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APPROACH TO CLD / ASCITES

Symptomatology :

1. Hematemesis :

- Onset
- Frequency
- Volume
- Colour – bright red/coffee
- Postural symptoms – giddiness, diaphoresis
- Associated melena or hematochezia
- Pain abdomen or dyspeptic symptoms
- Blood transfusion/ IV fluids/ pressors support
- Any hospitalization
- Vomiting/ retching/ alcohol binge - preceeds
- Drug intake – NSAIDS/steroids
- Jaundice
- Fever – children with EHPVO

2. Jaundice :

- In cirrhosis - Mild jaundice
- Deep Jaundice: Budd chiari/ obstruction/alcoholic hepatitis/HCC

3. Abdominal distension :

- Onset – Sudden(Budd chiari/CHF/Pancreatic ascites) or Gradual
- Progression
- Generalized or localized
- Duration
- Associated pedal edema/reduced urine output/facial puffiness/anasarca/breathlessness
- H/o paracentesis – colour/volume/frequency
- Response to drugs – diuretics
- Low grade fever/ chronic cough/ night sweats
- Weight loss/ loss of appetite
- Associated pain abdomen/ jaundice

4. Awareness of lump :

- Onset
- Progression

- Duration
- Size - lemon/fist/handful
- Site
- Shape
- Associated
 - Pain abdomen
 - Jaundice
 - Vomiting
 - Altered bowel habits
 - Early satiety
 - Fever

5. Altered sensorium :

- Onset
- Progression
- Duration
- Sleep disturbances
- Irritability
- Difficulty in concentration – reading newspaper/driving/office work
- Tremoulness/incoordination
- Associated jaundice/abdominal distension/GI bleed/reduced urine output/vomiting/diarrhoea

6. Growth retardation : EHPVO

- Developmental milestones
- Comparing with sibblings
- School performance

7. Loss of appetite :

- Diet details
- Calories intake - prior and present

8. Weight loss :

- Loosening of clothes
- Thinning of limbs
- Documentation of weight loss

Negative history :

- History of tattooing, blood transfusion, sexual promiscuity, IV drug abuse
- Prolonged drug intake – native or alternative medicines – OTC/CAM

- Joints pain, skin rashes or pigmentation, acnes, thyroid nodule, heat or cold intolerance, palpitation, eye redness
- Abnormal behavior, psychiatric disorders – depression/anxiety, movement disorders, tremoulness, ataxia or incoordination and poor school performance.
- Neonatal h/o umbilical sepsis, mode of delivery
- H/o DVT, hypercoagulable state, young stroke, MI, headache
- Pain abdomen, fever, jaundice, pale stools, pruritis
- Polyuria, polydipsia and polyphagia
- Diarrhoea, bleed PR, joints pain, petechiae, ecchymosis, night blindness.

TREATMENT HISTORY :

- Paracentesis
- Blood transfusion
- Diuretics
- Endoscopy/ EVL- frequency
- Shunt surgery
- Hospitalization

PAST HISTORY :

- Diabetes mellitus
- Tuberculosis
- Decompensation – ascites/bleed/altered sensorium

PERSONAL HISTORY :

Alcohol :

- 1 unit = 8 grams
- 1 unit = 284 ml of Beer (4%) = 88 ml of Wine (12%) = 50 ml of Fortified wine (20%) = 25 ml of spirit (40%)

Calculation :

- 1 unit = volume of drink x percentage strength of drink
- Smoking
- Diet
- Female – OC pills, recurrent abortion, irregular menses

PERINATAL HISTORY :

- Mode of delivery
- Antepartum drugs
- Perinatal umbilical sepsis
 - Vaccination
 - Growth milestone

FAMILY HISTORY :

- Pedigree chart
- Family h/o Wilsons disease, CLD, Autoimmune diseases
- Young CVA, MI, DVT, Hypercoagulable state

PROVISIONAL DIAGNOSIS

- SYNDROMIC – CLD/DCLD/ACLF/BCS/NCIPH
- ETIOLOGY - viral/alcohol/metabolic/hypercoagulable state
- Portal hypertension
 - Ascites
 - Bleeder / post secondary EVL status
 - Splenomegaly
- COMPLICATIONS :
 - SBP
 - Hepatic encephalopathy
 - AKI/HRS
- COMORBIDITIES : DM, HIV
- PERFORMANCE STATUS

EXAMINATION – GPE

Built – short stature in childhood disease

Nutrition assessment :

- BMI (Quetelet index)
- Mid arm muscle circumference
- Skin fold thickness
- Waist hip ratio - for obesity

Male - > 0.9

Female - > 0.85
- Malnutrition universal screening tool

SKIN FOLD THICKNESS : measuring of fat stores in mm

- Triceps – most common
- Biceps
- Infrascapular area
- Suprailiac (iliac crest)
- Measured in vertical plane
- Relaxed arm hanging side by during measurement
- < 3mm - indicates complete exhaustion of fat stores

Adults Normal nutrition moderate depletion severe depletion

- Male 12.5 10 7.5
- Female 16.5 13 10

MID UPPER ARM CIRCUMFERENCE (MUAC) : bedside

- Sitting or standing position
- Non dominant hand
- Inbetween olecranon process and acromion process

Clinical use :

$$\text{MUAC} = \text{BMI}$$

- $>25 \text{ cm} = >20$
- $<23.5 \text{ cm} = <18.5$
- $>23.5 - <25 \text{ cm} = 18.5 - 20$

MID ARM MUSCLE CIRCUMFERENCE (MAMC) :

- $\text{MAMC} = \text{MUAC} - [0.314 \times \text{SFT}(\text{mm})]$
- Useful in CLD patients with ascites and pedal edema without fluid accumulation in arms.

Pallor – GI blood loss

- Hemolysis in AIH, Wilsons
- Zieve syndrome
- Nutritional deficiency in alcoholics
- Spur cell anemia
- Splenic sequestration in hypersplenism

Icterus – hepatocellular dysfunction/ portal biliopathy

- Clubbing – PBC
- Cyanosis – HPS
- Edema – decompensation/IVC obstruction
- Lymphadenopathy – HCC
- Eyes – KF ring

Nail changes :

- Muehrcke's lines – multiple white transverse lines
- Blue lunulas – half moon sign (Wilson's disease)
- Terry nails - CLD

STIGMATA OF CHRONIC LIVER DISEASE :

- Diminished body hair
 - Alopecia
 - Loss of beard and axillary hair
- Parotid swelling
- Fetor hepaticus – sweet ammonical odour
- Spider naevi

Also seen in – normal individual

 - Pregnancy
 - Hyperthyroidism
- Gynaecomastia – breast tissue diameter >5cm
- Dupytrens contracture
- Palmar erythema – redness over thenar and hypothenar prominence +/- sole
- Hepatic flaps
 - Other causes – renal failure, hypercapnia, dyselectrolyemia
 - Unilateral flaps – genu and anterior portion of internal capsule lesion or ventrolateral thalamic lesion
- Testicular atrophy – using orchidometer
 - Diameter <3cm
 - Loss of testicular sensation

Xanthoma – cholestatic disease

- Tendon xanthoma – over Achilles tendon
- Tuberous xanthoma – over knee, elbow
- Plane xanthoma – over palmar crease
- Xanthelesma – on eyelids

PER ABDOMEN EXAMINATION :

INSPECTION :

- Shape of the abdomen
- Umbilicus position and shape
- Flanks
- All quadrants moves equally with respiration or not
- Visible veins and back veins
- Scars/sinus
- Visible pulsations
- Hernial orifices
- External genitalia

PALPATION :

- Superficial palpation – local rise of temperature, tenderness, guarding or rigidity
- Deep palpation – organomegaly
- Confirm all other inspectory findings
- Veins – site and direction of flow
- Hernia orifices – cough impulse
- External genitalia
- Distance from xiphi sternum to umbilicus, umbilicus to pubic symphysis and spinoumbilical lines in women, abdominal girth at umbilicus if necessary
- Back examination

PERCUSSION :

- Note
- Shifting dullness
- Fluid thrill
- Liver span
- Traube's space

AUSCULTATION :

- Bowel sounds
- Arterial bruit
- Venous hum – Cruveilhiers Buamgarten syndrome

PER RECTAL EXAMINATION :

Palpable mass/Pelvic deposit(Blumers shelf)

Respiratory & Cardiovascular system:

Cardiomegaly, murmurs, JVP and breath sounds at both lung bases

Investigations:

- Biochemistry/serology
- Ultrasound abdomen: 100mL of ascites+
- CLD evidence on USG- coarse liver, portal vein > 10mm, splenomegaly, hepatofugal flow in portal vein
- CT Abdomen: For detection of primary tumor
- Endoscopy: for detection of esophageal varices and portal gastropathy
- Ascitic fluid analysis: TC, DC ,Protein, Albumin with SAAG, Malignant cytology
- Diagnostic laparoscopy: Gold standard for malignant and tubercular ascites

APPROACH TO DIARRHOEA

Diarrhea is defined as the passage of loose or watery stools, typically at least three times in a 24-hour period.

Acute — 14 days or fewer in duration.

Persistent diarrhea — more than 14 but fewer than 30 days in duration.

Chronic — more than 30 days in duration.

- Onset
- Progression/course
- Stool frequency
- Volume
- Consistency
 - Mucoid
 - Blood mixed
 - Undigested food particles
 - Greasy/oily
 - Hard
- Duration - acute/chronic
- Nocturnal frequency
- Response to fasting
 - Improves in osmotic diarrhoea
 - Persistent in secretory diarrhoea
- Odour - foul smelling in protein malabsorption

Association with

- Pain abdomen
- Worms
- Vitamin deficiencies :
 - Fat soluble vitamins
 - A – Night blindness
 - D – Bone pain, back ache, muscle pain
 - E – Extremities paresthesia, imbalance
 - K – Easy bruising, bleeding tendency
 - B complex – Glossitis, cheilitis, recurrent oral ulcers,
 - C – Gum bleeding, bruises

- Anemia symptoms :
 - Easy fatigability
 - Exertional breathlessness
 - Palpitation
 - Chest pain
 - H/o blood transfusion
- Macronutrients malabsorption :
 - Carbohydrates - abdominal bloating, excessive flatulence, perianal rashes
 - Protein - weight loss, limb thinning, proximal muscle weakness, edema feet
 - Fat - weight loss, thinning of cheeks, limbs
- Intolerance to food :
 - Gluten free diet – in celiac disease
 - Milk and milk products – in lactose intolerance
- Drug history :
 - Antibiotics
 - Acid reducing agents – PPI, H2RA
 - Antacids – magnesium combinations
 - Antiarrhythmics – quinidine
 - Anti inflammatory – NSAIDs, 5 ASA, gold salts
 - ART
 - Colchicine
 - PAS
 - Olmesartan
 - Metformin
 - Orlistat
 - Herbal products
 - Vitamin and mineral supplements
- Radiation exposure in the past
- Abdominal surgeries in the past – Crohns disease, SIBO, short GUT
- Intestinal obstruction features : vomiting, abdominal distension and pain
- Awareness of lump or swelling in other parts of body

Negative History :

- IBD – joints pain, backache, skin rashes, eyes reddening, oral ulcers, perianal disease (fissure/fistula).
- Abdominal Tuberculosis – anorexia, weight loss, evening rise of temperature, night sweats.
- Celiac disease – anemia, symptoms onset after weaning, positive family history.
- Eosinophilic disease – allergy, eczema, food intolerance, respiratory symptoms, positive family history.

- SIBO – Prior h/o surgeries, radiation exposure.
- HIV – h/o blood transfusion, skin tattooing, sexual promiscuity.
- CVID – recurrent respiratory infections.
- Thyroid disease – heat intolerance, excessive sweating, palpitation.
- Carcinoid tumour – flushing, bronchospasm.
- Diabetes Mellitus – polyuria, polyphagia, polydipsia.
- Chronic laxative use.
- Prolonged drug intake/ alternative drugs use.
- Worms infestation – passing worms in stool, perianal pruritis
- Colon polyps
 - Skin nodules – Neurofibromatosis
 - Buccal and perioral pigmentation – Peutz Jeghars syndrome
 - Alopecia
 - Dystrophy of nails
- H/o jaundice with diarrhea
 - IBD and PSC
 - Celiac disease with NCIPH/Autoimmune hepatitis
 - Carcinoid with liver metastasis
 - HIV

Treatment History :

- Course
- Any hospitalization
- Investigations – UGIE, LGIE +/- biopsies, ERCP
- Drug history- ATT, OCPs
- Drug allergy

Past History :

- Tuberculosis
- Diabetes Mellitus

Personal history :

- Alcohol
- Smoking – alpha 1 antitrypsin deficiency
- Diet – purely vegetarians – Vit B12 defecency
- Allergy
- Education

Family History :

- Pedigree chart
- Similar history in other family members
- Malignancy

Females :

- Menstrual history
- OCPs

Children :

- Prenatal history – complication
Teratogenic drug ingestion

- Delivery – Home/hospital
 - Normal /LSCS/ complications
 - Preterm or term birth
- Post natal history – immunization
 - Weaning
 - Developmental milestones
 - Growth retardation

EXAMINATION :

GPE :

- Pallor, Icterus, Clubbing, Cyanosis, Edema and Lymphadenopathy
- Hair – pigmentation, texture, curling (vitamin C deficiency), alopecia
- Eyes – Bitots spot, episcleritis
- Oral cavity – oral ulcers, cheilitis, stomatitis, oral hygiene, glossitis, macroglossia
- Buccal pigmentation, oral candidiasis
- Neck – lymphadenopathy, goitre
- Nails – Clubbing, koilonychia, brittleness, dystrophic nails (Cronkite Canada syndrome)
- Skin – eczema, Petechie, ecchymosis, nodules
- Dermatitis herpetiformis, pyoderma gangrenosum, erythema nodosum, flushing
- Joints – arthritis, sacroileitis

Vitals signs :

- Pulse
- BP – Postural hypotension
- Fever
- BMI

Features of Diabetes Mellitus – acanthosis nigricans, candidiasis

PER ABDOMINAL EXAMINATION

- Splenomegaly/ hepatomegaly
- Ascites
- Abdominal lump (lymphadenopathy - Tuberculosis)

PER RECTAL EXAMINATION

- Perianal fistula/abscess
- Sphincter tone
- Mass
- Perianal excoriation – carbohydrate malabsorption/worms infestation

CVS

- Murmur (TR) – Carcinoid tumour

RS

- Carcinoid – wheeze(bronchospasm)

CNS

- Motor system – reflexes, power
- Sensory system – sensation, proprioception, ataxia, Rombergs sign

Clinical associations :

DIARRHEA + RASH + SKIN LESIONS

- Celiac disease – Dermatitis Herpetiformis
- Eosinophilic enteritis – eczema
- Tropical sprue – hyperpigmentation
- IBD – erythema nodosum, pyoderma gangrenosum, pyoderma vegetans, oral ulcers, granulomatous chelitis, perianal disease, metastatic Crohns disease
- Amyloidosis – skin nodules, pinch purpura, macroglossia
- Glucaganoma – Necrolytic migratory erythema
- Carcinoid – flushing
- HIV – Herpes zoster, Kaposi sarcoma

DIARRHEA + HEPATOMEGALY

- Carcinoid + liver metastasis
- Amyloidosis with liver infiltration
- Lymphoma
- Tuberculosis

- IBD + PSC
- Pancreatic NET + Metastasis
- HIV
- Colonic malignancy + metastasis

DIARRHEA + JAUNDICE

- IBD + PSC
- HIV – drug induced jaundice, HIV cholangiopathy
- Tuberculosis – disseminated
- Carcinoid with liver metastasis
- Paraneoplastic syndromes
- Lymphoma
- Celiac disease + AIH

DIARRHEA + SPLENOMEGLY

- Lymphoma
- Tuberculosis
- HIV
- IBD + PV/SV thrombosis
- Celiac disease + NCIPH
- Amyloidosis

DIARRHEA + ASCITES

- Tuberculosis
- Lymphoma
- Carinoma colon with metastasis
- Amyloidosis
- IPSID
- Eosinophilic enteritis
- Carcinoid with cardiac involvement
- CLD – Hepatitis B, C , alcohol

DIARRHEA + CARDIAC

- Amyloidosis
- Carcinoid
- Tuberculosis
- Whipples disease

POST SURGERY DIARRHEA

- SIBO
- Post Vagotomy
- Post Gastrectomy
- Bariatric surgery
- Short bowel syndrome
- Recurrence of Crohns disease
- Tuberculosis recurrence

DIABETIC DIARRHEA

- Drug related – Acarbose, Metformin
- Autonomic dysfunction
- Glycosylated product – ICC loss – dysmotility
- Sympathetic hypoactivity
- Pancreatic cause – steatorrhoea
- Celiac disease – association
- Fecal incontinence
- Increased motility

DIARRHEA + PRESERVED APPETITE

- Chronic pancreatitis
- Diabetes Mellitus
- Hyperthyroidism
- Laxative abuse

DIARRHEA WITHOUT MALABSORPTION

- IBS
- Hyperthyroidism
- Diabetes Mellitus
- Drugs

Diarrhea summary :

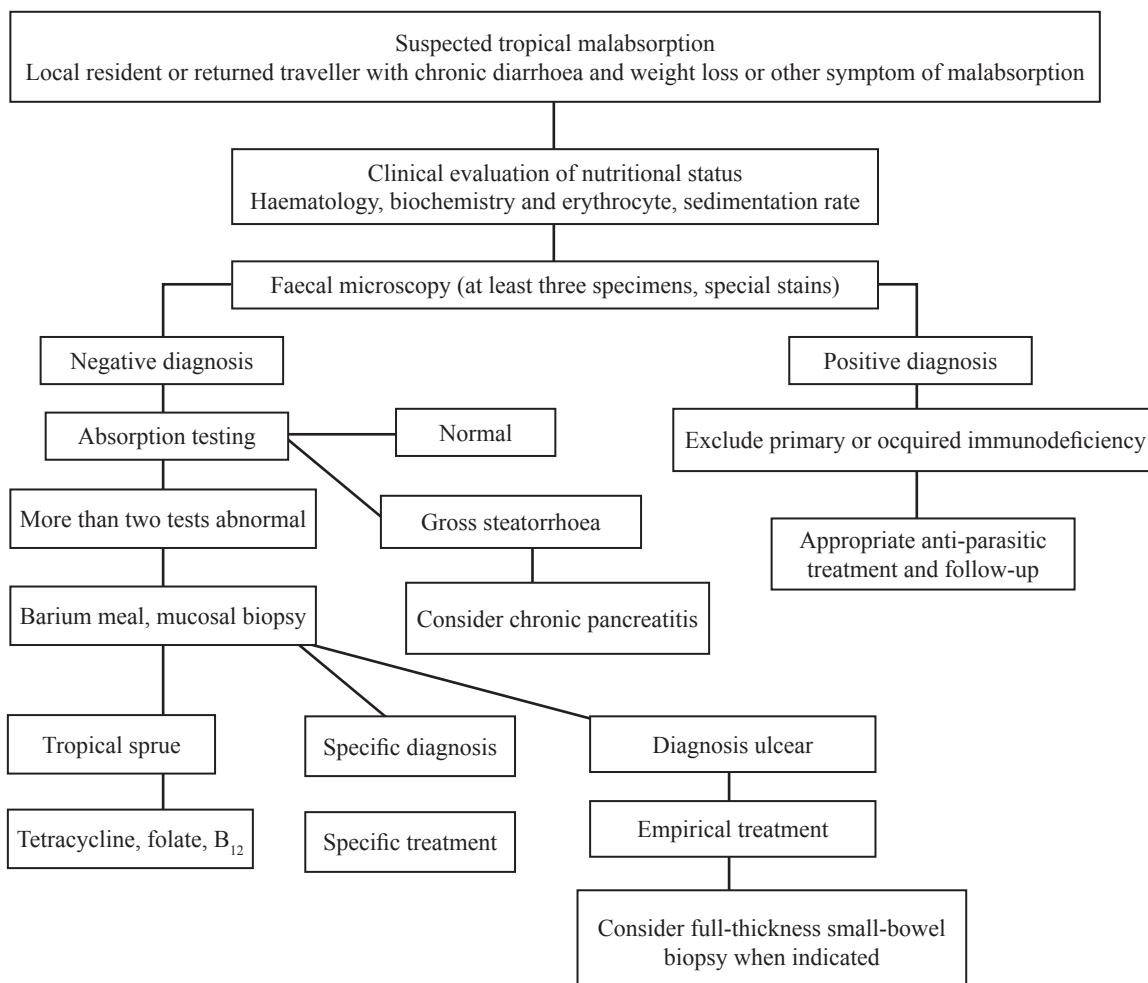
- Age
- Small volume/ large volume
- Painless/ painful
- Features if malabsorption – macronutrients or micronutrients

