Lecture 3 [2hrs]

GASTRITIS

Inflammation of the gastric mucosa in response to infection or injury.
Gastritis is a histological diagnosis and can be classified after a biopsy from the body and antrum of the stomach.

Types of gastritis

1-**Acute gastritis**

Maybe erosive or hemorrhagic. Neutrophils are the predominant inflammatory cell in the epithelium.

Causes of acute gastritis include *Aspirin, NSAID.*H.pylori. Alcohol*iron preparation.*Sever physiological stress [burn, multiorgan failure, CNS trauma].*Bile reflux.*Viral infection [CMV, HSV in AIDS].

Clinical presentation* gastritis May be asymptomatic. Or presented with
*Dyspepsia, anorexia, nausea or vomiting, Hematemesis or melena
Many cases resolve quickly but sometime endoscopy and biopsy may be necessary to exclude PUD or malignancy.

2-Chronic gastritis maybe

***Specific.**

Causes include .CMV, TB . Crohn's disease, Sarcoidosis ,Eosinophlic Lymphocytic. Hypertrophic [menetriers disease].

***Non-specific.**

Autoimmune Chronic gastritis [type A].

involves the fundus and body with antral sparing. This form of gastritis associated with circulating antibodies against parietal cells and intrinsic factor. Parietal cells are the source of intrinsic factor and HCL .lack of intrinsic factor will lead to vitamin B12 deficiency and its sequelae (megaloblastic anemia, neurologic dysfunction) and achlorhydria. Because gastric acid plays an important role in feedback inhibition of Gastrin from G cells achlorhydria leads to hypergastrinaemia. Gastritis itself is asymptomatic but some patients have evidence of another organic specific autoimmunity like [thyroid disease]. This type of gastritis has an increased risk of gastric cancer.

Chronic Gastritis due to H.pylori infection [type B].

The site of involvement in the antrum of the stomach. The predominant inflammatory cells are lymphocytes and plasma cells with very scant neutrophils. H.pylori positive antritis predisposes to duodenal ulceration in 2-20% and increases the risk of gastric cancer 2-5 folds.

Menetriers Disease

Hypertrophic chronic gastritis not associated with significant mucosal inflammation of unknown etiology. Characterized by
A-protein Losing gastropathy due to Increased intracellular permeability and wider tight junctions between cells leads to loss of albumin.
B-Loss of parietal cells.
C-Large gastric folds.
The differential diagnosis of large gastric folds includes 1-ZES .2- lymphoma.
3- Adenocarcinoma.
4-infection (CMV, histoplasmosis, syphilis). 5- Sarcoidosis.

Clinical features

*Epigastric pain, nausea, vomiting, anorexia, and weight loss.
*Protein-losing gastropathy accompanied by Hypoalbuminemia and edema.

Investigation

*Gastric acid secretion is usually reduced or absent because of the replacement of parietal cells

and chief cells by mucus-secreting cells.
* Endoscopy shows-Large gastric folds, do not flatten with maximal insufflation.
deep mucosal biopsy (and cytology) is required to establish the diagnosis.
*EUS to exclude other causes of large gastric folds.
Treatment with
Za1*anti-Secretory drugs may reduce protein loss
*surgery for un-responsive patient's.

Gastroparesis

Defective gastric emptying without the mechanical obstruction of the stomach or duodenum may be *Primary - due to inherited or acquired disorders of the gastric pacemaker.
*Secondary to disorders of autonomic nerves system ex-diabetic neuropathy, systemic sclerosis, myotonia dystrophia, and amyloidosis.
Drugs such as opiates, calcium channel antagonists, tricyclic's, phenothiazine's.

Clinical features

*Early satiety and recurrent vomiting *abdominal fullness
Examination revealed a succussion splash heard through a stethoscope placed on the abdomen during side to side movement of the abdomen .

Treatment

*Small, frequent, low-fat meals.
*Prokinetics drugs [metoclopramide and domperidone].
*Jejunostomy feeding or total parenteral nutrition In severe nutritional failure.
*Surgical insertion of a gastric pacing device in some cases but remains experimental

Gastric tumors

1-Gastric Adenocarcinoma

It is more common in men and the incidence rises after the age of 50y.

