitting disease and the ensuing inflammation causes recurrent or chronic diarrhea which over time result in significant loss of macro- and micronutrients and weight loss. Gallstones may cause pancreatitis by impacting in the ampulla of Vater. Persistent stone impaction can cause severe pancreatitis combined with ascending cholangitis. The ensuing inflammation causes escape of activated enzymes from acinar cells and pancreatic ducts and set the stage for the autodigestive process that represents acute pancreatitis. The pain from the ensuing inflammation causes anorexia with reduced food intake which over time results in weight loss.

Neoplasm: Malignant transformation and proliferation of gastric cells result in gastric carcinoma. As the cancer advances, malabsorption occur causing weight loss. Malignant transformation and proliferation of small intestinal cells result in tumours like adenocarcinomas, carcinoids, lymphomas, and leiomyosarcomas. The duodenum is the most frequently affected site and when the peri-ampullary region is involved, it may cause obstructive jaundice and malabsorption leading to weight loss. Hepatocellular carcinoma, or hepatoma, is an epithelial tumor arising from malignant transformation of the hepatocyte. As the tumour mass increases, it may invade or compress the biliary tract leading to obstruction and inability of digestive enzymes to access the gut causing malabsorption, nutrient loss and eventual weight loss.

Trauma: Surgical excision of a considerable length of the intestine will cause a short bowel syndrome. This will lead to malabsorption, intestinal hurry, loss of nutrients and will result in weight loss.

45. XANTHOMATA AND XANTHELASMAS

Definition: Xanthoma is the deposition of yellowish cholesterol rich material in tendons or other parts of the body. It is a cutaneous manifestation of lipids in large foam cells within the skin. Xanthelasma, a type of xanthoma, is a sharply demarcated yellowish deposit of cholesterol under the skin, usually on or around the eyelids.

Pathophysiology: Pathological processes resulting in xanthomata and xanthelasma include the following.

Deranged metabolism: The liver is primarily responsible for removing cholesterol from the body by its direct secretion into bile or its conversion to bile acids. In cholestasis, the serum concentrations of unesterified cholesterol and phospholipids increase. A major fraction of the increased plasma unesterified cholesterol is accounted for by an abnormal low-density lipoprotein designated LpX. Severe sustained increase in LpX result in the deposition of cholesterol within the skin forming xanthomas and xanthelasma.

Dysgenesis: Defect of LDL receptors or lipoprotein lipase deficiency or apolipoprotein C-II deficiency results in the body's inability to properly utilise circulating LDL cholesterol. This results in elevated serum LDL cholesterol which is deposited in tendons, eyelids and other parts of the body forming xanthomas and xanthelasma.

46. XEROSTOMIA

Definition: Xerostomia is dryness of the mouth from a variety of causes.

Pathophysiology: Change in the composition of saliva or reduced salivary flow will lead to dryness of the mouth and result in xerostomia. Pathological processes that results in xerostomia include the following:

Degeneration: Degeneration of the salivary glands with aging will lead to reduced production of saliva and result in dry mouth.

Deranged immunology: Autoimmune damage to the salivary glands (Sjogren's syndrome) will lead to hyposalivation which will lead to dry mouth and result in xerostomia.

Deranged metabolism: Anticholinergics or sympathomimetic drugs reduce the production of saliva from the salivary glands and will result in dry mouth and xerostomia.

Inflammation: Enteric pathogens may infect the GI tract and incite an inflammatory reaction which may result in destruction and loss of enterocytes (gastroenteritis) effectively reducing the absorptive capacity of the gut and causing diarrhaea. In addition, some organisms may increase the secretory functions in the mucosal crypts, increasing the volume of fluid in the gut and causing secretory diarrhoea. Large volumes of fluid loss in diarrhoea result in dehydration, which may be severe. Severe dehydration with loss of body water causes dryness of the mouth.

Trauma: High dose radiation within the field of the salivary glands may result in destruction of the gland and as such lack of production of saliva leading to dry mouth.

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