- Associated weight loss/ appetite loss
- Complications
- Extraintestinal manifestations

PROVISIONAL DIAGNOSIS:

- Acute / Chronic
- Syndromic – Small bowel/Large bowel type
- Etiology – Watery/ Inflammatory/ Fatty (Watery – secretory/osmotic)
- Complication – features of malabsorption
- Extra intestinal manifestations
- Comorbidities
- In case of malignancy – Performance status

Small bowel diarrhea	Large bowel diarrhea
Large quantity, less frequent stool offensive, steatorrhea, periumbilical pain, weight loss, symptoms of malabsorption	Small quantity, more frequent stool associated with blood and mucus, rectal symptoms of urgency, tenesmus and incontinence, hypogastric pain



Tropical Malabsorption - Small intestinal disease

Infectious

- Protozoa
 - Giardia intestinalis/Isospora belli/Cryptosporidium parvum/Enterocytozoon bieuneusi/Encephalitozoon intestinalis/Cyclospora cayetanensis/Leishmania donovani
- Helminths
 - Strongyloides stercoralis/Capillaria philippinensis
- Bacteria
 - Mycobacterium tuberculosis
- Viruses
 - Human immunodeficiency virus
- Inflammatory and immune related
 - Coeliac disease/ Crohn's disease/ Primary immunodeficiency
- Malignant
 - Immunoproliferative small - intestinal disease and small - intestinal lymphoma
- Pancreatic disease
 - Tropical pancreatitis

Tropical Malabsorption- Unknown aetiology

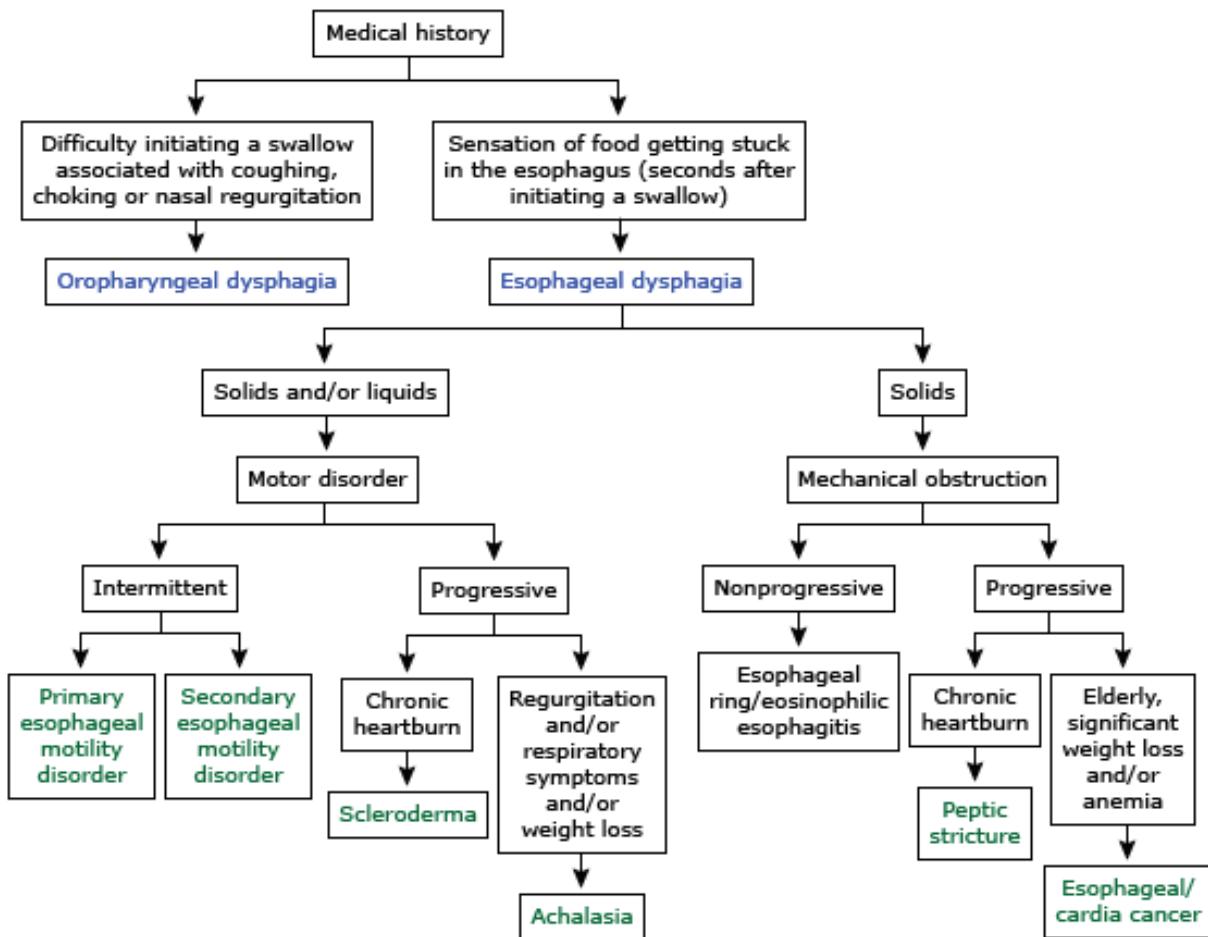
Tropical enteropathy/ Tropical sprue

DYSPHAGIA

Def: Subjective sensation of difficulty or abnormality of swallowing. Dysphagia to solids if esophageal lumen <13mm

Odynophagia - Painful swallowing

Globus - Lump in throat in the absence of dysphagia/odynophagia



History:

Food and progression: Liquids and solids from onset- motility

- Progressive dysphagia - solids → liquids- mechanical
- Intermittent dysphagia - lower esophageal ring/web

Pointing Sign: ask pt. to identify the site of pathology

Cervical - oropharyngeal and retrosternal in esophageal

Aggravating/relieving factors: Repeated swallows/valsalva maneuver- motility (cold precipitates and hot food reduces)

Associated symptoms:

Heartburn – reflux and scleroderma

Heartburn(reflux/hypomotility), weight loss (malignancy), hematemesis, coffee ground emesis (reflux), anemia, regurgitation of food particles (oropharyngeal), and respiratory symptoms (Achalasia), swallowing with a neck swelling/gurgling noise (zenkers), Cough while swallowing (oropharyngeal /tracheo esophageal fistula), change of voice (vocal cord palsy- malignancy)

Past history of [surgery](#) on larynx/esophagus/stomach

Past history of [Radiation](#) to the neck

[Medications](#) - potassium chloride/alendronate/ferrous sulfate/ascorbic acid/tetracycline/aspirin/NSAIDS- pill esophagitis

Past history of [corrosive](#) intake

Past history of Barretts/Reflux esophagitis/eosinophilic esophagitis

Causes of Esophageal Dysphagia:

Mechanical lesions - Intrinsic

- Benign tumors
- Caustic esophagitis/stricture
- Diverticula
- Malignancy
- Peptic stricture
- Eosinophilic esophagitis
- Infectious esophagitis
- Pill esophagitis
- Postsurgery (laryngeal, esophageal, gastric)
- Radiation esophagitis/stricture
- Rings and webs
- Lymphocytic esophagitis

Mechanical lesions – Extrinsic

- Aberrant subclavian artery
- Cervical osteophytes
- Enlarged aorta
- Enlarged left atrium
- Mediastinal mass (lymphadenopathy, lung cancer, etc)
- Postsurgery (laryngeal, spinal)

Motility disorders

- Achalasia
- Chagas disease
- Primary motility disorders
- Secondary motility disorders

Functional

Functional dysphagia

Physical examination: Depending on condition

Age > 40 years, presence of alarm features (anemia, weight loss, GI bleed)- malignancy

Dysphagia, iron deficiency anemia, atrophic glossitis, angular stomatitis, koilonychia, female in fourth decade, pre malignant for post cricoid malignancy- needs follow up, dilation as treatment - [Plummer vinson syndrome](#)

Bulbar (LMN - flaccid) or **pseudobulbar** (UMN- Spastic) palsy of IX-XII: Dysphagia, nasal regurgitation, slurred nasal speech, wasted tongue with fasciculations, absent gag in Bulbar P- Emotional lability, spastic tongue with brisk jaw reflex, frontal release signs- Pseudobulbar P.

Right supraclavicular adenopathy is associated with cancer in the mediastinum, lungs, or esophagus. Left supraclavicular adenopathy ("Virchow's node") suggests abdominal malignancy (eg, stomach, gallbladder, pancreas, kidneys, testicles, ovaries, or prostate)

Dysphagia, food impaction, asthma, heartburn, chest pain, vomiting, food allergies - [Eosinophilic esophagitis](#)

Management:

Endoscopy: Can determine etiology, procure biopsies and dilation is possible if required. Extrinsic esophageal compressive lesions can be missed

Barium studies: As initial test (prior to upper endoscopy): ? proximal esophageal lesion (eg, surgery for laryngeal or esophageal cancer, Zenker's diverticulum, or radiation therapy) or complex (tortuous) stricture (eg, post-caustic injury or radiation therapy)

Motility studies: negative endoscopy and strong suspicion of motility disorder is noted

Other investigations:

- Plain x-rays: for example, foreign body identification, cervical osteoarthritis
- CT/MRI head: for example, stroke
- Chest CT: for example, idiopathic achalasia
- pH monitoring in GERD

APPROACH TO CASE OF JAUNDICE / EXTRAHEPATIC BILIARY OBSTRUCTION

JAUNDICE :

- **Onset :** acute vs insidious
- **Duration**
 - Progression - slow
 - Rapid – acute viral hepatitis/ACLF/acute biliary obstruction/ ligation of HA
 - Intermittent – BRIC, Biliary Ascariasis, AIH, Flare of Hep B, Gilberts syndrome
 - Persistent – viral hepatitis/biliary cause
 - Fluctuating – periampullary malignancy/CBD stone/stricture/ PSC / relapsing hepatitis A
- **Prodromal symptoms** – rash/arthalgia/anorexia/diarrhoea/headache
- **Urine colour**
 - High coloured – hepatocellular/obstructive
 - Normal colour – hemolytic
 - Cola colour – intravascular hemorrhage(hemoglobinuria)
- **Eye colour**
 - Lemon colour – hemolytic
 - Orange – hepatocellular
 - Yellowish green – obstructive
- **Pain abdomen**
 - Painless
 - Painful – biliary pain (Steady pain, RUQ/epigastric, increases in 15 min-plateaus in 1 hour and decreases in <6Hrs) or Pancreatic (Dull continuous epigastric pain, radiating to back, relieved by muslim prayer posture) or Solid organ pain (dull, continuous pain due to stretch of capsule)
 - Fever – high grade with chills (cholangitis), low grade (neoplasm), Prodrome (viral hepatitis)
- **Pruritus**
 - Grading or pruritus
 - 0 – none
 - 1+ - mild, itching only when awake
 - 2+ - moderate, awakeness at night, finding self scratching
 - 3+ - moderately severe, constant itching without excoriation of skin or bleeding
 - 4+ - severe, constant itching with excoriation, bleeding, marked insomnia and irritability.
 - Hepatocellular
 - Extrahepatic

- **Stools:** Clay colour – cholestasis
 - Silvery colour – periampullary malignancy (acholic + blood)
 - Steatorrhoea – chronic pancreatitis
 - Easy fatigability
- **Drug History:** oral medication/herbal/OTC/ATT
- **Weight loss**
- **Relief of jaundice by drug or any intervention** – drain/ERCP
- **Abdominal distension/leg swelling**
- **GI bleed** – melena/hematemesis → portal hypertension/ Periampullary carcinoma
- **Surgery/trauma**
- **Altered sensorium**
- **WEIGHT LOSS:** Significant – loss of 5% over 6-12 months – Harrisons/ loss of 10% over 6 months – Sleisenger

Negative history :

- Surgery/trauma
- Biliary colic/cholangitis/gall stone
- Parasites

Recurrent severe pain – chronic pancreatitis

- HIV – SSC – Blood transfusion/sexual promiscuity
- CLD – Portal biliopathy/ascites/altered sensorium/G I bleed
- PSC-IBD – Extra articular manifestations (eye redness, joints pain, oral ulcers, perianal disease)
- Night sweats, evening rise of temperature, chronic cough
- Prolonged drug intake – herbal/ATT/OTC
- Fat soluble vitamin deficiency features – A: Night blindness; E: Cramps; D: Bone pain and myalgia; K: Easy bruises
- Awareness of abdominal lump – splenomegaly/distended GB/liver/pancreas
- Bleeding PR – IBD/Polyposis – oral pigmentation

PAST HISTORY:

- Gallstone disease/recurrent biliary colic
- Surgery
- Endoscopic intervention
- Tuberculosis – lymphnode compression at porta

TREATMENT HISTORY :

- Endoscopic intervention
- Antibiotics
- Drugs - OCPs
- Current treatment history in detail

PERSONAL HISTORY :

- Alcohol/ Smoking/Use of mineral oil
- Geographic location – Ganges belt – gallstone disease

FAMILY HISTORY :

- Malignancies – biliary
- BRIC/Wilsons-Jaundice
- PFIC/α1AT def- cholestasis

Summary at the end of history :

- Provisional diagnosis : components
- Syndromic : EHBOJ/Hepatocellular
- Benign/malignant
- Etiology – Ca GB/Pancreatic/Choalngio/Periampullary/HCC
- Complication - cholangitis
 - Hepatomegaly – mass/abscess
 - GOO

Comorbidities : DM/HTN/COPD/CVA

Performance status :

GRADE	ECOG PERFORMANCE STATUS
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

EXAMINATION :

- Eyes – Bitots spot/ KF ring/ Episcleritis/ Dryness of eyes/ Xanthelesma/ Pallor
- Skin – scratch marks, shiny nails, xanthoma
- Petechie, ecchymosis, gum bleeding
- Lymphadenopathy, Clubbing, Cyanosis, Icterus, Pedal edema

Abdomen :

- Scar
- Liver – hepatomegaly
 - Firm
- GB palpation – soft cystic – periampullary malignancy
 - Hard mas - GB malignancy
- Ascites – CLD, Portal hypertension, Peritoneal metastasis
- Splenomegaly – PVT/Portal biliopathy/portal HTN
- GOO – succession splash
 - Saline load test
 - Scratch test

INVESTIGATIONS

- Hemogram
 - Hb – anemia, hemolysis
 - TLC – cholangitis
- Creatinine – sepsis/ to decide on imaging
- LFT

Bilirubin – Conjugated - > 50% direct of total
Unconjugated - > 85 % indirect of total

Sequence of events in obstructive jaundice and relief of obstruction follows the same order

- Alkaline phosphatase increases
- AST/ALT increases
- Bilirubin increases

Serum Albumin – for surgery

USG abdomen :

- Sensitivity 60-70%. Bed side. Localise/extent/etiology of block
- GB status
- Ascites/portal hypertension
- Lymphnodes/Mass

MRI + MRCP:

- Better for
- biliary anatomy
 - vascular anatomy
 - to assess encasement
 - hepatoduodenal ligament

T2W MRI - **World War II** - Water is white in T2. Reverse is true in T1W MRI. Static fluid in CBD and PD as white against dark (fat) background.

CT abdomen :

- Better for – Lymphnode
 - Ascites
 - Distant metastasis

Choice of investigation ?

- Depends on availability
- Personal expertise
- Cost
- Ferumoxide MRI contrast for cholangiocarcinoma

EUS :

- Hilar lesion – not useful
- For assessment of pancreas and periampullary lesions – best
- Useful in – FNAC from indeterminate mass/lymphnodes

PET SCAN :

- Diagnosis of cholangiocarcinoma
- Intrahepatic cholangio ca – 93% sensitivity, 80% specificity
- Extrahepatic cholangio ca – 55% sensitivity, 33% specificity
- False positive – inflammation

ERCP:

- Therapeutic for decompression of CBD
- Gold standard for choledocholithiasis

Diagnostic laparoscopy/laparotomy :

- Pancreatic ca - > 2cm head lesion/ body or tail lesions – laparoscopy before surgery
 - CT scan resectable – but diagnostic lap – 25% unresectable
 - Further yield by peritoneal washing – 10% unresectable
- GB ca - CT scan resectable – but diagnostic lap – 40-50% unresectable
- Yield of percutaneous FNAC in Ca GB > 90%

TUMOUR MARKERS :

CA 19-9	Sensitivity	Specificity
Ca GB (>20 IU)	- 75%	75%
Ca Pancreas (>37 IU)	- 87%	85%
CEA	Sensitivity	Specificity
Ca GB	- 50%	90%

TISSUE DIAGNOSIS :

- Cholangio ca - Tissue diagnosis not must before surgery
 - But for palliative must
- Pancreatic ca – biopsy not needed before surgery in all cases
- Ca GB
 - Not necessary if potentially resectable
 - Must if unresectable and nonsurgical management planned
 - Extended cholecystectomy if GB ca suspicious is high

CHOLELITHIASIS:

- Fair: more prevalent in Caucasian population
- Fat: BMI >30
- Female gender
- Fertile: one or more children
- Forty/Fifty: age ≥ 40
- Familial

Symptoms:

- Asymptomatic - 75%; Biliary colic- 20%; Cholecystitis-10%
- 15% of gall stones have choledocholithiasis but 95% of CBD stones have GB stones
- Development of biliary colic is 2% in 1 year with complication of 0.2% with development of carcinoma $< 0.02\%$ per year

Differentiation of Intrahepatic and extrahepatic cholestasis:

Intrahepatic cholestasis	Extrahepatic cholestasis
Prodroma, Drugs, risk factors, family history of cholestasis, Stigmata of cirrhosis, encephalopathy	Signs of cholangitis, prior hepatobiliary surgery, PT/INR normalizing with Vit K

APPROACH TO ABDOMINAL LUMP/MASS

Common symptoms :

1. Awareness of lump

- Onset
- Duration
- Progression – slow/rapid
- Site
- Size – lemon/fist/handful
- Direction of growth/change of position
- Change in size – increasing or decreasing
- Associated with pain/ dragging sensation/ heaviness/ sudden severe pain
- Relation with meals/posture/movement/defecation
- Associated backache or lower back pain
- Urinary symptoms – increased frequency/burning micturition/hematuria
- Neurological compression symptoms – pain/paresthesia/sciatica
- Edema feet/varicocele
- Vomiting /abdominal distension
- Hematemesis/melena/bleed PR
- Jaundice/pruritis/clay stools
- Altered bowel habits – constipation/diarrhoea
- Fever/cough/expectoration/hemoptysis
- IBD – joints pain/eye redness/perianal disease

2. Abdominal pain

- Relation to lump
- Did lump change the character of pain
- Progress of lump and pain whether simultaneous or disproportionate

Simultaneous	Disproportionate (lump progress + pain static)
Stomach	Spleen
Bowel	Retroperitoneal
Pancreas	

3. Early satiety
4. Intestinal obstruction – vomiting, abdominal distension, constipation
5. Anorexia
6. Weight loss
7. Scrotal swelling
8. Jaundice
9. Pressure symptoms

Negative history :

1. Pancreas - recurrent severe epigastric pain, back radiation of pain, vomiting, abdominal distension, steatorrhoea, DM
2. Luminal - hematemesis, melena abdominal distension, vomiting, altered bowel habits
3. Biliary - jaundice, pruritis, clay stools, silvery stools
4. Tuberculosis - low grade fever with evening rise, loss of appetite and weight
5. Crohns disease - eye redness, joints pain, perianal disease
6. Urinary - hematuria, increased frequency, burning micturition
7. Neurological compression - pain, paresthesia, sciatica
8. NET - flushing, headache, irritability, hyperpigmentation, skin lesions
9. Vascular pressure – varicocele, hydrocele, chronic non healing ulcer

PAST HISTORY :

- Diabetes Mellitus
- Hypertension
- Tuberculosis
- Surgery for – testicular teratoma/scrotal
 - Melanoma
 - Perineal diseases

TREATMENT HISTORY :

- Antitubercular drugs
- Intervention – endoscopy +biopsy, ERCP
- Ascitic fluid aspiration
- Blood transfusion

PERSONAL HISTORY :

- Smoking
- Alcohol
- Diet
- Females – OCPs, menstrual history
- Pet – dogs
- Risk behavior – injection drug abuse, needle sharing, blood transfusion, sexual promiscuity
- Occupational exposure – rubber industry

FAMILY HISTORY :

- Early age malignancy
- Chronic disease
- Pedigree chart
- Diabetes mellitus
- Hypertension
- Tuberculosis

PROVISIONAL DIAGNOSIS : Components

- LUMP
 - Intraperitoneal /Extraperitoneal
 - Organ of interest
 - Compartment of lump
- Benign /malignant
- Complications – jaundice/hematemesis/melena
 - Early satiety/GOO/intestinal obstruction
 - Pressure symptoms
- Comorbidities - DM/HTN/COPD
- Etiology
- Performance status