Etiology

1-Chronic H. pylori infection classified as class 1 carcinogen. cancer arises from gastric intestinal metaplasia in patients who develop chronic atrophic gastritis.
*hypo or achlorhydria [leading to bacterial growth in the stomach which leads to the transformation of dietary nitrites to nitrosamines which is carcinogenic].
*Chronic inflammation with the generation of reactive oxygen species and depletion of antioxidants like ascorbic acid.
2-Alcohol 3-Smoking
4-Dietary associations [rich in salted, smoked foods. diets lacking fresh fruit and vegetables
5-Adenomatous gastric polyps.6-Pernicious anaemia.7-Previous partial gastrectomy for more than 20 years.
8-Familial adenomatosis polyposis.9-Cancer risk is increased two to threefold in first degree relatives of patients.10-Blood group A is associated with a 20% increase in risk.

Clinical features include

*Early gastric cancer is may be asymptomatic
*abdominal pain
*weight loss * Anorexia and nausea.
*Early satiety, hematemesis, melena.
*Dysphagia occurs in tumors of the gastric cardia which obstruct the gastro-esophageal junction.
*gastric outlet obstruction occurs in distal gastric cancer *Anemia from occult bleeding.

Examination

*maybe normal in early gastric cancer or
*signs of weight loss, anemia or a palpable epigastric mass.
*Jaundice or ascites. Occasionally tumor spread occurs to the supraclavicular lymph nodes (Troisier's sign), umbilicus ('Sister Joseph's nodule'), or ovaries (Krukenberg tumor).
*Enlarged liver due to metastasis.

*Para neoplastic phenomena, such as acanthosis nigricans, thrombophlebitis (Trousseau's sign), and dermatomyositis.
* Metastases occur most commonly in the liver, lungs, peritoneum, and bone marrow.

Investigations

*Hemoglobin level may be normal but typically is low in advanced gastric cancer.
If the patient has pernicious anemia the anemia may be macrocytic.
*CEA elevated inpatient with advanced gastric cancer.
*Elevated alkaline phosphatase level indicate metastases to the liver.
*Upper gastrointestinal endoscopy is the investigation of choice and should be done in any dyspeptic patient with 'alarm features'.
* Multiple biopsies from the edge and base of a gastric ulcer are required.
*Barium meal is a poor alternative approach and any abnormalities must be followed by endoscopy to obtain a biopsy.
*Once the diagnosis is made, further imaging is necessary for accurate staging and assessment of resectability. CT may not demonstrate small involved lymph nodes but will show evidence of intra-abdominal spread or liver metastases.
*EUS to show gastric wall involvement.
* Laparoscopy some time is required to determine whether the tumor is resectable and detect peritoneal spread.

Pathology.

All tumors are adenocarcinomas
Histologically Gastric adenocarcinomas maybe
1-Diffuse type lacks glandular structure and worse prognosis.
*Occur in younger patients.
*Develop throughout the stomach more common in the antrum and lesser curvature.
* Poorly differentiated and ulcerative.
2-Intestinal type. Gland like tubular structure [Arising from areas of intestinal metaplasia].
Distribution of gastric cancers-[50% occur in the antrum, 20-30% occurs in the gastric body on the greater curve and 20% occur in the cardia**]**.
Anatomically gastric adenocarcinoma classified into
*Proximal tumors[oesophagogastric junction, cardia] .
*Distal tumors [fundus, body, and antrum]**.**
Macroscopically tumors may be classified as [1-Polipoidal 2-Ulcerating. 3-Fungating. 4- diffuse infiltration (*linitis plastic*)].
Early gastric cancer is defined as cancer confined to the mucosa or sub mucosa regardless of lymph node involvement.

Treatment

Surgery

*Complete surgical removal of the tumor with resection of adjacent lymph nodes offers the only chance for cure in a patient with early gastric cancer.
*A subtotal gastrectomy is the treatment of choice for patients with distal carcinomas.
*Total or near-total gastrectomy is required for more proximal tumors.
EMR [endoscopical mucosal resection, ESD[endoscopical mucosal dissection] may be used in early gastric cancer limited to mucosa and sub mucosa .

Adjuvant therapy

Postoperative chemotherapy combined with radiation therapy may reduce the recurrence rate and prolong survival. Prognosis is very poor.