General Physical examination:

- Anemia – G I blood loss
- Icterus – biliary cause/metastatic
- Clubbing – IPSID
- Edema

- Lymphadenopathy
 - Left supraclavicular lymphadenopathy (Virchow's node/ Troisier's sign)
 - Sign of inoperability
 - Seen in
 - Breast carcinoma
 - Pancreatic carcinoma
 - Gastric carcinoma
 - Colon carcinoma
 - Testicular malignancy
- Varicocele, scrotal swelling
- Varicose veins

VITAL SIGNS

- Pulse
- BP – Hypertension in Pheochromocytoma
- RR
- JVP
- Temperature

Cutaneous markers of internal malignancy :

Esophageal malignancy :

- Tylosis palmaris at plantaris (Howell Evans syndrome)
- Acrokeratosis paraneoplastica (Bazex's syndrome) – periungual skin thickening with nail atrophy and rash

Gastric malignancy :

- Dermatomyositis – Gottron's papule, heliotrope rash, shawl sign, mechanics hand
- Tripe palms (acanthosis palmaris)
- Acanthosis nigricans
- Lesser Trelat (multiple seborrhoeic keratosis)

Pancreatic malignancy :

- Subcutaneous fat necrosis
- Trousseau's sign (superficial migratory thrombophlebitis)

Colon malignancy :

- Hypertrichosis lanuginose
- Skin tags

Neuroendocrine tumours :

- Flushing – Carcinoid tumour
- Necrolytic migratory erythema – Glucagonoma

PER ABDOMEN EXAMINATION : LUMP

INSPECTION :

- Condition of the overlying skin – tense, red, shiny, pigmented
- Position or site
- Size
- Shape – spherical or globular
- Surface
- Number of lump
- Pulsation
- Peristalsis
- Left to right – Gastric outlet obstruction
- Right to left – Colon malignancy
- Step ladder pattern – Small bowel obstruction
- Movements with respiration
- Impulse on cough
- Pressure effects – edema feet
- Hernial site
- Scrotum

PALPATION :

Superficial palpation – Local rise of temperature/ tenderness/ guarding/ rigidity

Deep palpation - Description of lump

- Position
- Size
- Shape
- Surface – smooth/nodular
- Margin – well defined/ ill defined
- Can get above or below the swelling
- Consistency – soft/cystic/hard
- Movements

With respiration – Liver/Gall bladder/Stomach/Spleen/Kidneys

Mobile

- In all direction – small bowel mass
- Diagonally – mesenteric cyst
- Vertically – Liver/ Spleen/ GB/ Stomach
- Horizontally – GB mass

Restricted mobility

- Retroperitoneal tumours
- Severe chronic inflammatory mass
- Locally advanced intraperitoneal tumours

Ballotment – Kidneys

Bimanually palpable - Colon/Retroperitoneal mass

- Pulsation - Transmitted or expansile
- Other organs – Liver/ Spleen/ GB/ Kidneys
- Hernial orifices/ cough impulse
- External genitalia
- Per rectal examination
- Per vaginal examination – if necessary

Differentiation between Extraabdominal and Intraabdominal mass

	Extra abdominal	Intra abdominal
Head rising test	Prominent	Disappears
Leg rising test	Prominent	Disappears

Differentiation between Intraperitoneal and Retroperitoneal mass

Except for Kidney tumour – moves	Retroperitoneal mass
Moves with respiration (Stomach/Liver/GB/Spleen)	Does not moves with respiration Except for Kidney tumour – moves
Mobile	Immobile
Knee elbow position (Prominent)	Disappears

PERCUSSION :

- Note over lump
- Band of colonic resonance
- Loin percussion (Renal angle)
- Shifting dullness
- Hydatid thrill

AUSCULTATION :

- Arterial bruit - Abdominal aortic aneurysm/ hepatic artery aneurysm/ HCC
- Venous hum
- Friction rub

RIGHT HYPOCHONDRIUM: IN RELATION TO:

- Liver/ GB
- Rt. Hepatic flexure
- Stomach
- Rt.kidney / Adrenal
- Pancreas
- Appendix (subhepatic)
- Retroperitoneum

FEATURES OF LIVER SWELLING:

- Mass in rt .hypochondrium/ epigastrium
- Intraabdominal
- Intraperitoneal
- Moves with respiration freely
- Liver border felt, sharp/ rounded
- Surface may be smooth or nodular
- No inherent mobility
- Liver span is usually around 15cm in anterior axillary line in adults
- Upper border goes under the rib cage, hence , digital insinuation not possible
- There may be upward enlargement
- Dull on percussion which is continuous with liver dullness
- Liver swellings may be bimanually palpable, but not ballotable
- Hepatic swellings may be classified as those involving only a part of the liver or entire liver..
- If a part is involved., it may be cyst, abscess , riedel's lobe, tumour.. Primary or secondary.
- If entire liver is involved.. All the medical conditions come under this category..plus . Multiple secondaries, polycystic disease, hydatidosis,

FEATURES OF SPLENIC SWELLING: (Remember 1,3, 5, 7, 9, 11)

- Size 1", 3 ", 5", 7 ounces & located under 9-11 ribs (left posterior axillary line) in line with 10th rib
- Located in left hypochondrium , loin or umbilical region
- Intraabdominal
- Intraperitoneal
- Moves freely with respiration
- Grows towards right iliac fossa, crossing the midline (b'coz of the phrenicocolic ligament which limits downward growth)
- Rounded anterior border with a notch
- Fingers cannot be insinuated between the swelling & costal margin
- No transmitted pulsations felt
- If it enters the loin, it may be binually palpable, but not not ballotable

- Venous hum may be appreciated over the mass & the epigastrium
- If the colon is distended, anterior colonic band of resonance can be appreciated
- Splenomegaly in jaundice case- portal HTN

EPIGASTRIC MASS - CAN BE

- Stomach
- Liver
- Lesser sac (pseudocyst of pancreas)
- Transverse colon
- Omentum
- Retroperitoneum
- Lymphnodes
- Aorta
- Body of pancreas
- Gastric swellings
- Leiomyoma (GIST)
- Bezoars
- Perigastric abscess
- Gastrinoma (rare)
- Lymphoma

FEATURES OF RENAL MASS:

- Hypochondrium/ loin
- Intaabdominal
- Retroperitoneal
- Vertically placed
- Rarely crosses midline
- Limited movement with respiration
- Bimanually palpable, ballotable (only if it is small)
- Digital indinuation possible
- Can be pushed into renal fossa

ABDOMINAL PAIN: SOCRATES:

- Site
- Onset
- Character
- Radiation
- Alleviating factors / Associated symptoms
- Timing (duration, frequency)
- Exacerbating factors
- Severity
- Alternatively, Signs and Symptoms with the 'S'

ABDOMINAL SWELLING: 9 F's:

- Fat
- Feces
- Fluid
- Flatus
- Fetus
- Full-sized tumors
- Full bladder
- Fibroids
- False pregnancy

DIFFERENTIAL DIAGNOSIS: "A VITAMIN C"

A and **C** stand for Acquired and Congenital

VITAMIN stands for:

- Vascular
- Inflammatory (Infectious and non-Infectious)
- Trauma/ Toxins
- Autoimmune
- Metabolic
- Idiopathic
- Neoplastic

LUMP: 6 Students and 3 Teachers go for CAMPFIRE":

Site, Size, Shape, Surface, Skin, Scar

- Tenderness, Temperature, Transillumination
- Consistency
- Attachment
- Mobility
- Pulsation
- Fluctuation
- Irreducibility
- Regional lymph nodes
- Edge

SURFACE MARKING

LIVER

Rt. Lobe upper border: 5th rib- 2cm medial to the Rt.mid clavicular line (1cm below the right nipple)

Lt. Lobe upper border: 6th rib at a point in the Lt. mid clavicular line (2cm below the left nipple)

Lower border: 9th Rt → 8th left costal cartilage.

GALLBLADDER

Fundus : Junction of outer border of Rt.rectus abdominis muscle with Rt. costal margin

Grey Turner method: Lt. Spinoumbilical line extended tort. Costla margin- useful in obese

METHOD OF EXAMINATION

LIVER

- Lower edge - palpate just lateral to the Rt. rectus muscle. Liver movement is 1-3cm downward with deep inspiration.
- Common causes of a liver palpable below the umbilicus: malignant deposits, Polycystic or Hodgkin's disease, amyloidosis, congestive cardiac failure.
- Enlarged caudate lobe as epigastric mass - Budd-Chiari syndrome or with some cases of cirrhosis, may be palpated as an epigastric mass.
- Firm liver - Cirrhosis and hard in malignancy
- Pulsatile liver: Tricuspid regurgitation
- Anterior liver span: Vertical distance between the uppermost and lowermost points of hepatic dullness by percussion in the right midclavicular line. This is usually 12-15cm.
- Friction rub- palpable/ audible → Recent biopsy/HCC/ perihepatitis
- Venous hum of portal hypertension-Between the umbilicus and the Xiphisternum
- Arterial murmur over the liver → Primary liver cancer or alcoholic hepatitis.

GALLBLADDER-

- Palpable only when it is distended
- Pear shaped cystic mass
- 7 cm long
- Moves down on inspiration
- Mobile laterally but not downwards.
- Dull to percussion - Directly impinges on the parietal peritoneum(colon is rarely in front of it)
- Better seen than felt
- Inflammation of GB → positive Murphy's sign

Meckel's diverticulum:

- 2 inches long.
- 2 feet from end of ileum.
- 2 times more common in men.
- 2% occurrence in population.
- 2 types of tissues may be present.

Retroperitoneal structures: SAD PUCKER

- Suprarenal glands
- Aorta & IVC
- Duodenum (half)
- Pancreas
- Ureters
- Colon (ascending & descending)
- Kidneys
- Esophagus (anterior & left covered)
- Rectum

MALABSORPTION

Maldigestion: Defective digestion of complex nutrients to smaller molecules

Malabsorption: Defective mucosal absorption

History:

- Diarrhea
- Abdominal pain - unusual except in transmural diseases - Eosinophilic enteritis, crohns disease,TB, lymphoma, chronic pancreatitis.
- Celiac disease - Childhood history of diarrhea, positive family history, gluten hypersensitivity, anemia, growth retardation, mild elevation of liver enzymes, T1DM
- Past history of surgery
- Recurrent peptic ulcer - ? ZES
- Signs of nutrient MAS
- Alcohol
- Steatorrhea

Signs and symptoms of malabsorption

MAS	Clinical features	Diagnosis
Carbohydrate	Watery diarrhea, excess non fowl smelling flatulence and abdominal distension- more after 90 minutes of carbohydrate ingestion.	Hydrogen breath test D- Xylose test
Protein	Fowl smelling flatulence, Ascites, pedal edema, muscle atrophy, amenorrhea	Hypoalbuminemia Hypoproteinemia
Fat	Pale voluminous stool, steatorrhea, no flatulence	Stool fat >6%
Vit B12	Macrocytic anemia, Ataxia/tingling both LL	Vit B12, MMA
Iron	Microcytic anemia,glossitis, pagophagia	Iron, ferritin,TIBC
Vit B	Cheilosis, glossitis,angular stomatitis,Macrocyclic anemia	Folate
Calcium, Vit D	Paresthesia, tetany, pathological #	Calcium, Alkaline phosphatase, Vit D3, Bone densitometry
Vit A	Follicular hyperkeratosis, night blindness	Retinol decreased
Vit K	Hematoma, bleeding disorders	PT prolonged
Vit E	Parasthesias, Muscle cramps	

Diagnosis:

Clue: decreased- hemoglobin, serum folate, iron, ferritin, B12, calcium, magnesium, cholesterol, albumin, Vit D3

Increased: PT/INR, TIBC, Oxalate in urine

Investigations:

- Qualitative stool fat followed by quantitative stool fat (72 hr- Van De Kramer method) for fat MAS
- D-Xylose, Breath H₂ test, lactose tolerance test, stool pH<5.5 for carbohydrate MAS
- Protein, albumin, citrulline, α 1 AT for protein MAS
- Decreased triglyceride in abetalipoproteinemia
- Endoscopy and Duodenal biopsy - cobble stone, aphthous ulcers in crohns, white spotted appearance in lymphangiectasia, multiple ulcers in ZES and scalloping in celiac disease. On biopsy- examine for atrophy
- Biopsy confirmatory in Abetalipoproteinemia - lipid accumulation in enterocytes, collagenous sprue- collagen band in sub mucosa, mycobacterium avium complex- AFB and foamy cells and whipples disease with foamy macrophages and PAS positive inclusions.
- Ultrasound abdomen- thickened bowel loops/ evidence of chronic liver disease
- Barium series - flocculation, dilution of barium
- CT abdomen - Chronic pancreatitis/pancreatic hyper secretory tumor/ crohns disease/lymphoma
- Serological tests - IgA Anti TtG Ab- celiac, Ig profile- CVID, HIV- AIDS, ANA - vasculitis
- Bacterial overgrowth - Glucose/lactose hydrogen breath test, quantitative culture of jejunal aspirate

GASTRO

Associated factors in disease

CONDITION	FACTORS	GENES
EoE	Th2 reponse, IL-13, TGF beta	Eotaxin-3 overexpression TSLP gene (chr 5)
Eosinophilic gastroenteritis	Th2 response, IL4, IL5, IL13 ↓ IgA associated, ↑ IgE IL-9 driven mast cells cause diarrhea Peripheral eosinophilia and in gut Extracellular MBP and ECP (eosinophilic)	Eotaxin-1
Eosinophilic colitis	Non IgE disease STAT-6 dependent Blood and stool eosinophilia Bimodal	
Pancreatitis	IL-6	
GERD	IL-6, TNF α	
Gastric Carcinoma	IL-6, IL-11	
Ophisthorchis Cholangitis	IL-6	
Alcoholic Liver Disease	IL-6, IL-8, IL-18, TNF- α	
Giardia	Il-6	
Post operative ileus	IL-6, IL-8, Tryptase	
H Pylori	IL-8, PAF	
Hypoclorhydria	IL-1 β	
Parasitic Infections	IL-5	
NK Cells	IL-5	
IBS	Mast cells, T lymphocytes, Serotonin	SCN5A
Inflammatory GI neuropathies	CD3, CD4, CD8 T Cells near myenteric plexus	
Post infectious IBS	CD3, CD4, CD8 lymphocytes, macrophages, mast cells	
H pylori infection	Th1	
CD	Th1	
UC	Th2	
Lymphomatous and collagenous colitis	CD8 T cells	

CONDITION	FACTORS	GENES
LCD ????	CD3 & CD8 T cells	
IC	HLA A1	
IBS	Mast cells	
Post infectious IBS	CD3, CD4, CD8 T Cells, IL10/12 ratio	
EPEC	IL-8	
AIH	HLADR-3 associated with poor immune suppression outcome post LTx	
Tropical enteropathy	Fecal neopterin	
Not sprue	A marker of inflammation	
Epithelial hemangioendothelioma	CD 31 or CD 34 factor VIII associate antigen	
Cavernous hemangioma	Mast cells	
Angiosarcoma	Thorium dioxide Arsenic Vinyl chloride	
Hepatopulmonary syndrome	TGF beta → ET1 TNF alpha Endotoxemia eNOS VEGF iNOS heme oxygenase	
Splanchnic vasodilation	O pro co no gluco Opiates Prostacyclin CO NO Glucagon Adrenomedullin	
Kidney injury other than HRS	IL-18 uNGAL	
Esophageal atresia	Adriamycin = doxorubicin	
Banty's disease = NCPF = Idiopathic PHTN = Hepatoportal sclerosis	Arsenic Vinyl chloride Hypervitaminosis A ET-1	

Bacteria

	VIBRIO (non invasive)	SHIGELLA	SALMONELLA	CAMPYLOBACTER	YERSINIA
CHARACTERS	Gram negative Polar flagella Motile High O ₂ demand Alkaline media High salt Epi/pandemic by O1/O139 Mortality: adult 1%; child 3%	Gram; Non motile <i>Lactose negative</i> <i>No gas from glucose (except sonnei)</i> Survive acidic media Best is alkaline media Sensitive to heat / drying	Gram negative, Motile Little/no gas from glucose Affects extreme of ages S.Enteritidis 90% infn (not in Asia) Predispose for nontyphi infection: Malaria, Bartonella, SCA, Schizostoma IL-12/23 defect, UC, Neoplasia, HIV S.Typhi not affected by HIV	Shape like vibrio Gram negative rods Polar flagella, comma shape Motile Reduced O ₂ tension Requires CO ₂	Gram negative rod Urease positive Grows in Fe++ media Non lactose fermenting Needs lower temperature Becomes nonmotile at 37°C
IP	Hours	Fever – 2 days Diarrhea – 4 days Dysentery – 7 days	6-72 hrs (non typhoid) 7-14 days in Typhoid F. (lasts 4 wk)	1-3 days DOI = 7 days (recurs in 25%)	1-2 days DOI – 1-2 days
ACTION AT	Duod. & upper jejunum	Colon & ileum > SI	SI (ileum) > colon		Terminal ileum
TOXIN	Cholera toxin → A + 5 B Bind GM1 on BLM Inc. cAMP ZOT Accessory toxin (ACE)	Invasion plasmid: • IpaA, IpaD • IcsA- actin polymers Injected via T3SS IL-8 = calls neutrophils ShET1, ShET2 act on SI Stx only by S. dysenteriae	Intracellular proliferation + in RES T3SS is important SCV helps immune evasion SCV – salmonella cont. vacuole SPI (patho. Island) Main host defens is TLR & NLR Vi antigen on SPI-17 prevents TLR	Adhesion factor : CadF Adhesion and invasion CadF mediated internalisation Cytotoxic disten. tox (CDT) CDT cause DNA damage Early mucosal damage	Adhere mucosa and invade M cell → submucosa → peyer's patches pYV - plasmid of virulence Invasion is by : Inv; YadA; Ail HPI found in 1B / O:8 produce Yersiniabactin
INOCULUMS	10 ⁸ -10 ¹¹	10 bacilli Feco-oral – 20% SAR MSM / person-person	10 ³ -10 ⁶ (10 ⁷ -10 ¹⁰ for S.Typhi) person-person transmission		Feco-oral route
RESERVOIR	Copepods, Zooplankton Aquatic plants, Water fowl	DOI = 3 days in children 7 days in adult	Chicken, eggs (for non typhoid) Only Humans in S.Typhi / paratyphi	Cattle, Sheep, Swine, Birds, Poultry, Dog	Pigs & other cattle
NOTES	El-tor is hardier but milder El tor → current pandemic Seventh pandemic is on Stool infectious till 5-24 hrs Stool is iso-osmolar Don't invade -except O-139 Endoscopy normal Hypokalemic acidosis No bacteremia & sepsis (except non-cholera vibrio) 2 Oral killed vaccine tried	Most severe- S.dysenteriae 1 Mortality 5-15% ; 10% IBS S.Sonnei (4)– mildest ds Spreads within mucosa Not beyond mucosa Unless compromised Cell to cell transmission+ Recurrent symptoms + Cross react to HLA-B27 Toxic colon / perforation HUS / TTP / rose spot Severe protein loss E.nodosum / myocarditis Meningismus/seizures +	Highest rate in <1 yr & > 60 yr Attacks ileum Small ulcers (not in S. typhi) MC C/F – enterocolitis Non typhoid bacteremia → aorta IL12/23 defect in invasive ds. No recurrent sympt (like shigella) S.Typhi → cholecystitis Only S.Typhi has Vi Ag → virulence Vi ↓ PMN activation locally ViaA & viaB on SPI 7 has Vi genes SPI specific to S.Typhi = 15,17,18 Typhoid F: no GI symptom in 50% Pea soup diarrhea/perfo. by III wk	In children < 5 yrs Spread by uncooked meat Poultry is MC source Can cause bacteremia Diarrhea in 90% Fever in 70-90% Can cause meningitis Reactive arthritis in HLA 27 Can cause GBS, IPSID	Children < 5 yr – high incidence Feco-oral route Found in cooler climates Microcolonies in peyer patches High virulence biotype : 1B Young children : self limiting Mesenteric adenitis + Affects terminal ileum Mimics UC Arthritis in HLA 27 + in 2-3 wks Bacteremia in compromised

	VIBRIO (non invasive)	SHIGELLA	SALMONELLA	CAMPYLOBACTER	YERSINIA
Investigation	Hanging drop	Stool culture + till 3-4 wks Sometimes 3-4 months	BASU (gold std → BM culture) Blood/BM, Ag/AB, stool, urine	Acute only by stool Culture Dark microscopy (darting)	Culture of stool and body fluids
TREATMENT	Stat dose of : Doxycycline 300 mg Azithro 1000 mg in pregn. Zn ± reduce duration/severe	Rx – FQ → prevent HUS Azithro or CS-III in kids No antimotility drugs Zn, Green banana(SCFA) NO amox or TMP/SMX	FQ if complicated (nontyphoid) Rx of typhoid, always → FQ 2nd choice - III gen CS or azithro No ampicillin / chloramphenicol Treat carrier with FQ if its S.Typhi Ty21a:live attenuated/oral – 5 yrly booster ViCPS:fractionated /parenteral -2 yrly booster	No AB in mild infections Rx with FQ or macrolide Single dose Azithromycin Produce β lactamas thus Resistant for III gen CS But imipenem is effective	No AB in mild infections In severe disease only : Rx with tetracycline, cotrimox III gen CS, carbapenem <i>Resistant to I gen CS & penicillins</i>

EPEC	ETEC – india	EIEC	EHEC (STEC / VTEC) verocytotoxic	EAEC
IL-8 release Defective NaCl transport Attachment effacement (LEE pathogenic island for effacement) Typical and atypical forms Bundle forming pilus	Colonisation factor plasmid CFA (I,III,IV) & CS Stable toxin- ST 2 kd, On both LI & SI More potent , act Via cGMP Resist 100 degrees Labile toxin - LT (cholera) 84 kd, Affects only SI Act as CT / Via cAMP	Has toxin & virulence factors of shigella Has invasion plasmid pINV	O-157 & non O-157 Shiga like toxin (A+5B) Stx2a gene of shigella (1&2)- A+5B Attachment effacement lesion like EPEC LEE pathogenic island like EPEC Toxin inhibits protein synthesis /microthrombi S/M lesions resemble ischemic colitis Thrombocytopenia + Can cause HUS (O157-H7)	No attachment effacement seen Attach in stacked brick pattern Toxins : eat shit & hemolysis EAST ShET1 Hemolysin
Children < 1 yr age & HIV	< 2 & > 15 yrs Incubation 1-2 days Duration of illness is 3 days		Children 1-4 yrs of age 1 day – 14 days (DOI 3-8 days) Longer in children and bloody diarrhea cases Peak in june-september	Children , HIV , Travellers
Forms pores in cells	Adhere with tia & tib Do not invade mucosa/blood Cholera like symptoms +	Bloody dysentery may be seen	Begins as non bloody and progress to Classical bloody (more with O-157) Left shift in leukocytes	Acute and persistent Diarrhea Bleeding in 1/3rd children seen Has been linked to :HIV, Trav Diarrhea
Self limiting disease Persistant form is seen No Rx unless complicated	Self limiting disease No treatment required Recombi. whole cell vaccine +		No need of Rx mostly Rx with FQ can cause HUS	No need of Rx unless : O44-H18 → more pathogenic In Europe it acquired O104-H4 - adults
Disruption of tight junction (IL8) Disrupts NaCl transport Breast feeding is protective aEPEC is more important	MCC of community dia. MC cause of traveller's dia. Can cause severe dehydration Whole cell vaccine tested ST diarrhea is more severe!		By hamburger meat, milk, person – person Most important reservoir is cattle MC site of ulcers – ascending colon MC for site segmental colitis – Asc.Colon Thumbprinting → ascending & transverse Diagnosis by: Screen in sorbitol agar (O-157 don't ferment) Confirm with culture and toxin assay both Confirm with culture if EIA + (to R/O false +) PCR isn't FDA approved , but is used	Cause travellers diarrhea along with : ETEC

Adhesion(can rarely cause acute or persistant diarrhea in children) → Aggregation → Toxic → Invasive → Pathogenic → Hemorrhagic
(STEC) E.Coli is gram negative rod, motile, has pilus, grows best @ 370; heat labile

Aeromonas	Fresh and Brackish water, summer months, psychrophilic, 22-25 degrees, MC strain is A. Salmonicida Affects extremes of ages (< 2yrs & > 80 yrs) ; acute self limiting diarrhea for 3-10 days, Can cause segmental colitis, ischemic colitis or HUS; FQ or III gen. CS for chronic symptoms rarely (resistant to penicillin)
Plesiomonas	G-; fresh water, P. Sheigelloides can cause travelar's diarrhea Diarrhea often associated with pain, fever, vomiting; or III gen. CS for complicated cases rarely (resistant to tetracyclin)

DRUGS CAUSING MALABSORPTION	
A	Acarbose, Antacids, Azathioprine
B	Biguanides
C	Carbamazapine, Colestyramine, Colchicines
E	Ethanol
F	Fibre
G	Glucocorticoides
H	H2 Receptor Blockers
L	Laxatives
M	Methotrexate, Methyldopa
N	Neomycin
O	Orlistat , Olestra, OCP
P	Phenytoin, PPI, Pyrimethamine, PAS Phytates
S	Somatostatin Analogue, Sulfasalazine, Sulfonamides
T	Tetracycline, Thiazide, Triamcinolone

Extras for GOLD

Extrahepatic manifestations of PBC:

- Sjogren's syndrome (MC association)
- RTA
- Arthritis, arthropathy, Osteoporosis
- Gall stones
- Thyroiditis NO PANCREATITIS
- PSS and CREST
- LP, DLE, pemphigoid
- Celiac disease,
- Hepatocellular carcinoma (19 times higher)

Extrahepatic manifestations of AIH:

- RA, SLE, EN, nephritis
- Coombs + anemia
- Pernicious anaemia,
- Systemic sclerosis, celiac
- Thrombocytopenia,
- Cryoglobulinemia,
- Leukocytoclastic vasculitis
- Fibrosing alveolitis

Extrapancreatic manifestations of AIP :

- Biliary stricture
- Hilar lymphadenopathy
- Sclerosing sialadenitis
- Retroperitoneal fibrosis
- Tubulointerstitial nephritis
- Pseudotumor – lung, liver, pancreas, kidney

Paraneoplastic syndrome of gastric cancer

- Nephrotic syndrome
- DIC
- Thrombophlebitis (Buerger's syndrome)
- Acanthosis
- Seborrheic dermatitis = senile warts
- Pruritus = sign of lesser tretat
- Bazex syndrome
- Triple palms

Extrahepatic manifestations of HAV

- Evanescence Rash
- Arthralgia
- Glomerulonephritis
- Arthritis
- Leukocytoclastic Vasculitis
- Cryoglobulinemia (Igm Anti HAV)
- Necrolysis
- Fatal Myocarditis
- Renal Failure
- Optic Neuritis/Polyneuritis
- Transverse Myelitis
- Cholecystitis
- Aplastic Anemia
- Pure Red Cell Aplesia
- Thrombocytopenia

Extrahepatic manifestations of HBV:

- Arthritis/dermatitis /vasculitis
- Polyarteritis nodosa (1&30%)
- Glomerulonephritis
- Membranous > MPGN
- MC mode : nephrotic
- Cryoglobulinemia
 - II → PM (monoclonal against IgM)
 - III → PP

Extrahepatic manifestations of HCV:

- RA
- Lichen planus, PCT, EMC, leukocytic vasculitis
- MPGN > membranous
- Hypothyroidism
- Cryoglobulinemia in 50%
- Mooren's corneal ulcer
- NHL
- Local lymphocytic sialadenitis

EXTRAINTESTINAL MANIFESTATIONS OF UC:

Cutaneous/oral :

- Drug reactions / photosensitivity due to sulfasalazine → MC skin manifestation in UC
- Angular stomatitis → vitamin B deficiencies
- Aphthous oral ulcerations (in 10%) → correlate with severity of colitis
- Aphthous stomatitis
- Erythema nodosum (2-4%) – due to panniculitis – self limiting in 30 days
- Pyoderma gangrenosum (1-2%) → just relate with the activity of colitis, but not parallels
- Pyostomatitis vegetans → pustular lesions of oral cavity → cobblestoning seen
- Pyoderma vegetans of hallopeau
- Sweet syndrome (acute febrile neutrophilic dermatosis)
- Psoriasis

Ophthalmologic :

- Conjunctivitis
- Episcleritis (MC along with uveitis)
- Scleritis
- Uveitis / iritis
- Retinal vascular disease

Musculoskeletal :

- AS – 1-2% (B27 +) → no relation with disease activity
- Osteopenia/malacia/necrosis/porosis
- Peripheral arthropathy → responds to Rx → (type I – pauci, large joints, more frequent, < 10 wk duration, self limiting)
- Sacroileitis – 10-15% (B27 negative) → no relation with disease activity

Hepatobiliary :

- AIH / PSC
- Cholangiocarcinoma
- Hepatic steatosis
- Pericholangitis

Hematologic :

- Anemia of chronic disease
- Iron deficiency anemia (and other vitamin , Zn deficiency)
- Coomb's positive haemolytic anemia (due to sepsis and G6PD deficiency by sulfasalazine)
- **Hypercoagulable states – DVT, pulmonary embolism** (anticoagulant don't increase colonic bleeding)
- Increased WBC & platelets
- Decreased WBC & platelets

CVS and others :

- Pericarditis
- Pleuropericarditis (also due to mesalamine therapy)
- Constrictive pericarditis
- Decrease in pulmonary reserve and pulmonary diffusion capacity
- Bronchiectasis, bronchiolitis, fibrosing alveolitis , pulmonary vasculitis
- Systemic amyloidosis → mainly affects kidney

EXTRAINTESTINAL MANIFESTATIONS OF CD:

Cutaneous/oral :

- Aphthous ulcers
- Metastatic chronic's (ear, perineum, feet, leg, penis)
- Erythema nodosum
- Pyoderma gangrenosum
- Leukocytoclastic vasculitis
- Sweet syndrome
- Epidermolysis bullosa acquisita
- Psoriasis
- Cutaneous PAN

Ophthalmologic :

- Episcleritis (CD>UC)
- Uveitis (insidious)

Musculoskeletal :

- Clubbing is very common
- Peripheral arthralgia: MC in knee and ankle, non deforming, seronegative, no DIP
- Granulomatous vasculitis, periosteitis, amyloidosis
- Osteopenia/malacia/necrosis/porosis
- Pseudoarthritis, aseptic necrosis, osteomyelitis
- Sacroileitis (B27 positive in 75%; associated with iritis)

Hepatobiliary :

- Gall stones
- Mild enzyme elevations
- Small duct PSC and cirrhosis (UC>CD)
- AIH and fatty liver
- Hepatic steatosis

Others :

- Entrapment of ureter
- Renal stones
- MPGN
- Penile edema
- Renal amyloidosis
- Venous > arterial thrombosis
- Hyperhomocysteinemia
- Asthma / COPD
- All kind of - itis

EXTRAINTESTINAL MANIFESTATION OF IBS

- Headache migraine
- Backache
- Impaired sleep
- Chronic fatigue
- Increased urinary frequency
- Pelvic pain
- Fibromyalgia
- TM joint disorder
- Dysparunia
- IBS is associated with IBD (CD>UC) & CeD (in 1/3rd patients)

EXTRAGASTRIC MANIFESTATIONS OF H PYLORI INFECTION :

- Raynaud's syndrome
- Scleroderma
- Idiopathic urticaria
- Acne rosacea
- Migraines
- Thyroiditis
- GBS
- Thrombocytopenic purpura
- Iron deficiency anemia

Extraesophageal manifestations of GERD :

- Noncardiac chest pain
- Asthma
- Posterior laryngitis
- Chronic cough
- Recurrent pneumonitis
- Dental erosions

- Disordered sleep
- Interstitial pulmonary fibrosis
- Bronchitis
- Bronchiectasis

Associated conditions with microscopic colitis :

- Arthritis
- Celiac disease
- Autoimmune disorders

Para neoplastic syndrome of HCC :

- Musculoskeletal : HOPA, Hypercalcemia (sclerosing variety), Osteoporosis, Polymyositis
- Blood : Porphyria, polycyathemia, Erythrocytosis (10%), Thrombophlebitis Migrans
- Endocrine :
 - ▶ Isosexual Precocit, Gynecomastia, Feminisation,
 - ▶ Hypoglycaemia (A is mider & late & B is earlier, due to IGF II & is severe)
 - ▶ Thyrotoxicosis, HTN
 - ▶ Crcinoid syndrome
- Watery diarrhea syndrome
- Neuropathy
- Pityriasis rotunda circumscripta: African, scaly hyperpigmented on trunk and thighs, 0.5-25 cm

Lynch syndrome associated tumors: muir torre variant

- Endometrium
- Ovary
- Stomach
- SI
- Ureter / renal pelvis
- Pancreas
- Brain
- Hepatobiliary tract
- Multiple sebaceous adenoma & carcinoma
- Keratoacanthomas

Alagille syndrome :

- Cholestasis → in 96%
- Congenital heart disease
- Peripheral pulmonary stenosis → in 90%
- Cardiac murmurs
- Systemic vascular malformations
- Mild/moderate mental retardation
- Facies: broad forehead, deep & wide set eyes, prominent ears, small & pointed mandible, flat malar
- Posterior embryotoxon, retinal pigmentation
- Short stature
- Butterfly vertebra, hemivertebra, decrease interpedicular distance
- Decreased bone age
- Shortening of **distal** phalanges
- Hypogonadism, renal abnormalities
- **Increased GH & GHBP (due to reduced growth hormone sensitivity)**

GENES AND DISEASES

Tangier disease	ABCA-1 → chr 9	Alpha lipoprotein deficiency, Reduced HDL HSM +, clouding of cornea, neuropathy, Mild hyper triglyceridemia, orange tonsils
Sitosterolemia	ABCG5/ABCG8	Premature atherosclerosis Phytosterol is not excreted from body
Primary BA malabsorption	ASBT (SLC1A2)	Chronic diarrhea
PFIC 1	ATP8B1 → chr 18	Hearing loss
PFIC 2	BSEP → chr 2	Hepatic fibrosis & malignancy
PFIC 3	MDR 3 = ABCB 4	GGTP, gall stones, bile duct proliferation
Dubin jhonson	MRP2 = ABCC 2	Pigmented liver
Rotor	OATP1B1 → chr 12 OATP1B3	Defective anion secretion e.g. BSP, ICG
Wilson	ATP7B → chr 13	Defect in copper excretion in the canaliculi
Menke's	ATP7A	Defect in copper absorption
Hemochromatosis	HFE → chr 6	Irreversible gonadal, joint and P. endocrine disease
FAP	APC → chr 5	Multiple adenomatous polyps
HNPCC	MSH2 > MLH1> MSH6	High chance of cancer in polyps
Cholangio carcinoma	NKG2D – NK cell receptor K-ras IL-6 TP-53 P-16	
HCC	P-53	
Hepatoblastoma	APC → FAP Beckwith weidmann → chr 11	Age grp < 3 yrs of age
Microvillous inclusion disease	MYO5B	Autosomal recessive
Polycystic liver disease with ADPKD (AD condition)	ADPKD1 → chr 16 à polycystin 1 ADPKD2 → chr 4 → polycystin 2	
Isolated PCLD (AD)	PRKCSH → chr 19 SEC63 → chr 6	Isolated PCLD is only 7% of all PCLD
ARPKD	PKHD → chr 6 → fibrocystin	No gross cysts in liver Only microscopic cyst with fibrosis Fatal disease

NEMATODES

	Size	Epidemiology	Life cycle	C/F	Diagnosis	Treatment	Note
Ascariasis	Female 49 cm Male 10-30 cm Fertilized egg 35*55 mim Unfertilized 90*44 mim	25% of population	Ingestion of eggs with 3rd stage larva Incubation for 10-15 days in soil Viability 7-10 yrs 2 lacs eggs per day	Pneumonia after 2 wks of ingestion.	Endoscopy Retention of Ba	400 mg albendazole stat 100 mg BD; 3 days mebenda Glucocorticoids in pulmonary	Largest nematode SI obstruction with 60 worms 600 worms are fatal. Pregnancy promote biliary migration Visceral L.migrans Encapsulated eggs
Strongyloides	Filariform 500 mim Rhabditiform 250 mim Adult : 2 mm	Free living Embeds in jejunum	Filariform lava penetrates Rhabditiform passes in stool No eggs in stool	Larva currens (anal) Rt. sided colitis Sepsis (perforation)	ELISA IgG AB Rhabditiform L. Agar plates Serpentine tract	Ivermectin 200 mg stat Repeat dose in 1 wk 4 doses in I.compromised	Autoinfection Parthenogenesis seen Can cause fulminant disease No relation with sanitation Ass. S. Bovis meningitis,carditis
Capillaria		Birds are natural host	Eating raw fish	Protein loss Malabsorption Sprue like illness Death with CHF & Sepsis	Egg & larva in stool Egg resemble trichuris (bipolar plugs)	Albendazole 200 mg BD 10d	Autoinfection Mortality 30%
Ankylostoma Necator	Size 1 cm		Soil- human waste Rhabditifor larva – infective Also from oral route	Cutaneous L.migrans Blood loss: Necator .01-.04 ml/d Duodenale .05-.3 ml/d Pregnancy 2.14 mg/d Lactation .25 ml/d Menstruation .5 ml/d	Seen on endoscopy Eggs on stool Formaline fixed	Albendazole 400 mg stat	Iron deficiency Anemia Necator - south india; 10000 eggs/d Ankylostoma – 20,000 eggs/d Mod. Infn. 2000-4000 eggs/d Eggs are non encapsulated A.caninum → eosinophilic enteritis
Trichuris			Embryonated eggs – infective Lodges in caecum Eggs pass in stool Incubation in soil: 2-6 wks				20,000 eggs / day No autoinfection
Enterobius							
Trichenella							

NUMBER AND PERCENTAGES

NUMBERS	OTHER FACTS
<ul style="list-style-type: none"> • Incidence of ulcer after EST → 25-75% • Incidence of perforation in EST → 1-3% • Perforation in diagnostic endoscopy → 0.03-0.1 % • Onion skin fibrosis is seen in 50% of PSC cases • Post cholecystectomy diarrhea in 5-40% (20%) • Achalasia is equal in males and females • Transhepatic cholangiography below 10th ICS • Type I choledocal cyst is 80-90% of all • 5 yr survival of alcoholic hepatitis = 50-75% • Average no. Of cholesterol polyps in GB is 8 • Distance of Z line or GEJ from incisors is 35-40 cm • Post sphincterotomy bleeding = 2% • ERCP complications : <ul style="list-style-type: none"> ▶ Pancreatitis : diag → 3-5% ; Rx → 7.5 %; SOD → 15-20% ▶ Perforation : 0.1% ▶ Mortality : 0.01 % • SCFA , butyrate provides : <ul style="list-style-type: none"> ▶ 60-70% of colonic energy needs ▶ 10% of total body energy needs • Toxic megacolon in : <ul style="list-style-type: none"> ▶ Clostridium difficile → 5% ▶ Amoebic colitis → 0.5% • Daily minimum requirement of EFA : <ul style="list-style-type: none"> ▶ 5% of total daily energy intake (2/3rd as LA & 1/3rd as LLA) ▶ 10% of total fat intake • Mortality in diagnostic endoscopy → 0.001 % • Budesonide has 90% first pass metabolism • NAFLD in India 32% • Drug induced AIH → 42 days median • Frequency of overlap syndrome with AIH is 7-18% • Frequency of PSC in AIH with cholestasis → 6-11% • T1/2 of prednisolone = 3.2 hrs • Budesonide T1/2 = 2.8 hrs • Azathioprine metabolite peak in plasma , 4 hrs after oral ingestion • Full action of azathioprine takes 4 months to develop • Steroid related cosmetic effects → 80% in 2 yrs • Tumor occurrence with azathioprine → 3% after 10 yrs 	<ul style="list-style-type: none"> • Maximum risk of bacteremia after endoscopic dilatation → 45% • Earliest and most common manifestation of MEN-1 is hyperparathyroidism → 3rd decade • No purging in binge eating disorder, but concern for body weight is present • Blunted post prandial CCK response in bulimia (not in binge eating (BED) though) • Dysregulated PYY in AN & BN (not in BED - binge eating disorder) • Cl- secretion in GIT is an active process, K+ is absorbed passively • CoCo & LC are common in cecum and transverse colon, less common in left colon • Fat needed to induce GB emptying : 4-10 gm • Very low calorie diet : 800 kcal or less • Stomach HCO3 actively secreted by mucus cells ↓es with age , but not by vagal stimulus • α1 AT is excreted in stool of protein losing enteropathy (can be digested in pH<3) • Hp is gram negative, cause transient hypochlorhydria in acute infection • SI diarrhea → secretory, large volume, less pus cells, less bleeding & mucus • Salmonella doesn't cause sprue like illness • Parietal cells during secretion: pH 0.8, 160 mM of H+ → 17 mm Hg pressure • Gastric acid secretion like adult a by 2 yrs of age • Cathartic colon → ascending colon • Cardiac mucosa is absent in 50% • Stomach has 109 parietal cells, 106 gastrin cells • MC of exocrine pancreatic insufficiency in children → CFTR > SBDS • 1 isthmus produces 6 parietal cells in a month • Normally 85% of gastrin is G-17 (T1/2 is 3 min) • BAO upper limit in males = 10, in females = 5 • A 3 - to 4 - times increase in serum amylase levels 4 hours after ERCP predicts pancreatitis. • BAO decreases by vagotomy