2-Gastric Lymphoma

Gastric lymphoma is relatively uncommon, accounting for <15% of gastric malignancies and about 2% of all lymphomas. The stomach is the most frequent extra-nodal site for lymphoma. The disease is difficult to distinguish clinically from gastric adenocarcinoma. These are B-cell tumors, most of which are aggressive large-cell lymphomas, with a minority being low-grade mucosal-associated lymphoid tissue tumors ('MALT lymphomas') The macroscopic pathology of gastric lymphoma may mimic adenocarcinoma, consisting of either a bulky ulcerated lesion

localized in the corpus or antrum of a diffuse process spreading throughout the entire gastric sub-mucosa and even extending into the duodenum.
Infection with H. pylori increases the risk of gastric lymphoma.
The clinical presentation is similar to that of gastric cancer

Treatment

Primary gastric lymphoma is a more treatable disease than adenocarcinoma of the stomach. Antibiotic treatment to eradicate H. pylori infection has led to a regression of about 75% of gastric MALT lymphomas ,more aggressive lymphoma is treated by surgical resection with adjuvant chemotherapy and radiotherapy. The prognosis depends on the stage at diagnosis .stage 1 and 2 have a favorable prognosis.

3-Polyps

*Hyperplastic polyp and cystic fundal gland polyp are the commonest epithelial lesion and these polyps are without significance.
*Adenomatous polyps may be premalignant and must be removed.

4-Gastric carcinoid tumor. **5-Ectopic pancreatic exocrine tissue**.

6- Gastrointestinal stromal tumors [GIST].

Stromal tumors include those that arise in soft tissue like lipoma, hemangiomas, schwannomas, leiomyoma's, Leiomyosarcomas. GIST can occur anywhere in the gastrointestinal tract but usually affects the stomach and proximal small intestine. GIST showed histopathological similarities with the pacemaker cells of the gut known as interstitial cells of Cajal which normally are present in the myenteric plexus and serve to coordinate gut peristalsis .mutation in the c-kit proto-oncogene are associated with most GIST.

Presentation include

*Blood loss due to ulceration. *Abdominal pain*Abdominal mass.

Investigations

*Endoscopy- smooth sub mucosal mass, may be associated with ulceration of the overlying mucosa. The biopsy is helpful in 50% because of the sub mucosal location of tumors.
*EUS- with fine-needle aspiration
*CT, MRI

Treatment surgical resection, combination chemotherapy for patients with metastatic disease

Malabsorption

Malabsorption is defined as defective mucosal absorption.
Malnutrition means inadequate food intake.
Maldigestion means defective intraluminal hydrolysis of nutrients.
Malabsorption can be
*generalized affecting the absorption of a range of exogenous nutrients.
*specific where the absorption of only a single nutrient is impaired
* Failure to re-absorb endogenous substances such as bile acids.

Three mechanisms are involved in the pathophysiology of malabsorption: premucosal (luminal), mucosal and post mucosal (postabsorptive). Premucosal mechanisms lead to maldigestion, mucosal and postmucosal mechanisms lead to real malabsorption. Normally less than 5% of ingested carbohydrates, protein, and fat are excreted in the feces.

Etiology.

1-Intra-Luminal Maldigestion occurs when deficiency of bile or pancreatic enzymes results in inadequate solubilization and hydrolysis of nutrients.

Causes include

*Pancreatic disease [Pancreatitis, cystic fibrosis, and pancreatic cancer].
*Inactivation of pancreatic enzymes by gastric hypersecretion [ZE Syndrome].
*Impaired bile acid micelle formation [hepatocellular disease, ileal resection, bile duct obstruction, biliary cirrhosis, and bile acid deconjugation by bacterial over growth].
*Inadequate mixing of food, bile, and pancreatic enzymes occurs in gastro-jejunostomy.

2-Mucosal Malabsorption results from small bowel resection or conditions which damage the small intestinal epithelium leading to diminishing the surface area for absorption and or depleting

brush border enzymes. **Causes** include *Celiac disease,* tropical sprue, *hypogammaglobulinemia, *giardiasis, *amyloid *Crohn's disease, *disaccharide deficiency. Gastric cause include atrophic gastritis, autoimmune gastritis[pernicious anemia], gastric resection or bypass

3-Post-mucosal. The lymphatic obstruction prevents the uptake and transport of absorbed lipids into lymphatic vessels. Increased pressure in these vessels results in leakage into the intestinal lumen, leading to protein-losing Enteropathy.