NUMBERS	OTHER FACTS
<ul style="list-style-type: none"> Thickness of normal collagen band 4-5 mm In CoCo collagen band can be > 10 mm (usually 20-60 mm) Average stool in CoCo → 8/day i.e. 300-1700 gm/day Chronic DILI > 3months <p>AIH :</p> <ul style="list-style-type: none"> Asymptomatic in 35-45% Interface hepatitis in 9% Fibrosis in 40% In 6% present as fulminant Rx related Side Effects in 12% pts Rx failure in 9% Incomplete response in 13% after 3 yr Rx Drug tolerance in 13% S.IgG is normal in 25-35% 6 month mortality in untreated is 40% MELD > 12 fail with GC monotherapy Cirrhosis in 7-40% (varices develop in 13% of these) UGIB of any cause → 6% in 5 yrs MC cancer is HCC (1-9%) Annual rate of HCC in AIH with cirrhosis → 1.1 - 1.9 % (USG every 6 mon) Extrahepatic malignancy in 5% MC nonliver cancer is nonmelanoma skin cancer due to AZA 10 yr survival after LTx → 75% Need for retransplantation is 8% Mortality in these : <ul style="list-style-type: none"> ▶ UGIE → 0.01%; ▶ EST - sclerotherapy → 1.5% ; ▶ Endoscopic dilation → 0.01 % (equal to ERCP) ▶ Colonoscopic polypectomy → 0.05 % <p>Up to 5% can have bacteremia with diagnostic UGIE</p> <p>Liver stiffness on transient elastography if :</p> <ul style="list-style-type: none"> Normal liver stiffness is < 2.93 kilopascals > 17 kilopascals = cirrhosis > 21 kp = PHTN and complications <p>On ARFI: > 2.6 m/s indicates cirrhosis</p> <p>On MRE > 5.9 KPa indicate stiffness</p> <p>APRI > 2 indicates cirrhosis</p> <p>Bonacini cirrhosis discrimination score ≥ 7 → cirrhosis (no cirrhosis if < 3)</p> <p>Median survival of compensated cirrhosis = 9-12 yrs Median survival of decompensated cirrhosis = 2 yrs 10 yr probability of decompensation is 58%</p> <p>Annual rate of decompensation :</p> <ul style="list-style-type: none"> ▶ HCV cirrhosis – 4% ▶ Alcoholic cirrhosis – 6-10% ▶ HBV cirrhosis – 10% 	<p>BAO is ↑ in pernicious anemia, gastric CA, myxedema, rheumatoid arthritis.</p> <ul style="list-style-type: none"> Sham feeding increases acid by 50% Lowest BAO between 6-11 AM Highest BAO between 2-11 PM Increased BAO in late gastric phase III of MMC PAO (10-60) > MAO (5 -50) > BAO (5-10) MAO and PAO are high in men and smokers & correlate with parietal cell mass In ZES BAO/PAO is > 0.6 Hp reduces BAO and induced acid output H2RA reduces both basal and meal related acid secretion PPi reduce only meal induce avid secretion Stomach produces 60-80% of bodies gastrin Gastric lipase do not require co-lipase HRS-1 → CrCl ↓ by 50% or S. Cr doubles within 2 wks or to a level of 2.5 But definition of HRS is S. Creat > 1.5 in ascites, even after stopping diuretics etc Essential mixed cryoglobulinemia is seen in Rx with IFN MC site for intestinal atresia is duodenum Glucagon is spasmolytic MC site of GB polyp is fundus Nonspecific colon ulcer → proximal colon ,solitary, antimesenteric,40 yrs, demarcated, females MCC of Hypergastrinemia → Hypochlorhydria Most common surgical procedure during 1st 6 months of life → pylorotomy for IHPS cANCA in AIH, cANCA in PSC Prednisone is a prodrug Prednisone converted by 11beta HSD AIH improves during pregnancy but worsen after delivery Master regulator of bile acid synthesis → FXR Activation of FXR help in fat burning, dissipation CYP proteins are higher in zone 3 CYP2E1 increase by obesity, fat intake, fasting, DM, alcohol, INH Cirrhosis overall associated with reduced CYP enzymes MTX is dose dependent toxicity , avoid daily dosing NAFLD : fat in > 5% hepatocytes <p>• Heavy alcohol use is more than 3 drinks/day</p> <p>• MCC of mortality in cirrhosis = decompensation</p> <p>• MCC of mortality in compensated state → CVS cause !!!</p> <p>• Diuretics do not cause hepatorenal syndrome</p> <p>• Gastrinoma has no functionally coupled SST cells so secretin stimulates only gastrin</p> <p>• MUC-5 from surface cells</p> <p>• MUC-6 from MNC, mucus neck cells</p> <p>• Hp inhibits MUC-1</p>

NUMBERS	OTHER FACTS
<p>Level of von willibrand factor antigen above 315% → high decompensation risk. Acetaminophen can be given upto 2 gm in cirrhotics</p> <p>Survival in diuretic-resistant ascites is 50% at 6 mnth and 25% at 1 yr</p> <p>2 yr surviaval is ascite and cirrhosis is 50%</p> <p>Resistant ascites → excretion of sodium, frequently less than 78 mEq/day</p> <p>Diuretic sensitive ascites = urine sodium/potassium > 1</p> <p>Albumin for LVP(> 5 litre) = 6-8 gm / lit of ascetic fluid drain</p> <p>Ascites is diuretic resistant in 10 % of patients with cirrhosis and ascites</p> <p>K+ in gastric juice = 8-12 mMol</p> <p>Allowed sodium in cirrhotics → 2000 mg = 88 mEq = 5 gm of NaCl</p> <p>Only 10-15% of Hp patients have hyperacidity</p> <p>In ZES BAO > 15 ; BAO/PAO> 0.6</p> <p>25% of ZES have MEN</p> <p>PG-I is 80% of total pepsin → increases in pts on PPI & PG-II is 20% □ increases with Hp infection</p> <p>PG-I/PG-II < 0.3 is shows oxyntic atrophy</p> <p>Fasting serum gastrin > 400 pg/ml also indicate gastric atrophy</p> <p>PG-I/PG-II increase in renal failure</p> <p>ZES secretes G-34 > G-17</p> <p>Successful dissolution of gall stone → recurrence in 30-50%</p> <p>Least common stone is brown stone = 5%, black is 20%, cholesterol 75%</p> <p>Gall stone is max in 3rd trimester , increased parity in young is a risk</p> <p>Biliary sludge forms stones in 12-20% patients</p> <p>Gall stone seen in 30% of spinal injury patients</p> <p>Gall stone in CF = 10-30%</p> <p>IP of Cl difficile = 2 days , carriage is upto 2-6 wks following treatment</p> <p>In cl deficille 15-20% of pseudo membrane seen in proximal colon only</p> <p>15-25% of CDI can resolve eve without Rx over 2-6 wks</p> <p>Severe complicated CDI is seen in 10% , associated with high mortality</p> <p>25% of successfully treat CDI patients report recurrence , subsequent recurren rates are 40% & 50% for subsequent recurrences</p> <p>Only 10% of Cholangiocarcinoma are due to PSC</p> <p>Lifetime prevalence of Cholangiocarcinoma in PSC = 5-15%</p> <p>Annual prevalence of cholangiocarcinoma in PSC pts. = 0.5 -1.5%</p>	<ul style="list-style-type: none"> MUC5AC increases in Hp related gastric cancer Parietal cell migrate downward Earliest visceral manifestation to be described in PSS was esophageal disease Pain is not seen in esophageal scleroderma C/F of esophageal scleroderma : pain is not seen typically <ul style="list-style-type: none"> Reflux esophagitis & stricture formation Diffuse esophageal spasm Hypertonic upper esophageal sphincter Characteristics of GB colic are following : <ul style="list-style-type: none"> Peaks in 15 - 20 mins May last for 1 yr (not > 6 hr) Can lead to emergency visit Atleast once a yr Pain is not daily pain Right hypochondrial or epigastric Estogen increases cholesterol secretion in bile (affects negative feedback by SREBP) Statins and ezitimib are protective for gall stones , clofibrate predisposes HTG and low HDL associated with gall stones, not LDL cholesterol or total serum cholesterol Councilman bodies seen in hepatocytes with viral infection and yellow fever Most frequent complication of epidermolysis bullosa is esophageal stricture MCC of distal CBD obstruction is carcinoma pancreas MRI is best imaging for cholangiocarcinoma Pancreatic secretions during various phases : <ul style="list-style-type: none"> Cephalic – 20% Gastric – 5-10% Intestinal phase – maximum secretion

Numbers

- **Pancreatic ductal system constitutes 20-25% of pancreatic mass**
- **Normal cecal diameter :** 7.5 cm (widest part of colon)
- **Length of cecum = 6-8 cm**
- **Narrowest part of colon :** sigmoid = 2.5 cm
- **Toxic megacolon :** Transverse > 6 cm
- **Megacolon :** Rectosigmoid or descending >6.5 cm, Ascending > 8 cm, Cecum > 12 cm
- **Cecum > 10 cm** = ischemia , > 12 cm = imminent perforation in chronic obstruction cases
- **Cut off for impending perforation of cecum in Ogilvie syndrome = 9 cm**
- Chronic constipation : colon at pelvic brim > 6.5 cm
- Total bile duct length : 7 cm
- Sphincter of Oddi length : 7 mm
- Normal sphincter of oddi pressure : 7 (6-8) mm Hg
- Upper normal limit of baseline biliary sphincter pressure : 35-40 mm Hg
- Upper normal limit of baseline pancreatic sphincter pressure : ? mm Hg
- Pressure of biliary duct : 10-15 cm of water (bile flow slows @ 15, stops @ 30 cm of water)
- Pressure of pancreatic duct = 22 cm of water
- CBD : 4.5 cm length & 6 mm thickness at opening (12 mm at commencement)
- CBD thickness > 6 mm denotes choledocolithiasis (old records say 10 mm)
- Cystic duct : 4 cm
- GB : ? 7 x 3 cm (30 – 50 ml)
- Acute cholecystitis : GB wall thickness > 4 mm
- Gall stone ileus : 25 mm stone
- Esophagus : 18-26 cm length (2 x 3 cm)
- SI : 3-7 meter (0.3 + 2.5 + 3.5 m)
- Appendix : 9 cm (in ac. Appendicitis 7mm thick on USG and 6 mm thik on CT scan)
- IAS : 2-4 cm long and 3-5 mm thick
- Cecum length = 6-8 cm
- Ascending colon length = 12-20 cm
- Transverse colon length = 40-50 cm = longest and most mobile part of colon
- Descending colon length = 25-45 cm
- Sigmoid colon length = 35-40 cm
- Rectum = 10-12 cm (rectum does not have taenia coli)
- Anal canal : 2-4 cm
- Retal angle : 90 degree (110-130 @ defecation)

- No. Of columns of morgagni : 6-12, columns are joined by anal valves @ dentate line
- No. Of valves of huoston = ? 3
- Abnormal descent > 4 cm = perineal descent syndrome
- Resting anal canal presuure 80% by IAS, 20% is by IAS
- Esophageal capsule : 11 x 26 mm (14 fps), 50,000 pics, 0.1 mm resolution , 1560 captures
- LES : 2-4 cm
- Width of tenia coli= 6-12 mm (width increase from cecum to sigmoid colon)
- Pancreas : 12- 20 cm in length ; 70 -110 gm weight
- Villous height : 0.5- 1.5 mm (3-5 times the length of crypts)
- Villi increase the surface area by 400-500 times
- Each villous contain 2 central artery & 1 central lacteal except in duodenum where the number is 2
- Microvili increase the surface area by 14-40 fold
- Normal CD3+ cells in intestine : 30 cells per 100 epithelial cells
- Muscularis mucosa is only 3-10 cell thick
- Cell turnover in :
 - ▶ Gastric epithelium - 3 days
 - ▶ SI – 3-5 days- mature on reaching the upper third of the villus
 - ▶ Colon - 3-8 days
- Hypotensive peristalsis : < 30 mmHg
- Resting LES tone : 10 -30 mmHg
- Resting UES tone 70-80 mmHg
- To prevent GER : 5-10 mmHg
- Crural contraction produces : 5 – 10 mmHg
- Resting anal tone : > 60 mm Hg
- Anal tone on squeeze : > 180 mHg
- CBD normal pressure : 10-15 cm of H₂O
- Bile flow decrease if > 15 cm of H₂O
- Bile flow stops at > 30 cm of H₂O
- Mean colonic transit time : 34 hrs
- Fasting gastric pH : 2
- pH of saliva : 6.4-7.8
- Portal vein : 7.5 cm in length, upper 5 cm has no tributaries
- Portal vein in PHTN : >6 mm Hg & >13 mm in diameter
- Varices 10 @ mmHg, bleed @ 12 mmHg , treatment goal <12 mmHg; high rebleed @ > 20mm Hg
- Portal hypertension : hepatic sinusoidal pressure > 6 mmHg
- 30 % of blood and 60 % of oxygen to liver is supplied by hepatic artery

- Lipase & amylase half life = 10 hrs
- Daily GI secretions :
 - ▶ Biliary : 500 ml
 - ▶ Intestinal : 1000 ml
 - ▶ Pancreatic : 1500 ml- 2500 ml (0.2 ml/min @ rest; 4 ml/min @ feed; has 120 mEq of HCO₃-)
 - ▶ Salivary : 1500 ml
 - ▶ Gastric : 2500 ml
 - ▶ Dietary : 1500 ml
- Daily water absorption from :
 - ▶ Jejunum & Ileum : 7 L
 - ▶ Colon : 1.4 L
- Duodenum : 30 cm as whole (5+10+10+5), 3rd part is longest of all
- Length of jejunum = 2.5 meter, ileum = 3.5 meter, colon = 1.5 meter
- RDA of fibre = 25-30 gm per day, provided as mainly insoluble fibres
- Stomach has 109 parietal cells and 106 gastrin cells
- Gastric cardia (transition zone) 0-9 mm long
- Pancreatic secretion 0.2 ml/min in resting state, 4 ml/min in fed state
- Pancreatic weight = 70-110 gm
- 1 isthmus of parietal gland produces 6 acid producing parietal cells in a month
- Turnover of parietal cells : 54 days
- ENS has 106 neurons
- Parietal cell acid secretion at concentration of 160mM pr pH 0.8
- K⁺ in gastric juice = 8-12 mM/L
- BAO = Males ; 10 mmol/hr, Females ; 5 mmol/hr
- MAO = 5-50 mmol/hr , PAO= 10-60 mmol/hr
- Bile acid concentration in intestine : 5-10 mmol/l
- Bile acid concentration required for micelle formation : 1.5 mmol/l
- Concentration in portal blood : 20-50 micro mol/l
- Concentration in systemic blood , fasting : 2-5 micromol/l, postprandial : 5-15 micromol/l
- Total bile acid pool 2-4 gm
- Maximum rate of synthesis : 4-6 gm/day
- BA pool cycles daily : 6-10 times (2-3/meal)
- Daily reabsorption of bile : 10-30 gm
- Bile excreted in stool : 0.2-0.6 gm/d
- GB stores 30 ml of 10X concentrated bile
- Bilirubin production per day : 4 mg/kg/day
- T_{1/2} of bilirubin = 4 hrs

- Colon receives 10-30% of cardiac output
- 1 gm wheat = 2.5 gm stool
- 1 mmol of Mg++ = 7.5 gm stool
- 200 ml N₂ is evacuated from rectum per day
- Angiectasia : 2-10 mm
- Normal blood loss in stool : 0.5 – 1.5 ml/ day
- Normal production of bilirubin : 4 ml/kg/d
- Length of rigid sigmoidoscope : 20 cm
- Length of flexible sigmoidoscope : 60 cm (many use gastroscope instead)
- Length of gastroscope : 100 cm
- Length of side viewing scope : 120 cm
- Length of colonoscope : 160-180 cm
- Length of single/double balloon : 200 cm
- Length of push enteroscope : 220-250 cm
- Proctoscope(uses fibre optic light) : length – 25 cm , diameter – 10-20 mm
- Anoscope(obturator and sheath) : diameter - 20 mm
- Volume in SBT : 200-400 ml
- Volume of minesotta tube bulb : 500 ml
- Volume in linton nachlas tube : 600 ml
- Albumin forms 75% of oncotic pressure
- Body has 300-350 gm of albumin
- Albumin produced in body : 15 gm/day
- Daily Albumin loss in stool : 2-15% of total loss
- Daily ULN of fecal fat loss 7 gm (7% of 100 gm)
- REE : 1 kcal/kg/hr
- Energy expenditure : 70% in REE, 20% in activities, 10% in thermal effects
- RDA for protein : 0.8 gm/kg/day (15-20 %should be from EAA)
- 1 gm nitrogen = 6.25 gm of amino acids = 30 gm of muscle
- 5-20 gms of soluble and insoluble fibres are taken daily
- A healthy excretion of 12 gm Nitrogen in urine = 80 gm of protein (amino acids)
- 95% of REE is in lean body mass, only 5% in fat (28% of body weight)
- Total body albumin pool : 4.7 gm/kg in male , 3.9 gm/kg in female
- Daily albumin synthesis in body : 0.15 gm/kg/day
- Enteric loss of albumin = 2-15% of total body albumin degradation daily (average is < 10)
- T1/2 of albumin is 15-33 days
- Muscle mass of 22% of body weight

- Normal PaO₂ > 80 mm Hg
- PCWP = 6-12 mmHg
- Pulmonary resistance < 250 dynes
- P(A-a)O₂ = 5-10 mmHg
- RV pressure → systolic = 15-30 mmHg, diastolic = 3-8 mmHg
- PAP → systolic = 15-30 mmHg, diastolic = 4-12 mmHg, mean PAP = 10-20 mmHg
- Normal SvO₂ = 65-70%
- Portopulmonary hypertension :
 - ▶ mPAP > 25mmHg at rest and > 30 mmHg on exercise
 - ▶ pulmonary capillary wedge pressure < 15mm Hg
 - ▶ pulmonary vascular resistance > 240 dynes/s/cm²
- Pancreatic ducts form 20-25% of pancreatic mass.
- Diameter of pancreatic duct 3,4 & 5 mm in head, body and tail
- Pressure of pancreatic duct : 22 cm of water
- HSC constitute 5% of liver cells, hepatocytes constitutes 60% of liver (by number), 70% (by volume).
- Physiologic hypoganglionic segment = 1 cm above anal verge
- RMC = rectal motor complexes = during sleep = 15-60 mm Hg, 15-30 minutes retrograde contractions
- Normal fat loss in stool :
 - ▶ Adult < 5%
 - ▶ Infants 10-15%
 - ▶ Premature infants 25-35%
- Frequency of slow waves in :
 - ▶ Stomach: 3 cpm
 - ▶ Duodenum; 12 cpm
 - ▶ Ileum : 7 cpm
 - ▶ Ileocecal junction : 6 cpm
 - ▶ Colon : 2-4 cpm
- Pneumatic dilation in c/o :
 - ▶ Achalasia – 3 cm
 - ▶ GOO : 1.5 cm
 - ▶ Esophageal stricture : ? 1.5 cm
- Bleeding after RBL ligation of internal hemorrhoides : 4-7 days ,
- Sepsis after RBL - 2-8 days (in compromised)
- Thickness of collagen plate in colon normally : 4-5 mm (> 10 mm , usually 20-60 mm in CoCo)
- Excessive perineal descent : > 3 cm
- Target goal of dilation esophageal Strictures in EoE = 15-18 mm (3mm in one sitting)