Causes include *Intestinal Lymphangiectasia, *lymphoma,*TB *Whipple disease.

Diagnosis of Malabsorption include the following steps

1-Documentation which includes [clinical features and investigations].

***Clinical features** include

Malasie, anorexia, abdominal bloating, diarrhea[bulk stool rather than frequency compared with the colonic disease], weight loss.Steatorrhea due to fat malabsorption[pancreatic and small bowel disease]

Edema, ascites- due to protein malabsorption

Paraesthesiae, Tetany- due to Calcium or magnesium malabsorption

Skin rash- due to zinc or vitamin B malabsorption

Cheilitis, glossitis- due to vitamin B malabsorption

Neuropathy-[subacute combined degeneration of spinal cord] anemia due to vitamin B12 malabsorption.

Night blindness- due to vit A malabsorption

Bruising- due to vit K or C malabsorption.

Bone pain, myopathy, osteoporosis- due to Vit D malabsorption.

Anemia is due to (iron, folate, or B12 deficiency).

Increased Prothrombin time due to (vitamin K deficiency).

2- investigations Identify the Site of Malabsorption

***Plan film of the abdomen**-may show pancreatic calcifications that indicate chronic pancreatic insufficiency.

***Small bowel follow-through and small bowel enteroclysis** to identify #Focal or diffuse abnormalities like thickening of intestinal folds caused by lymphoma, Whipple's disease or amyloidosis, #Narrowed irregular terminal ileum caused by Crohn's disease, lymphoma, TB

#Diverticuli, fistulas, and surgical alteration in bowel anatomy.

***Abdominal CT with oral or iv contrast agents to detect**

#Focal intestinal lesions like Crohn's disease, lymphoma, intestinal fistula, and dilated bowel loops

#Diffuse thickening of small bowel seen in Whipple disease

Abdominal lymph nodes may be seen in Whipple disease, small bowel lymphoma, or Crohn's disease

#Calcifications of the pancreas dilated pancreatic ducts

***MRI of the small intestine** for detection

Segmental bowel wall thickening with inflammation of mesentery, ulcerations, fistula formation may be seen in Crohn's disease**,** Small intestinal dilatation, mucosal thickenings, tumors

Flattening of duodenal and jejunal folds

***Endoscopy with biopsy** is the definitive investigation for mucosal lesion may shows

Serrated or scalloping of duodenal folds highly suggestive of celiac disease

Aphthous ulcer suggest Crohn's disease

Diffuse white-yellowish punctate lesions can be seen in lymphangiectasia

***Aspiration of jejunal juice** may detect G.lambilia.

***Video Capsule endoscopy and Enteroscopy** useful in the diagnosis of [lymphangectasia, Crohn's disease]

Fecal fat determination useful in the diagnosis of malabsorption of fat

The stool is collected over 72 hrs. in a large sealed container most normal people excrete less than 7 gr pr 24 hrs. on a diet that contains 80-100 gr of fat

Stool fat > 7gr / 24 hrs. can be seen in pancreatic insufficiency, bile acid deficiency, mucosal disease, or lymphatic obstruction.

Pancreatic exocrine function tests

Collection of pancreatic secretion from the duodenum and the content of bicarbonate and enzymes can be measured after stimulation of pancreatic secretion with secretin test .for example bicarbonate concentration < 90 mmol/L suggest pancreatic insufficiency.

The bentiromide test

The test is performed by administering a single oral dose of 500 mg of bentiromide after overnight fast and the urine is then collected for 6 hrs.

Pancreatic enzyme chymotrypsin cleaves the molecule within the lumen of the small intestine releasing para-aminobenzoic acid[PABA]. Then PABA is absorbed and excreted in the urine

Less than 60% excretion of PABA suggests pancreatic insufficiency although mucosal disease, renal disease, severe liver disease, and diabetes also can cause low PABA excretion.

Bile acid breath test

Normally about 95% of bile acids that secreted in the duodenum are absorbed in the terminal ileum if radiolabeled [14 c]- glycocholate is given orally about 5% of it enters the colon and undergoes bacterial deconjugation .the CO2 released is absorbed and excreted by the lungs and measured in expired air**.**

Bacterial overgrowth in the small intestine promotes earlier bacterial deconjugation of C14 –glycocholate and consequently a larger amount of 14 CO2 is measured in expired air

Similarly, resection or terminal ileal disease allows more bile acids to pass into the colon and undergo bacterial deconjugation increasing expired carbon dioxide.

Xylose tolerance test

D-Xylose is a five sugar that remains intact when it is absorbed across intestinal mucosa for that reason can be used as a screening test for diffuse small bowel mucosal disease

After the patient drinks 25 gr of xylose dissolved in 500 ml water and patient encouraged to drink an additional 1 L of water for good hydration we can do 2 thinks

1-Collecting urine for next 5 hrs normally patient excrete > 5 gr of xylose. Causes of low levels occur in small bowel overgrowth, decrease circulatory volume, massive ascites, and renal disease.

2-Collecting blood sample for blood xylose level at 2 hrs. after ingestion for the patient with the renal disease the normal 2 hrs. the blood level is above 40 gr /dL

The hydrogen breath test.

Bacterial metabolism of carbohydrates results in the accumulation of hydrogen which then absorbed by colonic mucosa and excreted in the breath. Using lactose or fructose can be used to detect malabsorption of these carbohydrates.

Lactose H_2 breath test .increase in breath hydrogen concentration greater than 20 parts per million over the baseline occurs [30,60,90,180,240 minutes] after ingestion of 50 grams of lactose.

The lactose tolerance test is an indirect measurement of the activity of intestinal lactase a brush border enzyme that hydrolyzes lactose to glucose and galactose a fasting blood glucose level is drawn and the patient drinks 50 g of lactose mixed with 500 ml water then the blood glucose level checked after 15,30,60, and 90 min in lactase deficiency the blood glucose level fails to rise more than 20 mg% above the fasting level.

Vit B12 absorption [schilling] test.

When the intrinsic factor is given with vitamin B12, the test measures terminal ileal or pancreatic function. Dietary vit B12 is bound in the stomach with an endogenous protein called R protein .pancreatic enzyme to degrade R protein in the proximal small bowel resulting in the transfer of Vit B12 to IF. The Vit B12 to IF complex continue to the terminal ileum where it binds to specific receptors on the epithelial cells .thus lack of

sufficient pancreatic enzymes or terminal ileal disorder may result in abnormal Vit B12 excretion

The test is done by giving cobalt-labeled vit B12 and measures the 24 hrs. urinary excretion.

Conditions Associated With Malabsorption

Pancreatic Exocrine insufficiency.

Results from a chronic inflammatory disease of the pancreas, rarely pancreatic carcinoma Pancreatic insufficiency leads to panmalabsorption.

Clinically

it is suspected in a patient with chronic relapsing pancreatitis, abdominal pain, and wt loss

investigation

*abdominal plain X-ray shows pancreatic calcification.

Laboratory-

*24 hrs fecal fat quantitive - is elevated sometimes >30 gr

*Schilling test-may indicate malabsorption of vit B12

*The bentiromide test it is usually abnormal in a patient with pancreatic insufficiency

Treatment

Pancreatic enzyme supplement is given before, during and after each meal

PPI prolonged the activity of pancreatic enzyme supplement.

A low-fat diet, fat-soluble vitamins, and calcium supplement

Bile acid insufficiency

Insufficient bile acids result from the following disorders

*Severe liver disease*bacterial overgrowth of the small intestine*disorders of the terminal ileum

Diagnosis

*Small bowel x-ray may show abnormality when there is small bowel stasis or Diverticuli

*Steatorrhea

*The bile acid breath test is abnormal if bacterial overgrowth or terminal ileal disorders.

Small bowel bacterial overgrowth [SIBO]

SIBO results from dysmotility, altered anatomy and hypochlorhydria

Clinical Manifestations are variable and range from anemia results from iron or Vit B12 deficiency or frank Steatorrhea with protein-losing Enteropathy**.**

Treatment

***Treating the underlying disease

*Treating bacterial overgrowth by giving AB like [ciprofloxacin, norfloxacin, metronidazole, Rifaximin].