- In PSC for cholangiocarcinoma :
 - ▶ CEA > 129 is diagnostic
 - ▶ CEA > 1000 is non resectable
 - ▶ Biochemical index { Ca 19-9 + CEA } > 400
- Median survival of cholangio carcinoma = 5 months
- Only 5-40% of gut bacteria can be cultured normally
- Gut bacteria concentration :
 - ▶ Stomach : 10^3
 - ▶ D & proximal J : 10^2 - 10^3
 - ▶ Ileum : 10^{7-8}
 - ▶ Colon : 10^{10-12}
- SIBO seen in 45-55% of scleroderma patients
- SIBO is the cause for 10% of non responsive celiac disease
- For diagnosis of SIBO from jejunal aspirate : 10^5 CFU ; 10^7 for south Indian patients, in one study.
- Breath test positive for SIBO if among HBT → LHBT is more specific but less sensitive than GHBT
 - ▶ LHBT (10 gm): H₂ > 20 ppm within 180 min or rise from baseline within 90 mins
 - ▶ GHBT (50-75 gm) : baseline H₂ > 12 ppm or rises by 12 ppm after 2 hrs
- 12 hrs of fasting needed before HBT
- Antibiotic renders breath test negative in 40-7-% of SIBO cases
- CLINICALLY significant B12 mal-absorption – on 60 cm or more ileal resection
- Fat malabsorption occurs when > 100 cm of ileum is resected (affecting bile acid enterohepatic circulation)
- Ileal resection of < 100 cm → bile acid diarrhea , because liver can compensate
- Ileal resection of > 100 cm → fatty acid diarrhea , liver is exhausted of synthesizing BA
- A minimum of 100 cm of jejunum is needed to prevent intestinal failure
- SBS @ < 150-200 cm of total SI → 50-70% requiring TPN can be weaned
- Colon can absorb upto 3-4 litres per day
- Colon can absorb 500-100 Kcal per day
- Normaly 2-20% of ingested starch escapes SI absorption
- 90% of SCFA are absorbed in colon , 20-90% of gases produced are absorbed
- 45 gm of carbs should reach colon to cause diarrhea
- 80 gm of carbs daily can be metabolise to SCFA in colon
- Human can tolerate upto 25 gm of fructose per day
- 100 gm of fruit or soft drink contains 8 gm of fructose
- Human phasic small intestinal contraction lasts 0.8 - 6 seconds
- Within 10-20 minutes of meal ingestion IDMC (MMC) is abolished , and re-emerges in 4-6 hrs
- Post prandial orocecal time is usually less than 6 hrs
- Median duration of IDMC = 90-120 minutes

- Excitatory motor neurons project orad upto 10 mm, closely associated to ICCIM and fibroblast like cells
- Inhibitory neuros : are larger, fewer and project aborally for 1-15 mm , are tonically active
- Law of intestine → helped by interneurons
 - ▶ Ascending direction – orad contraction upto 40 mm
 - ▶ Descending direction – aborad relaxation upto 70 mm
- Daily effluent as stool 200-400 ml (100- 150 ml is water)
- Sympathetic system for colon L2-L5, via inferior mesenteric ganglion
- Pelvic floor muscles and external anal sphincter are innervated by S3-S4 pudendal nerve
- Net flow rate through gut = 1 cm / hr
- **ICC_{MY}** :
 - ▶ Faster/smaller amplitude/myenteric potential oscillations (MPO)
 - ▶ 12-20/min
 - ▶ Spread in both longitudinal and circular smooth muscles
- **ICC_{SM}** :
 - ▶ Slower/larger amplitude
 - ▶ 2-4/min
 - ▶ Spread only in circular smooth muscle cells
- Gap junctions allow upto 1000 kd molecules to pass through.
- Even nonpropagating contractions of colon (2-4 cpm) can propagate upto < 9 cm.
- Rectal motor complexes : amplitude 15-60 mmHg, duration of 3-30 minutes, prevalent during sleep.
- Resistance at ileocecal junction is maintained by 6 cpm phasic contractions
- Preparatory phase of stool expulsion : commence upto 1 hr before stool expulsion
- Gastrocolic response – 1-2 hrs after meal, suppressed at night
- 300 kcal for gastrocolic reflex, 200 kcal for increasing rectal tone
- Daily GI tract processes 8-9 lit of fluid
- Only 100-200 ml is excreted daily
- Microvilli increase surface area by 600 times → 3300 square cm to 20,00,000 square cm
 - ▶ Plica circularis → 3 times
 - ▶ Villi → 10 times
 - ▶ Microvilli → 20 times
- Zone of maximum UES pressure is 1 cm (encircled by cricopharyngeus) → manometric assessment is difficult
- We swallow 600 times in a day
- Laimer's triangle = 3 cm distal to cricoid cartilage
- Time between UES relaxation and opening is 0.1 sec
- Oesophagus is 20-22 cm long
 - ▶ 5% is striated
 - ▶ 35-40% is mixed
 - ▶ 50-60% is smooth

- Esophageal emptying is difficult if emptying pressure > 30mm Hg
- Shortening of longitudinal muscle during swallowing = 2-2.5 cm
- Contraction rate of esophagus = 2-4 cm/s
- LES length is 3-4 cm
- During MMC-III LES pressure may exceed 80 mmHg
- Resting LES tone range from 10-30 mmHg
- EGJ high pressure zone :
 - ▶ From 1-1.5 cm proximal to SCJ
 - ▶ To 2 cm distal to SCJ
- Dilation done in achalasia treatment = 3 cm
- Dilation of pylorus in PUD related GOO is 4 cm ???
- Dysphagia is observed when esophagus diameter is < 13,mm
- 1-5%of hyperemesis gravidarum may require hospitalization
- 30% of GERD with asthma hav no esophageal complaints
- Prevalence of GERD in general population is 35-90%
- 30-80% of pregnant females C/O heartburn mainly in first trimester
- After heller myotomy 10-20% can develope GERD
- 90% of patients with PSS have GERD
- Only 20-60% of GERD patients have endoscopic findings
- Pigbel – clostridium perfringens → 40% mortality
- Beginning at age 60 yrs, body wt reduces by an average of 0.5% every yr
- 175 molecules of water can be transport with each ion of solute
- K⁺-Cl⁻ → 500 water molecules
- Na⁺K⁺2Cl⁻ → 590 molecules
- SGLT can transport 210 water molecules per turnover, can absorb upto 5 lit of water
- Channels can conduct 106 ions/sec; along electrochemical gradient (carriers conduct at a slower rate)
- 5-15% of diverticulosis develope diverticulitis and bleeding, 90% of bleeding diverticula are right sided
- In healthy individuals esophagus is exposed to acid in 10% time of the day
- Alagille syndrome (AD) →
 - ▶ Ratio of bile duct to portal tracts is < 0.4
 - ▶ Chronic cholestasis is found in 95% of patients (though of variable degree)
 - ▶ Jagged1 (JAG1) gene is found in 94% of the patients
 - ▶ S. Bilirubin level of 2-8 mg / dl → intermittent rise
 - ▶ S. Cholesterol > 200 mg/dl
 - ▶ STG > 500-1000 mg/dl
 - ▶ 20 yr life expectancy is 75%

- ▶ Poor prognosis in alagille syndrome :
 - Total bilirubin >6.5 Mg/dl
 - Conjugated > 4.5 mg/dl
 - Cholesterol > 520 mg/dl in children < 5 yrs of age
- MELD awarded for HCC = 22 points
- MELD score of < 10 is ineligible for listing in liver transplantation
- Patients with MELD score < 15 have better survival without liver transplantation
- CPS of < 7 was a contraindication for liver transplantation
- Liver transplantation is best done for MELD between 15 – 34
- For TIPS : do it between MELD score of 14 – 24 (outside this range is bad)
- For hepatic re-transplantation : maximum utility is seen at MELD score of
 - ▶ HCV : MELD 21
 - ▶ Non HCV : MELD 24
 - ▶ Benefit start declining@ MELD > 28
- Patients with MELD > 18 or pts with ascites shouldn't be treated with IFN- α
- Do a resection of HCC nodule if its satisfying resection criteria and MELD is 9 or less
- In acute pancreatitis :
 - ▶ Ranson score : < 2 = lives ; > 3 = dead
 - ▶ BISAP score > 4-5 is associated with 10 fold increased organ failure
 - ▶ APACHE-II : < 10 (9 or less) survives; > 13 high death rate
 - ▶ For every 5 mg BUN rise mortality increase by 2.2 times (best predictor)
 - ▶ Hct > 44 % is indicative of severe necrosis
 - ▶ CRP cut-off for severe acute pancreatitis is 21 mg/dl (> 150)
 - ▶ GCS equal to more than 3 is severe disease
 - ▶ UTAP > 30 nmol/ml is severe disease
- Composite risk scoring system/rockall scoring system (in bleeding from gastric ulcer)
 - ▶ 0-2 = excellent prognosis
 - ▶ Equal or more than 9 = high risk of death
- CDAI : <150 = remission; > 450 = attack , response to Rx is fall by 75
- Activity in UC :
 - ▶ Fecal calprotectin level < 50 = remission; > 250 = active disease
 - ▶ Mayo score(0-12) : 2 or less = remission; > 10 = severe ; response = fall by 3
 - ▶ True love and witt's
- Median interval between symptom onset and diagnosis of UC is 9 months
- Crypt density in UC < 6 crypts/mm
- Length of ileum used in ileal pouch = 20 cm
- Number of stools per day after IPAA – 4-7 stools / day ; 1-2 nocturnal stools
- Time of ileostomy closure after IPAA = 2-4 months post IPAA formation

- Toxic megacolon not responding to medical Rx (50%) in 48 hrs should go for colectomy
- Mortality with free perforation in UC toxic megacolon = 50%
- Risk of malignancy in UC = 7-10% in 20 yrs (0.5%- 1% per yr after 8-10 yrs of disease)
- Acute pouchitis < 4 wks, chronic > 4 wks (common in UC than in FAP cases, highest in first 6 months)
- pANCA > 100 U/mL is associated with chronic pouchitis and not acute.
- Lifetime risk for cholangio carcinoma in PSC = 10-15%
- Scoring system for diagnosis of AIH : definite is 7 or more, probable is 6 or less
- Tropical pancreatitis (SPINK-1 mutation in 40%)
 - ▶ Exocrine insufficiency in 25%
 - ▶ Diabetes in 50%
- Caloric values of SCFA 3.5 – 6 kcal/gm
- LCFA > 12C can cause diarrhea in colon
- Carbohydrate malabsorption = stool pH < 5.5
- US of celiac disease : bowel wall thickness > 3 mm & bowel diameter > 2.5 cm
- Refractory celiac disease type 2 if >2/3 of
 - ▶ < 10 folds per 5 cm of jejunum
 - ▶ Mesenteric fat infiltration
 - ▶ Bowel wall thickening
- Fecal fat < 7 gm per day on a 100 gm fat diet is normal (14 gm if associated with diarrhea)
- Acid steatocrit of < 31% is normal, its a semiquantitative method
- Normal stool fat on slide < 100 fat globules / hpf; of size < 4mm
- Serum test for fat malabsorption : photometric measurement of beta carotene @ 456 nm
 - ▶ < 100 mg / 100 ml → suggestive of steatorrhea
 - ▶ < 47 mg/100 ml → strongly indicate
- 18% of normal population is hydrogen non excretors on hydrogen breath test
- Diagnosis of lactose malabsorption :
 - ▶ H₂ breath test < 20 ppm H₂ after 20-50 gm lactulose; samples in 30, 60, 90, 180, 240 mins
 - ▶ Lactose challenge test : 50 gm → serum rise of less than 20 mg/dl in 30 mins; less sensitive test
- D Xylose test :
 - ▶ 25 gm eaten → collect 5 hr urine sample
 - ▶ 50% of absorbed xylose is metabolised
 - ▶ Normal excretion in 5 hr 6 gm ± 1.5 gm
 - ▶ Abnormal excretion is < 3.5 gm in 5 hrs → suggest malabsorption
 - ▶ Abnormal is also a serum concentration of < 20 mg/dl @ 1 hr (less sensitive than urine test)
- Peyer's patches :
 - ▶ Appear at 60 days intrauterine
 - ▶ Develop @ 120-130 days of gestational period
 - ▶ Numbers peak @ age 15-25 yrs → 30 is maximum

- 50% of patients with imperforate anus have down syndrome
- 95% of pts with down syndrome have imperforate anus
- Deletion of chromosome 6 = anorectal malformations
- Deletion of chromosome 17 = hirschsprung disease
- 10% of babies with down syndrome have hirschsprung disease
- Congenital birth defect seen in 5-33% of hirschsprung disease cases
- Suspect HD if meconium not passed in 48 hrs
- Physiologic aganglionic segment = 1 cm above anal verge
- 15% of children with meconium plug have HD
- Acute renal dysfn occur in 15-25% of hospitalized patients with cirrhosis, HRS is found in 10-30 % of these
- HRS develops in 30% of patients admitted with SBP or other infection, in 25% with severe alcoholic hepatitis
- Ectopic pancreatic tissue : 0.6- 13.7% of population
- Portal vein thrombosis can occur in 25% of patients with cirrhosis
- Lifetime cholangiocarcinoma in PSC = 10-15%, MC in perihilar and CHD
- 10% of cholangio carcinoma are attributed to PSC.
- Annual incidence of cholangiocarcinoma in PSC is 0.6-1.5%
- 90% of all PSC patients have concomitant IBD.
- Small duct PSC is 5-20% of all PSC.
- S. Bilirubin > 1.5 mg/dl is independently associated with poor prognosis in PSC .
- Median survival of cholangiocarcinoma = 24 months .
- 80-90% of cholangiocarcinoma are extrahepatic .
- Risk of recurrence :
 - ▶ PBC = 11-34% (associated with tacrolimus use)
 - ▶ PSC = 5-21% (but more graft loss than PBC)
 - ▶ AIH = 17%
 - ▶ Roughly 25% recurrence in 10 yrs for PBC & PSC
- After refractory ascites development 1 yr survival is only 25%
- MELD score and mortality

MELD score	3 month mortality
<9	2%
40	70%

- Recurrence free interval in C/O non hepatic malignancies undergoing LTx for hepatic causes = 2 yrs , except in cases of colon ca, breast ca, malignant melanoma
- Hepatopulmonary syndrome in age < 65 yrs (> 65yrs):
 - ▶ PaO₂ < 80mmHg (<70mmHg)
 - ▶ A-a gradient > 15mm Hg (> 20 mmHg)

- SpO₂ > 96% rules out HPS, corresponds to PaO₂ > 70 mmHg
- High perioperative risk in PPH if :
 - ▶ MPAP > 35 mmHg
 - ▶ Pulmonary vascular resistance > 300 dynes
 - ▶ Cardiac output < 8 lit /min
- For LTx in HIV positive patients CD4 count should be
 - ▶ > 100 if never had opportunistic infection
 - ▶ > 200 if H/O opportunistic infections
- 40% of alcoholics resume alcohol after LTx
- Traditionally 6 months of abstinence from alcohol is required before LTx
- Severe alcoholic hepatitis : Maddrey's discriminant factor > 32
- Nonresponsive to medical therapy in ALD =
 - ▶ Liley score > 0.45 after 7 days
 - ▶ Persistent rise in MELD score
- Frequency of FCH in post transplant HCV = 5-10%
- Clinically significant recurrent HCV infection post LTx :
 - ▶ Grade 3 or 4 hepatic inflammation
 - ▶ Fibrosis stage F2 or more
- ALF is defined as development of HE within 26 wks of initial recognition of acute liver disease
- Patient with PBC and PSC should be referred for LTx if their Mayo risk score suggest 1 yr survival < 95%
- Post LTx - survival for Milan criteria satisfying HCC & decompensated cirrhosis is same = 75 % in 4 yrs
- Expanded Milan : (no additional MELD points awarded if this criteria is used)
 - ▶ Solitary tumor < 6.5 cm
 - ▶ No more than 3 lesions with largest < 4.5 cm with total tumor diameter < 8 cm
- HCC receives 22 MELD points & 10% point increment every 3 months of waiting
- At least 5% of HBV carrier also carry HDV virus (total 15-20 million cases)
- HBV vertical transmission :
 - ▶ 60-90% if HBeAg +
 - ▶ 5-15% if HBeAg -
- HCV perinatal transmission : 5% if mother is viremic
- Mortality of SOS (zone 3 necrosis & fibrosis) is 25%
- Pediatric recipient of liver → lobes 2,3
- Adult recipient (right trisegment) → 4,5,6,7,8
- Nomenclature of grafts in live donor :
 - ▶ Right → segments 5,6,7,8,
 - ▶ Extended right → 4,5,6,7,8
 - ▶ Left hepatic → 2,3,4

- Mortality in liver donor in first 90 days : 1.7/1000 donors, but not in long term
- Acute cellular rejection post LTx – within a wk → 7 days and beyond
- Post liver transplant :
 - ▶ Discharge → by second wk
 - ▶ Bacterial infection risk is maximum in first 3-4 wks post LTx → AB prophylaxis given
 - ▶ CMV prophylaxis → risk is after 3 wks post LTx → gancyclovir prophylaxis for minimum 3 months
 - ▶ Fungal prophylaxis : 7-14 days with fluconazole/liposomal amphotericin B
 - ▶ Pneumocystis prophylaxis → 1 yr with co-trimoxazole (others are pentamidine, atovaquone, dapsone)
 - ▶ Prophylaxis for PTLD (HBV) → if the patient has risk factors
- Poor long term outcome after liver transplant in alcoholics :
 - ▶ Males 30 gm/day
 - ▶ Females 20 gm/day
- Patients undergoing retransplantation experience approximate 20% reduction in survival a/c/t first transplant.
- In triphasic CT
 - ▶ Arterial phase = 35 sec
 - ▶ Venous phase = 75 sec
- Markers :
 - ▶ Hepatocytes – CK 8, 18
 - ▶ Bile duct cells – CK 8, 18, 19
 - ▶ Cells in fibrolamellar carcinoma – CK 7 (absence of glypican 3)
 - ▶ Intra hepatic cholangio carcinoma – CK 7, negative or weak CK 20
 - ▶ Progenitor cell HCC – carry CK 19 (arise from stem cells in canal of hering)
 - ▶ NASH → CK-18, CK-18 fragments & soluble Fas, most studied, a marker of apoptosis
- HCC will develop in 25% of HBV carriers
- HBV infection accounts for 80% of HCC
- HBV DNA is integrated in Hepatocyte DNA in 90% of HBV related HCC
- Long term HCC risk increases if HBV DNA is > 10⁴ copies/ml
- Cirrhosis is seen in 70-90% of HCC
- Relative risk of HCC in children exposed to HBV in young age = 100 times
- Aflatoxin B1 inactivates third base of codon 249 in P53 – in HCC
- HCC develops in 45% of patients with hemochromatosis, can occur without cirrhosis
- AFP > 10,000 ng/ml is considered diagnostic of HCC; > 400 in background of liver mass is also diagnostic
- AFP > 1000 associated with poor outcome and recurrence in LTx.
- Fucosylated AFP (lens culinaris agglutinin reactive = AFP-L3) > 10-200ng/mL is suggestive of HCC
- Jaundice & hepatic bruit in only 5-25% cases of HCC
- Smaller liver tumors < 5 cm are often hypoechoic

- For diagnosis of HCC nodule

	Sensitivity	Specificity
USG	48%	97%
CT	67%	92%
TPCT	67% ?	100% (95% if < 1 cm)
MRI	80%	84%

- Only 30% of liver nodules < 2 cm are malignant
- On triphasic CT if suspected HCC nodule has no typical features :
 - ▶ If > 1 cm size do a biopsy to confirm
 - ▶ If < 1 cm do serial imaging to see if it's growing
- HCC infiltrating variety : rarest HCC, portal vein is infiltrated as small nodules in 70% of cases @ biopsy
- HCC is metastasized in 50% @ the time of diagnosis → MC site is lung
- Natural H/O of HCC : death in 2-4 months
- Early HCC in BCLC : (constitute 30% of all HCC) → 5 yr survival is 40-70%
- LTx in patients satisfying Milan criteria :
 - ▶ 5 yr survival : 70-75%
 - ▶ Tumor recurrence rate is 10-15%
- In noncirrhotic HCC undergoing resection → minimum 40% of liver should be left after Sx
- Recurrence after resection of HCC is 50%
- Even among patients satisfying Milan criteria, these ones perform poor :
 - ▶ Nodule size 3-5 cm
 - ▶ MELD > 22
 - ▶ S.AFP level > 455 ng/ml
- If the waiting time for LTx in HCC is > 6 months, use either TACE or RFA to keep the patient in Milan
- Response of chemotherapy in HCC is 20%, no survival advantage
- Person in whom HCC surveillance may be indicated :

Patient group	Annual incidence of HCC
HBV cirrhosis	3-8%
HCV cirrhosis	3-5%
PBC cirrhosis	3-5%
Hemochromatosis cirrhosis	> 1.5%
Antitrypsin deficiency cirrhosis	> 1.5%
HBV carrier male > 40 yrs	0.4-0.6%
HBV carrier female > 50 yrs	0.3-0.6 %
HBV carrier with F/H/O HCC	?
HBV carrier – African	0.5%
Any cause of cirrhosis	?