*Correction of nutritional deficiencies**.**

Terminal ileal disorders

Patents may have malabsorption of vit B12 and bile acids

Clinical features

When there is bile acid malabsorption in the terminal ilium .the bile acids pass to the colon where it inhibits water absorption and electrolytes. Thus these patients may have both Steatorrhea as a result of bile acid deficiency and watery diarrhea from the effects of bile acids on the colon**.**

Management

*Cholestyramine which binds bile acids taken orally to treat watery diarrhea.

*Restriction of long-chain triglycerides and supplemental medium-chain triglyceride

*Monthly Vit B12 inj**.**

Small Bowel Diseases.

Coeliac Disease [Gluten-Sensitive Enteropathy] [CD].

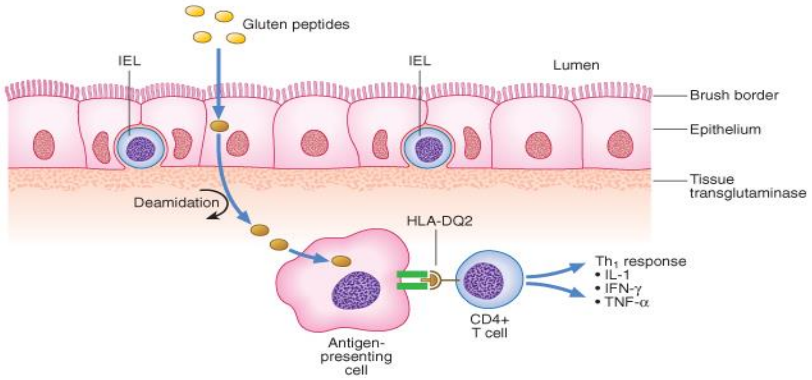
CD is an immune-mediated disorder affecting the small intestine precipitated by the ingestion of gluten in genetically predisposed children and adults,. Gluten is a family of proteins found in cereals wheat, barley, and rye(but not rice or oats).

Histological is defined as small intestinal villous atrophy that resolves when gluten is withdrawn from the diet. The histopathological changes are more severe in the proximal small bowel. This probably reflects the exposure of the intestinal mucosa to varied amounts of dietary gluten.

Pathophysiology

Celiac disease is considered an immune disorder that is triggered by an environmental agent gliadin in a genetically predisposed person. All patients with celiac disease are positive for HLA-DQ2 (or DQ8).

Patients with celiac disease have an inappropriate mucosal T-cell response to ingested gluten from diet resulting in intestinal injury. Gliadin forme an immunogenic complex with tissue transglutaminase [tTG]This tTG forms the substrate for antigliadin,antiendomysial, and anti tTG antibodies .the resulting both humoral and T-cell mediated small intestinal mucosal damage. leads to Lymphocytes infiltration of lamina propria, increased intraepithelial lymphocytes (IEL), crypt hyperplasia and villous atrophy.



Presentation

Classic[typical] With sign and symptoms of malabsorption].

Atypical [more common],anemia, chronic fatigue, fibromyalgia, short stature ,infertility ,seizures, osteopenia and osteoporosis.

Clinical features

Coeliac disease may present at any age.

Infant . after the introduction of cereals usually after 6 m of age .presentation include* impaired growth *diarrhea* vomiting * abdominal distention, abdominal cramping

Older children may present with diarrhea *anemia* short stature* delay pubertal *recurrent abdominal pain. *behavioral disturbance, occasional constipation.

Adult peak onset is in the 5th decade and females are affected more than males. The presentation is variable depending on the severity and extent of small bowel involvement some patient have *Malabsorption while others develop non-specific symptoms such as* Tiredness,* Weight loss,*Folate deficiency or* iron deficiency anemia in the absence of any gastrointestinal symptoms *oral ulceration

* Dyspepsia, *Bloating**.***

Diarrhea in celiac disease may be secondary to

1-Steatorrhea which is primarily a result of the changes in jejunal mucosal function.

2-Lactase deficiency a consequence of changes in jejunal brush border enzymatic function;

3-bile acid Malabsorption resulting in bile acid-induced fluid secretion in the colon in cases with more extensive disease involving the ileum.