- Patients with 2B & 3A caustic injury has 70-100% chances of stricture formation
- Chances of cancer in barrett's esophagus : 0.5% per yr → now it is 0.16-0.33% / yr = 0.25% per yr
- Prevalence of barrett's = 1.6-6.8 %
- Malignancy in high grade dysplastic barrett's = 6% per yr
- Upto 4% of benign looking ulcer on EGD are malignant, hence do repeat endoscopy after 8 wks of PPI
- Delayed gastric emptying :
 - ▶ > 10% retained in 4 hrs
 - ▶ > 60% retained in 2 hrs
 - ▶ > 10% retained in 1 hr ?
- 10-20% of GERD have short segment (< 3 cm) barretts
- Average age of barretts is 55 yrs.
- Classical triad of choledocal cyst : pain, mass, jaundice in only 20%
- Overall risk of cancer in choledocal cyst is 15-20%
- MC type of choledocal cyst : type 1 = 80-90%
- Reovirus is found in 78% of choledocal cyst by PCR.
- Nearly 100% of biliopancreatic malformations are associated with choledocal cyst.
- On the contrary 40% of the patients of choledocal cyst are associated with biliopncreative malformations.
- Biliary atresia : 1 in 10,000, forms 50% of pediatric liver transplantation referrals.
- Biliary atresia type I,IIA,IIB constitute only 10% of all, but they can be surgically corrected.
- S.Bilirubin in biliary atresia is 6-12 mg/dl.
- In biliary atresia prognosis is good if detected within 60 days, bad if detected after 120 days
- In biliary atresia extrahepatic anomalies found in 10-25% of individuals.
- In acute cholecystitis → 50% cases resolve in 1 wk without Sx.
- Charcot's triad is present in 70% cases : other symptoms as follows
 - ▶ Fever in 95%
 - ▶ Pain 90%
 - ▶ Jaundice 80%
 - ▶ Peritoneal sign 15%
 - ▶ Reynaud's pentad (+ altered mentation and shock) 15%
- Sensitivity in detecting CBD stone :
 - ▶ USG abdomen : 50%
 - ▶ EUS : 95%
 - ▶ ERCP : gold std ? 100%
 - ▶ Sensitivity order ERCP > EUS > MRCP > USG
- In acute pancreatitis: fluid therapy in first 48 hrs : 250-300 ml / hr
- High output gatro-enteric fistula is output > 500 ml/ day
- Gall bladder is anatomically related to segment 5 of liver

- HVPG : normal is 1-6 mm Hg .
- Varices develop at 10 mmHg
- Varices bled at 12 mmHg
- High chance of bleeding recurrence and poor bleeding control if HVPG > 18 mmHg
- In a compensated cirrhosis correlation of HVPG values :
 - ▶ 10 mmhg → clinically significant portal hypertension
 - ▶ 12 mmhg → risk of variceal bleeding
 - ▶ 16 mmhg → first clinical decompensation with ascites, mortality
- In a decompensated state, correlation of HVPG values :
 - ▶ 16 mmhg → risk of rebleeding, mortality
 - ▶ 20 mmhg → if bleeding varices, poor control of bleeding, high 1 yr mortality
 - ▶ 22 mmhg → increase mortality in alcoholic hepatitis and alcoholic cirrhosis
 - ▶ 30 mmhg → spontaneous bacterial peritonitis
- Other important points with HVPG :
 - ▶ Treatment goal < 12 mmhg
 - ▶ If > 10 mmhg → 70% chance of bleed
- Normal level of direct bilirubin in blood is < 15% of total bilirubin
- Resistance to lamivudine :
 - ▶ 10% in 6 months
 - ▶ 25% in 1 yr
 - ▶ 65% in 5 yrs
- Esophageal varices is present in 60% of patients with cirrhosis and ascites
- In portal hypertension :
 - ▶ Portal flow mean velocity < 12 cm/sec
 - ▶ Portal vein diameter > 13 mm
- Intrahepatic cholangio carcinoma is 10-20% of all primary hepatic malignancies
- CA 19-9 is undetectable in 7% of the population who are lewi blood group negative
- Metastasis is seen in 50% of cholangio carcinoma patients at diagnosis, 1 yr survival is 28%
- 50% mets are present in angiosarcoma at presentation
- In hepatic metastatic lesions :
 - ▶ 50% survive till 3 months
 - ▶ Only 10% survive till 1 yr
- Caroli's disease :
 - ▶ Caroli disease is associated with medullary sponge kidney in 60-80% pts
 - ▶ Occurance of cholelithiasis is 33%
 - ▶ Chances of cholangiocarcinoma is 10%
- Simple cysts = in 2.5% population, < 5 cm in size, 3 or less in number
- PCLD = > 3 cysts of size 1-10 cm

- Liver adenomatosis is > 10 adenomas
- OCP use for > 5 yrs is a risk for hepatic adenoma
- CURE liver failure chances :
 - ▶ HAV & HBV = 1%
 - ▶ Acetaminophen overdose = 0.2%
- Overall survival in ALF is 60%
- ALF category :
 - ▶ Hyperacute < 7 days → best prognosis of all
 - ▶ ALF 8-28 days
 - ▶ Subacute liver failure 4-24 wks
- Original definition of ALF : encephalopathy and coagulopathy within 8 wks of onset of illness
- MCC of ALF world wide is Acetaminophen toxicity constituting 28%
- Causes of ALF in India : HEV (38%) > HAV/HBV (33%) > seronegative hepatitis (24%)
- Maximum recommended therapeutic dose of acetaminophen is 4 gm/ day in adults
- Acetaminophen :
 - ▶ Mortality is very high @ 48 gm
 - NAC in PCM toxicity works best if given within 16 hrs(give if blood level of drug exceeds by 1 to 2 curves)
 - Patients with drug induced ALF are mainly females (70%)
 - Pregnancy related ALF → 0.0008% → in first and male fetus
 - WD can present as acute liver failure in 25%
 - In Wilsonian ALF :
 - ▶ SAP/TB < 4
 - ▶ AST/ALT > 2.2
 - Liver failure due to amanita phalloides → in 4-5 days
 - Briefest period between liver injury and hepatic encephalopathy is 3-4 days
 - Cerebral edema is seen in 80% of patients with grade 3 /4 encephalopathy (most common in hyperacute failure)
 - Patients with grade 2 or greater HE have bacterial infection in 80% cases, fungal in 30%
 - Renal failure in ALF cases requiring dialysis :
 - ▶ 75% in acetaminophen toxicity
 - ▶ 30% in other cases
 - ▶ Early renal dysfunction is also seen in WD, mushroom poisoning, pregnancy related syndromes
 - Management in ALF :
 - ▶ Ventilate in HE grade 3, maintain mild hypocapnia
 - ▶ Maintain CPP > 55 and ICP < 25
 - ▶ Maintain mean arterial pressure > 90

- Indian model for ALF prognosis :
 - ▶ Age > 50 yrs
 - ▶ Jaundice to encephalopathy time > 7 days
 - ▶ PT > 35 sec
 - ▶ S. Creatinine > 1.5 mg/dl
- Critical mass (volume) of hepatocytes in ALF for good survival = 25-40%
- ALF is 8% of all causes for LTx
- Auxiliary LTx in ALF serves for approx 3 yrs, 70% patients gain functionality of native liver by then
- Mortality rate in patients on wait list for LTx is 20-30%, maximum for acetaminophen toxicity
- 1 yr survival post LTx is 75%
- Head positioning in ALF / HE → 20-30% (0-10% if shock develops)
- Dose of mannitol in HE □ 0.25-0.5 gm/kg → repeat till osmolality is 320 mosm
- Hypertonic saline can be given in HE to maintain Sodium between 145-155 mmol/l
- Hypothermia done in HE 32-33 degree
- In ALF, maintain platelet between 50,000- 70,000 / mm³
- In ALF, high mortality (> 90%) if blood pH is < 7.3
- Nutrition goal in ALF : 25-30 Kcal / kg, started as enteral feed within 24 hrs of admission
- Alcohol gives 7 kcal/ gm
- Blood alcohol level for driving < 0.1 gm/dL
- Cirrhotic alcohol : males → 40-80 gm, female → 20-40 gm/day
- Hepatic steatosis in 90% of chronic alcoholics, cirrhosis in 10% over 5 yrs
- Alcoholic steatohepatitis is seen in 10-35% of heavy drinkers
- Alcohol % :
 - ▶ Beer 5% → for 14 gm required amount is 12 oz
 - ▶ Wine 12% → 5 oz
 - ▶ Hard liquor 40% → 1.5 oz
- Most common physical finding in patients with fatty liver & alcoholic hepatitis is:
 - ▶ Hepatomegaly → in 75%
 - ▶ Jaundice and ascites in 60% → more common in advanced disease
- Risk drinking :
 - ▶ Males > 5 drinks / day
 - ▶ Females > 4 drinks/day
- For diagnosis of NAFLD alcohol intake should be less than :
 - ▶ Males < 3 drinks/d
 - ▶ Females < 2 drinks/d

■ In ALD :

- ▶ Serum AST & ALT is almost always less than 300-500 IU/L (level doesn't correlate with severity),
- ▶ AST/ALT > 2
- ▶ Bilirubin is 20-40 mg%
- ▶ S. GGT is raised 8-10 times ULN/ persist even after 8 wks
- ▶ S. Albumin is as low as 1-1.5 gm%
- ▶ S. ALP range from normal to 1000

■ Patients with medry's discriminant score > 32 have 1 month mortality of 35-50%

■ 5 yr survival with alcoholic cirrhosis is 60-85%

■ 1 yr mortality in alcoholic cirrhosis patients :

- ▶ No complications → 15%
- ▶ Variceal bleeding → 20%
- ▶ Ascites → 30%
- ▶ Variceal bleeding and ascites → 50%
- ▶ Hepatic encephalopathy → 65%

■ Lifetime surveillance for HCC in alcoholic cirrhosis : USG every 6 months

■ Relative risk of HCC is 20-30 times higher among heavy drinkers and HCV infection

■ Poor prognosis in C/O alcoholic hepatitis :

- ▶ DF > 32
- ▶ MELD > 18
- ▶ Glasgow score > 9

■ 10% of patients undergoing TIPS show signs of liver failure

■ Adrenal dysfunction in cirrhosis – 10-90%

■ Gonadal dysfunction is seen in 70-80% of cirrhotics

■ Cardiomyopathy seen in 50% of cirrhotics

■ IFN therapy can cause hypo or hyperthyroidism in 10-15% of treated patients

■ LTx reverses HPS in 80% of the patients

■ Acute renal dysfunction is seen in 15-25% of hospitalized cirrhosis patients, HRS is seen in 10-30% of these

■ Annual incidence of HRS in cirrhosis with ascites : 8%

■ Incidence of HRS in hospitalized patients with :

- ▶ Infection = 30%
- ▶ Severe alcoholic Hepatitis = 25%
- ▶ Large volume paracentesis = 10%

■ Survival of type 2 HRS : 6 months

■ In cirrhosis, prevalence of :

- ▶ SBP → 10-30 % (21%)
- ▶ HE → 50-70%
- ▶ HRS → 8-40%
- ▶ HPS → 10-35%
- ▶ POPH → 5%

- Hepatic encephalopathy :
 - ▶ 1 yr survival → 42%
 - ▶ 3 yr survival → 23%
- Dose of rifaximine in HE (for both treatment and prophylaxis on risk patients) : 550 mg BD
- Menetrier's disease → thickening of 2nd layer in EUS (deep mucus layer)
- GVHD : rectosigmoid Bx for diagnosis
 - ▶ Acute → 21-100 days
 - ▶ Chronic → > 100 days
- To prevent bile acid reflux gastropathy :
 - ▶ Construct 30 cm roux-en-Y
 - ▶ 10-12 cm of isoperistaltic interposition
- Gastric radiation injury → 5000 cgy
 - ▶ Acute = 6 months
 - ▶ Chronic = 1 yr
- About 70% of population has patent duct of santorini
- Dieulafoy lesion → within 6 cm of GEJ, age of presentation 50 yrs
- Zenker's :
 - ▶ Prevalence → 0.1- 0.01 %
 - ▶ No Rx → < 2cm
 - ▶ Endoscopic Rx → 2-5 cm
 - ▶ Open surgery → > 5 cm
- Gastric volvulus : 2/3rd cases associated with diaphragmatic hernia
 - ▶ Organoaxial(acute) → 60%
 - ▶ Mesentericoaxial (chronic) → 40%
- Isolated esophageal atresia (without other anomalies) → 7%
- TEF associated esophageal atresia = 89%
- H type of esophageal atresia constitute only 3%
- 93% of ascites is due to PHTN, 85 %is due to cirrhosis
- Abdominal wall hematomas are seen in only 2% of paracentesis with severe coagulopathy
- Diagnostic Ascitic tap :
 - ▶ 1.5 inch long (3.5 inch in obese), 22 Gz needle
 - ▶ 5 mm increments with intermittent suction
 - ▶ Can be twisted 90 degrees
 - ▶ 30 ml fluid is obtained
 - ▶ 5-10 ml of fluid is inoculated in 50 ml bottle
 - ▶ 10-20 ml of fluid is inoculated in 100 ml bottle

- Therapeutic ascitic tapping :
 - ▶ 1.5 inch long, 16 -18 Gz needle (special 15Gz, 15 hole needles available)
 - ▶ 2-4 litre tapped in case of tense ascites
 - ▶ Total tap in diuretic resistance ascites
- Ascitic fluid WBC :
 - ▶ < 250 → transparent / slightly yellow
 - ▶ < 1000 → nearly clear
 - ▶ 5000 → cloudy
 - ▶ 50,000 → mayonese
- Ascitic fluid RBC :
 - ▶ < 10,000 → pink
 - ▶ > 20,000 → red
- Fat in ascites : chylous triglyceride concentration -
 - ▶ Opalescent → 50-200
 - ▶ Skimmed milk like → 100-200
 - ▶ By definition chylous ascitis has > 200 mg% of TG (usually is > 1000 mg%)
- Hepatocellular carcinoma ascites is often bloody but only 10% of peritoneal carcinomatosis is bloody
- Less than 5% of TB ascites is bloody
- Cause of ascites other than liver disease → 15%
- Cancer accounts for, 10% of ascitis cases
- Dipstick test can detect PMN in ascetic fluid within 90-120 secs
- In SBP, PMN is 70%
- 5% patients have mixed ascites
- Accuracy of SAAG is 97% for PHTN
- S. Albumin < 1.1 gm% is seen in 1% of ascitis patients
- 20% of patients with cirrhotic ascites will have ascitic fluid protein > 2.5 gm%
- In cardiac ascitis pts mostly have ascetic fluid protein > 2.5 gm% (SAAG narrows with diuretics)
- S. Pro BNP level in cardiac ascitis is > 6100 pg/ml
- Corrected SAAG in hypergammaglobulinemia :
 - ▶ Uncorrected SAAG x 0.16 x (S.Globulin + 2.5)
- Bedside inoculation of ascetic fluid culture yields bacteria in 80% cases
- For secondary bacterial peritonitis : ascetic fluid →
 - ▶ Total protein > 1 gm/dl (low total protein is a risk for SBP not secondary)
 - ▶ Glucose < 50 mg%
 - ▶ LDH > upper limit of normal (225 U/L)
- Biliary ascitis :
 - ▶ Ascetic fluid bilirubin > 6 mg%
 - ▶ Ascetic fluid/serum bilirubin > 1.0

- During 10 kg diuresis, ascetic fluid protein concentration doubles
- In uncomplicated ascitis ascetic fluid LDH and amylase values are half that of serum
- Gram stain of body fluids demonstrate bacteria @ concentration >10,000 bacteria/mL
- Median concentration of bacteria in ascetic fluid = 1 organism/mL, as in bacteremia
- Sensitivity of gram stain on a centrifuged sample of ascetic fluid with SBP → 10%
- Sensitivity of peritoneal Bx in TB peritonitis → 100%
- Only about 2/3rd of pts with malignant ascitis had peritoneal mets
- % of SBP in cirrhosis 10-30% (21%)
- 50% of tubercular peritonitis patients have underlying cirrhosis
- Cirrhosis is the cause of chylous ascitis in 90% of cases
- Hepatic vein thrombosis causes only 0.1 % cases of ascitis
- Liver receives 30% of total cardiac output
- Ascetic fluid protein < 1gm / dL is particularly susceptible for SBP
- Of patients with culture positive ascitis :
 - ▶ 2/3rd have SBP
 - ▶ 1/3rd have MNB
- Accidental bowel penetration in paracentesis occurs in 1/1000 cases, peritonitis develops in 1/10 with perforation and spillage of intestinal contents (not all with penetration will have spillage)
- Cumulative probability of infection during UGI bleed in ascitis pt is 40% (risk maximum @ 48 hrs)
- Renal impairment is seen in 33% of patients with SBP
- Duration of SBP Rx → 10-14 days for life threatening infections (few recommend 5 days treatment)
- Ascetic fluid culture becomes negative in 86% of SBp pts with single dose of cefotaxim
- No survivors of SBP once creatinine reaches 4 mg%
- Mortality in secondary peritonitis :
 - ▶ Without Sx □ 100%
 - ▶ With Sx □ 50-67%
- Hepatic hydrothorax has protein concentration higher (by 1 gm%) than ascetic fluid.
- Up to 20% with ascitis with cirrhosis have umbilical hernia at hospitalization (hernia recurs in 75% if Sx done without control of ascitis)
- Start prophylaxis (with norflox 400 mg OD for 1 yr) for SBP in a pt if :
 - ▶ Ascetic fluid protein < 1.5
 - ▶ T. Bilirubin >3
 - ▶ BUN > 25
 - ▶ Creatinine > 1.2
 - ▶ CTPS > 9
 - ▶ S. Sodium < 130

- Sodium given in cirrhotic ascitis : 5 gm NaCl = 2 gm Na = 88 mEq
- 1 tablespoon has 2.3 gm of Na+
- Indication of fluid restriction in ascitis : S. Sodium < 120 mEq
- Half life of spironolactone = 24 hrs normally, (5-6 days in cirrhosis -- Takes one month to reach steady state)
- Acceptable weight loss in ascitis patient : high SAAG → 500 gm/ day
- Beta blockers should be stopped in cirrhotic ascitis if :
 - ▶ HRS,
 - ▶ SBP,
 - ▶ Systolic BP < 100 mmHg &
 - ▶ Acute bleeding
 - ▶ Refractory ascitis (along with ACEI, ARB, NSAID)
- Diuretics should be stopped in patient with cirrhotic ascitis if :
 - ▶ HE is developing
 - ▶ Creatinine > 2
 - ▶ Na⁺⁺ < 120 mEq/L
- Diuresis increases the opsonic activity of ascitis 10 fold
- Ascitis is refractory to medical rx in 10%
- Mortality in a patient with ascitis : 50% in 2 yrs
- 12 month survival of patient with refractory ascitis is 32%
- Albumin in paracentesis : if > 5 lit is drained (6-8 gm/L of fluid removed)
- Stellate cells constitute 5-8% of all hepatic cells
- SOD has been described in 50-90% of chronic pancreatitis (25-60% of acute pancreatitis)
- Cholangiocarcinoma in :
 - ▶ PSC → 5-15%
 - ▶ Recurrent Pyogenic cholangitis → 3%
- In recurrent pyogenic cholangitis :
 - ▶ Ascending cholangitis 45%
 - ▶ Hepatomegaly 20%
 - ▶ Gall bladder enlargement 10%
- In GB adenomyomatosis,gall stones are present in 60%
- GB cancer develops in 1-3% of cholelithiasis patients
- In cholelithiasis patients GB cancer develops in 65-90%
- Risk of cancer in porceline GB → 20%, thus prophylactic cholecystectomy is done
- USG can detect gall stones upto 2 mm diameter, 90% stones larger than 2 mm
- USG detects 50% of choledocholithiasis

■ VARICES :

- ▶ Gastric zone → 2-3 cm below GEJ
- ▶ Palisade zone → 2-3 cm above GEJ, 4 groups, do not communicate, often bleeder
- ▶ Perforating zone →
- ▶ Truncal zone → 10 cm, 4 columns, unlikely to bleed

■ Laplace's law → $P = 2Tw/R$

■ HVPG is measured atleast 3 times, average is taken

■ Red wale signs :

- ▶ Cherry red spots → 2-3 mm
- ▶ Hematocystic spots → 4 mm
- ▶ Diffuse redness → ?