4-Endogenous fluid secretion resulting from the crypt hyperplasia.

Coeliac disease is linked HLA-DQ2, so is often associated with other autoimmune diseases like

*****Dermatitis herpetiformis (DH] .characteristized by itching blisters over extensor surfaces of the limbs and back. Almost all patients with DH have histopathologic changes in the small intestine consistent with celiac sprue.
*Insulin-dependent diabetes mellitus, pernicious anemia, myasthenia gravis. RA
*IgA deficiency.*Thyroid disease.*Primary biliary cirrhosis.*Splenic atrophy.*Down's syndrome.
*Inflammatory bowel diseases, pancreatic insufficiency, microscopic colitis. *Fibrosing alveolitis
*Hypothyroidism or hyperthyroidism*Sarcoidosis
*Neurological complications include [encephalopathy, cerebellar atrophy, peripheral neuropathy, Epilepsy with cerebral calcification]

Diagnosis

1-Hematologic, Biochemical tests, Radiologic, and Stool studies include.

*CBC and blood film (micro- or macrocytic anemia) .features of hyposplenism [target cells, Howell−Jolly bodies]. low [folate, Vit B12 ,iron].*Clotting screen (vitamin K malabsorption).
* low Ca, vitamin D, and albumin. osteopenia on the DEXA bone scan.
*Liver enzymes (elevated transaminases).
*Small bowel radiology (altered mucosal appearances, clumping of contrast).
*Intestinal permeability(increased).
*Fecal fat increased[due to fat malabsorption].

2- Serologic Studies include

Diagnostic Testing

*IgA and IgG gliadin antibodies are sensitive but nonspecific and should be avoided
*Endomysial IgA [EMA] and IgA anti-tissue transglutaminase (TTG) have 95% sensitive and specific• Alternative test IgG TTG. Because IgA deficient in celiac, IgA level should be determined if IgA. deficient
*Deamidated gliadin peptides (DGPs) [IgA, IgG]testing is used in the confirmation or exclusion of celiac disease
*<u>**Negative**</u> DQ2 and HLA-DQ8 is an excellent test to exclude celiac disease
*In children younger than 2 years, IgG TTG alone or with DGP should be done
*All patients should be on a gluten-containing diet before antibody testing

3-Duodenal biopsy –the gold standard for diagnosis –

Histological features are villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes.
Although these histopathologic features are characteristic of coeliac sprue, they are not diagnostic because a similar appearance can be seen in [tropical sprue, eosinophilic enteritis, milk-protein intolerance in children and occasionally in lymphoma, bacterial overgrowth, Crohn's disease, and gastrinoma with acid hyper secretion].
<u>The presence of a characteristic histopathologic appearance that reverts to normal following the initiation of a gluten-free diet establishes the diagnosis of coeliac sprue</u>

Confirmatory Testing

Duodenal biopsy (2 duodenal bulbs and 4 from second and third duodenum) Histologic findings consistent with Marsh or Corazza criteria
*The single most useful test for diagnosis and monitoring of celiac disease is IgA tTG assay.
a false-negative IgA EMA and tTG can occur with mild Enteropathy, in children younger than 2 years of age, and patients with IgA deficiency.

Complications

*T-cell Lymphoma and carcinoma of small bowel.*Squamous carcinoma of the esophagus,
*Ulcerative jejunoileitis [characterized by deep ulcers in the jejunum, Malabsorption, fever, pain, and perforation may occur]
* Non-responsive celiac disease .ongoing or recurrent symptoms and signs that suggest active celiac disease despite a strict gluten-free diet for more than 6-12 m.
*Collagenous sprue [a layer of collagen-like material is present under the basement membrane] .these patients generally do not respond to a gluten-free diet and have a poor prognosis.

Treatment

*A gluten-free diet must be taken indefinitely. This requires the exclusion of wheat, rye, and barley.

*Rice, maize, and potatoes are satisfactory sources of complex carbohydrates. On a gluten-free diet, the patient improves within 2 w.
* dietary supplements include iron, calcium, Vit B12,vit D, and B, folic acid, Vit A, thiamin, riboflavin, niacin.