■ PHTN on USG → PV diameter > 13 mm with absence of respiratory variations

■ 25% of cirrhosis patients have portal vein thrombosis

■ Bleeding in varices → dark red

■ Venous humm in PHTN is from falciiform ligament

■ Terlipressin has survival advantage in variceal bleeding

■ Somatostatin is 14 aa long, T $\frac{1}{2}$ is 1-3 minutes

■ Octreotide half life is 90-120 mins

■ Adequate hemodynamic response to beta blocker → HVPG falls to < 12 mmHg (or by 10%) in 20 mins

■ Interval used in variceal ligation 2 cm

■ 10-15% of variceal bleed are resistant to medical and endoscopic management → use balloon and TIPS

■ Tubes :

- ▶ SBT – 3 lumen – 200-400 ml
- ▶ Linton nachlas – 3 lumen – 600 ml
- ▶ Minnesota tubes – 4 lumen – 500 ml

■ Balloons can control bleed in 80% - 90% of patients for 24 hrs

■ TIPS is side to side shunt

■ TIPS mortality 1-2 %, may even be higher

■ Rosch needle for TIPS

■ TIPS complications, early in 30 days ; late in > 30 days

■ MC indication for TIPS; bleeding

■ Early TIPS → within 72 hrs of bleed even if bleeding controlled (they are at risk for Rx failure)

- ▶ CPS- C
- ▶ CPS - B with active bleeding
- ▶ MELD > 18
- ▶ > 4 PRBC needed during bled

- Stenosis in non covered TIPS → 20-78%, 15% with covered shunts
- TIPS shud be avoided if MELD > 24
- MELD can even be used for post TIPS survival prediction
- TIPS is offered for MELD between 15-24
- MC used selective shunt is distal splenorenal shunt,
 - ▶ Only GEJ & gastric varices controlled (not PHTN & ascitis as SMV isn't decompressed)
 - ▶ Portal azygos disconnection is done
 - ▶ Control variceal bleeding in 90%, ascites increased in 20%
 - ▶ Only mild increase in HE
- Partial shunt 8mm reduces HVPG to 12 mmHg, ascites may occur in 20%
- Complete shunting occurs with shunts > 12 mm in size, rebleed reduces to 10% but HE occurs in 30-40%
- Rex shunt is mesenterico- left portal vein bypass → done only in EHPVO
- Esophageal varices present in 40% of patients with cirrhosis, 60% of patients with cirrhosis & ascitis
- Development of varices in a newly diagnosed cirrhotic pt at a rate of 5% per yr
- Up to 25% of newly diagnosed varices will have bleeding in 2 yrs
- Risk of bleeding @ 2 yrs :
 - ▶ Small varices → 7%
 - ▶ Large varices → 30%
- Small to large varices conversion → 10% per yr
- Initial treatment leads to cessation of variceal bleeding in 80-90% of patients
- Of those patients who have stopped bleeding, 1/3rd will rebleed in 6 wks (40% of them within 5 days)
- Risk of death with variceal bleeding,
 - ▶ 5-8% @ 1 wk,
 - ▶ 20% @ 6 wks
- Absolute risk reduction with beta blocker for variceal bleed is 10% and for reducing mortality is 5%
- BB needs to be stopped in only 15% with HR < 55-60 or SBP < mmHg
- BB can be dose modified every 3-5 days to achieve HR of 55-60 bpm or HR reduction of 25%
- Goal of Rx is to reduce HVPG to < 12 mmHg or by 20% → bleeding risk reduces to less than 10%
- Predictors of rebleeding :
 - ▶ Active bleeding at endoscopy
 - ▶ Hypoalbuminemia
 - ▶ Bleeding gastric varices
 - ▶ Renal insufficiency
 - ▶ HVPG > 20 mmHg
- Only 30-40% of patients respond to BB, best response in preserved hepatic function patients
- Goal Hct in actively bleeding varices is 25%, maintain Hgb above 7 gm%
- Terlipressin improves survival in variceal hge, shud be continued for 5 days

- Variceal bleeding can be controlled in 80-90% of patients with EVL and vasopressors
- Uncontrolled bleed in 15-20% is defined as :
 - ▶ > 4 PRBC
 - ▶ SBP < 70 mmhg persistently or inability to raise BP by > 20mmhg
 - ▶ Persistant HR > 100
- Risk of rebleeding without prophylaxis → 80% @ 2 yrs
- Initial dose of ISMN in case if PHTN not controlling with BB → 30 mg/day, but EVL if bleed occurs
- 25% of PHTN patients will have gastric varices (70% of them are GOV1)
- Among gastric varices bleeding is MC with GOV2 & IGV1 (fundal varices)
- Large gastric varices > 20 mm with HVPG > 17 are at more risk to bled
- MCC of gastric varices – cirrhosis
- Best Rx for bleeding gastric fundal varices is cyanoacrylate glue
- Most difficult varices to obliterate IGV-1
- Bad ligation of gastric varices > 10 cm is unsafe
- TIPS can control bleeding gastric varices in 90%
- Ectopic varices constitute only 5% of varix related bleed
- MC ectopic varix is duodenal, typically associated with portal vein obstruction
- Collagenous sprue → subepithelial band > 10 micrometer
- Paraneoplastic cancer
 - ▶ Acanthosis Nigricans → triple palm → in pulmonary and gastric cancer
 - ▶ Bazex syndrome → upper aerodigestive carcinoma including esophageal
 - ▶ Dermatomyositis → MC with Gastric cancer (nasopharyngeal ca in Chinese)
 - ▶ Hypertrichosis lanuginose → lung > colorectal
 - ▶ Venous thrombosis → pancreatic cancer
 - ▶ Subcutaneous fat necrosis → pancreatic cancer
 - ▶ Lesser trelat sign → gastric carcinoma
- MC site for mucosal hyperpigmentation in PJ syndrome → lips
- MC GI abnormality associated with sjogren's disease → gastric atrophy
- MC malignancy associated with sweet syndrome → myelogenous malignancy
- MC GI feature of
 - ▶ MCTD → reduced esophageal motility
 - ▶ Sarcoidosis → chronic atrophic gastritis
 - ▶ PAN → pain, acalculous cholecystitis
- Diabetic diarrhea is more common in men

■ MCC of these conditions AIDS patient :

- ▶ Gastritis → CMV
- ▶ Focal ulcer in stomach → CMV
- ▶ GOO → Cryptosporidium
- ▶ Gastric mass in HIV → lymphoma > KS
- ▶ Enteritis → cryptosporidium
- ▶ Intestinal obstruction → lymphoma > KS
- ▶ Intestinal perfo → CMV (deep and large ulcers are seen as in idiopathic HIV ulcers)
- ▶ Colitis → enteric bacteria > CMV
- ▶ Colon perfo → CMV> lymphoma
- ▶ Appendicitis → Kaposi sarcoma > Cryptosporidium
- ▶ Liver / splenic infiltration → lymphoma > CMV
- ▶ Cholecystitis → CMV & cryptosporidiosis
- ▶ Pappilary stenosis → CMV & cryptosporidiosis
- ▶ Cholangitis → CMV
- ▶ Pancreatitis → CMV
- ▶ Pancreatic mass → lymphoma
- ▶ Acalculous cholecystitis → CMV > microsporidia, cryptosporidia, isospora
- ▶ LGI bleed → CMV & HSV ulcers
- ▶ UGI bleed → peptic ulcer not linked to AIDS
- ▶ Esophageal ulceration → candida (not so painful as in CMV)
- ▶ Diarrhea → protease inhibitor (MC is nelfinavir → Rx with crofelemer)
- ▶ MC Infective cause of diarrhea → Cryptosporidia (small intestine MC involved, Rx with HAART)
- ▶ Viral cause diarrhea → CMV (MC infection in colon, SI infection causes pain rather than diarrhea)
- ▶ Bacterial diarrhea → Cl. Dificille
- ▶ Chronic diarrhea with multiple negative stool samples → CMV
- ▶ MAC involvement MC in duodenum (diagnosis by Bx)
- ▶ MTB involvement MC in ileocecal and colonic sites
- ▶ Liver disease → viral hepatitis ?drug induced (but CMV rarely causes liver infection inHIV)
- ▶ MC specific hepatic finding in AIDS in late stages is MAC (MTB in developing nations)

■ MC identified infectious agent in AIDS → CMV (IHC is performed in sample from base of ulcer)

■ Nonspecific esophageal ulceration(punched out lesion) or idiopathic HIV ulcers

- ▶ Seen in **HIV patients** with CD4 count < 50
- ▶ Deep, big ulcers,
- ▶ Respond to GC in 90% cases
- ▶ Also respond to thalidomide (can cause rash, neuropathy, somnolescence)

■ TB is extrapulmonary in HIV patients → in 80% of cases

■ AIDS cholangiopathy → jaundice in only 10-20% patients

■ Sunlndac can cause pancreatitis

■ MC manifestation of NSAID enteropathy is chronic blood loss

- Gastric ulcer recurrence :
 - ▶ Without Hp eradication → 70-80%
 - ▶ With Hp eradication 5-15%
- Congenital diaphragmatic hernia :
 - ▶ Morgagni : right, anterior, small, present in adult
 - ▶ Bockdalec : left, posterior, large, present in infants
- Abdominal compartment syndrome :
 - ▶ Grade 1 → 12-15 mmHg
 - ▶ Grade 2 → 16-20 mmHg
 - ▶ Grade 3 → 21-25 mmHg
 - ▶ Grade 4 → > 25 mmHg
- Normal intra abdominal pressure → < 7 mm Hg
- Intra abdominal hypertension is > 12 mm Hg
- Anorectal varices seen in 10-40% of cirrhotics
- AIH is the cause of 4-6% of all LTx
- 8% of all aih have duct injury and cholestasis
- AIH asymptomatic in 35-45%
- Mortality in grade 4 caustic injury ulcer → 67%
- Natural, physiologic constrictions of esophagus = 23 mm
- 16-17 mm coin can negotiate through esophagus
- Will not pass through stomach pylorus → 5 cm X 2 cm object
- Caustic stricture in 1/3rd of patients → mainly within 2 months
- Dilation done in esophageal caustic strictures is 15 mm (incremental, progressive) or till dysphagia is relieved
- Perforation rate in caustic stricture esophageal dilation → 0.5% (10-50% will require Sx)
- MC site for acid stricture → antrum
- MC site for alkali stricture → esophagus
- MC site for gastric diverticula → cardia (posterior) → 75% → 1-3cm
- Esophageal pseudodiverticula → 1-4 mm, men, 7th decade, SM glands, diffuse, associated with stricture
- MC site of duodenal diverticula → juxtapapillary (present with pain and obstruction)
- MC site of SI diverticula is prox. jejunum (80%) □ 1% of population → on mesenteric border, multiple
- MC site for esophageal diverticula → middle or lower third
- Toupet → posterior ; dor → anterior
- Side of diverticula :
 - ▶ Zenker → left
 - ▶ Boyce's sign → left
 - ▶ Epiphrenic → right
 - ▶ Bockdalec → left
 - ▶ Morgagni → right

- SCC in zenker → 0.4-1.5%
- Prevalence of zenker → 0.1- 0.01%
- Zenker diverticula can cause weight loss
- Rx of Zenker : only when symptomatic
 - ▶ 2-5 cm → endoscopic (stapler can be used when size > 3 cm)
 - ▶ > 5cm → open surgical
- MC symptom of zenker's is dysphagia

Nutrition in GI Diseases

INDICATIONS :

- All patients who are not expected to be on normal nutrition within 3 days should receive PN within 24 to 48 h if EN is contraindicated or if they cannot tolerate EN.
- In the absence of indirect calorimetry, ICU patients should receive 25 kcal/kg/day increasing to target over the next 2–3 days.

Supplementary PN with EN :

- All patients receiving less than their targeted enteral feeding after 2 days should be considered for supplementary PN.

Carbohydrates :

- The minimal amount of carbohydrate required is about 2 g/kg of glucose per day.
- Hyperglycemia (glucose >10 mmol/L) contributes to death in the critically ill patient and should also be avoided to prevent infectious complications.
- Reductions and increases in mortality rates have been reported in ICU patients when blood glucose is maintained between 4.5 and 6.1 mmol/L. No unequivocal recommendation on this is therefore possible at present.
- There is a higher incidence of severe hypoglycemia in patients treated to the tighter limits.

Lipids :

- Lipids should be an integral part of PN for energy and to ensure essential fatty acid provision in long-term ICU patients. Intravenous lipid emulsions (LCT, MCT or mixed emulsions) can be administered safely at a rate of 0.7 g/kg up to 1.5 g/kg over 12 to 24 h B 6.8
- The tolerance of mixed LCT/MCT lipid emulsions in standard use is sufficiently documented. Several studies have shown specific clinical advantages over soybean LCT alone but require confirmation by prospective controlled studies. C 6.4
- Olive oil-based parenteral nutrition is well tolerated in critically ill patients. B 6.5
Addition of EPA and DHA to lipid emulsions has demonstrable effects on cell membranes and inflammatory processes. Fish oil-enriched lipid emulsions probably decrease length of stay in critically ill patients. B 6.6

Amino Acids

- When PN is indicated, a balanced amino acid mixture should be infused at approximately 1.3–1.5 g/kg ideal body weight/day in conjunction with an adequate energy supply. B 7
- When PN is indicated in ICU patients the amino acid solution should contain 0.2–0.4 g/kg/day of L-glutamine (e.g. 0.3–0.6 g/kg/day alanyl-glutamine dipeptide). A 8

Micronutrients :

- All PN prescriptions should include a daily dose of multivitamins and of trace elements. C 9
- Route A central venous access device is often required to administer the high osmolarity PN mixture designed to cover the nutritional needs fully.. C 1.3
- Peripheral venous access devices may be considered for low osmolarity.

PANCREATITIS :

International Consensus Guidelines for Nutrition Therapy in Pancreatitis

Indication for Nutrition Therapy

- Pancreatitis patients are at nutrition risk and should be screened.
 - For mild to moderate disease, analgesics, intravenous (IV) fluids, and nil per os (NPO) with a gradual advancement to diet (usually within 3–4 days) are recommended.
- The need for nutrition therapy (NT) by the enteral or parenteral route should be based on the extent of disease and nutrition status of the patient.
- NT is not generally needed for mild to moderate disease unless complications ensue.
 - NT should be considered in any patient regardless of disease severity if the anticipated duration of being NPO is >5–7 days.
 - NT is needed in mild to moderate disease when the patient has been NPO for 5–7 days.
 - Early NT is indicated for severe pancreatitis.
 - NT is useful in the management of patients who develop complications of surgery.

Use of Enteral Nutrition

- Enteral nutrition (EN) is generally preferred over parenteral nutrition (PN), or at least EN should, if feasible, be initiated first.
- EN may be used in the presence of pancreatic complications such as fistulas, ascites, and pseudocysts.
- Continuous EN infusion is preferred over cyclic or bolus administration.
- Nasogastric tubes may be used for administration of EN. Postpyloric placement is not necessarily required.
- For EN, consider a small peptide-based mediumchain triglyceride (MCT) oil formula to improve tolerance.

Use of Parenteral Nutrition

- Use PN if NT is indicated, when EN is contraindicated or not well tolerated.
- IV fat emulsions are generally safe and well tolerated as long as baseline triglycerides are below 400 mg/dL (4.4 mmol/L) and there is no previous history of hyperlipidemia.
- Glucose is the preferred carbohydrate source with metabolic control of glucose as close to normal as possible.
- Consider use of glutamine (0.30 g/kg Ala-Gln dipeptide).
- No specific complications of PN are unique to patients with pancreatitis. In general, avoid over feeding.
- Meet macronutrient requirements with NT.
 - ▶ Calories: 25–35 kcal/kg/d
 - ▶ Protein: 1.2–1.5 g/kg/d

CIRRHOSIS :

Enteral nutrition

General principles

- Avoid prolonged periods of fasting (frequent feedings, CHO-rich bedtime snack).
- Measure REE with indirect calorimetry instead of calculating REE with predictive equations.
- Assess and follow changes in body composition (DEXA is better than weight, height, skin folds, BIA).
- When oral intake is inadequate, consider high-calorie/low-sodium formulas, followed by enterostomy tube feedings and PN (last resort).
- Do not restrict protein below minimum daily requirements to prevent muscle catabolism.

Dietary intake

- Energy Adults: 25–40 kcal/kg/d a ; indirect calorimetry should be used to determine caloric needs.
- Children: requirements may be 130% predicted or less than expected for age.
- Protein Adults: well, 1.2 g/kg/d a ; stressed, 1.5 g/kg/d a ; medically refractory HE, 0.6–0.8 g/kg/d a + 0.25 g/kg/d a of BCAA (only for short periods, until HE resolves).
- Carbohydrate 45% – 65% of total daily calories.
- Avoid hypoglycemia (frequent meals).
- Fat 25% – 30% of total daily calories.
- Measure fecal fat to estimate potential additional fat requirements.
- No MCT if no significant steatorrhea.
- Consider screening for EFA deficiency by obtaining a fatty acid profile that includes AA, EPA, DHA.

Diet in ESLD :

Summary of Nutrition Management in End Stage Liver Disease.

Oral diet

- Small/frequent meals
- Bedtime snack or late evening meal
- High protein
- Avoidance of skipping meals
- ≤2000 mg sodium daily if ascites/edema present

Enteral nutrition

- Initiate if unable to meet protein-energy needs via PO diet
- Standard, energy-dense formula
- Nasoenteral tube
- Percutaneous gastrostomy tube relatively contraindicated
- Aspiration precautions

PARENTERAL NUTRITION

- Indicated only if nutrition needs cannot be met via oral and enteral routes
- Monitor glucose levels closely
- If hyperglycemia present, limit glucose to 2–3 g/kg/d
- ≤ 1 g/kg/d lipids
- Limit manganese and copper in setting of cholestasis
- Cyclic regimen recommended
- Concentrated solution to prevent fluid overload

POINTS FROM JOSHI

IN CRITICALLY ILL PATIENTS / IN ICU

- Immuno-nutrition : arginine , glutamine, nucleic acid, vit. A, C, E, omega -3 PUFA
- Typical anthropometric parameters are not useful in critically ill patients
- Max rate of glucose utilization in ICU patients is 4 mg/kg/min so limit glucose to < 5 gm/kg/day
- Limit glucose based non protein calories to $< 60\%$
- Insulin is used to maintain blood glucose between 80 -110
- Atleast 7% of calories should be from EFA
- Give 2-3 table spoon of PUFA/day
- Total fat should not exceed 30% of daily calorie intake
- Protein 1.2-1.5 gm/kg/day → titrate with urine urea nitrogen(to check nitrogen balance)
- IV fluids should have osmolality < 800 mosm/kg

IN LIVER FAILURE

CALORIES : 25-30 kcal / kg/ day (upto 50 kcal in malnourished)

Of daily calories 25-40 % should be provided from fat

In case of malabsorption give medium chain triglyceride for a short duration

Overfeeding of calories should be avoided

PROTEIN :

- Uncomplicated hepatitis : 0.8-1.0 gm/kg/day(1.2-1.5 in ESPEN guidelines)
- Cirrhosis without encephalopathy : 1.5 gm/kg/day
- Cirrhosis with encephalopathy : do not restrict dietary protein (1.2-1.5 in ESPEN guidelines)
- Cirrhosis with resistant encephalopathy : restrict dietary protein

ACUTE PANCREATITIS

Changes in acute pancreatitis :

- Increased insulin and glucagon
- Decreased insulin to glucagon ratio
- Increased glucose, urea, TG, AAA, peripheral lipolysis
- Decreased plasma total AA, BCAA, glutamine, gluconeogenic AA
- Mild pancreatitis increases energy and oxygen consumption, severe pancreatitis decreases
- Oral feeding in mild to moderate disease

Indication of TPN:

- Inadequate oral or tube intake
- Enteric fistula
- Pain on food intake
- Ascites

Lipid emulsion can be used if STG can be maintained below 400

Nasogastric or nasojejunal tube in severe disease

Calories : start with 15-20 kcal/kg/day(after 7 days gradually building dietary intake)

Calorie N = 100:1

Glucose or carbohydrates : 50-60 % or < 4 mg/kg/min

Protein 15-20 % or 1.2-1.5 gm/kg/day

Lipids 20-30% or 2 gm/ kg/day

PROBLEM WITH SBS AND MANAGEMENT

Resection length	Problems	Solutions
< 100 cm	Bile salt malabsorption causing secretory diarrhoea	Cholestyramine
> 100 cm	Malabsorption of fatty acids causing fatty diarrhoea	Fat restriction , MCT supplementation
More extensive resection	Carbohydrate malabsorption leading to osmotic diarrhoea Fatty stool cause Ca and Mg deficiency and nephrolithiasis Fat soluble vitamine deficiency Vit C and FA deficiency	Ca supplements (Mg supplements can cause diarrhoea) Multivitamine supplementation

Organisms Associated

IPSID (<i>G. lamblia</i> infestation is commonly seen)	Campylobacter jejuni is causative
PTLD	EBV transformed B cells
HIV with NHL	EBV
Primary effusion lymphoma = Castleman disease	HHV-8 (in HIV patients)
Zenker's diverticula	HSV-1
Achalasia	HSV-1
Tropical enteropathy (not sprue)	Citrobacter, Hookworm
HTLV-1 infection	Strongyloides stercoralis
MALTOMA	Hp infection
MC GI infection in CVID & IgA deficiency	Giardia
PBC	<i>E. coli</i>
PSC	Chlamydia
AIDS cholangiopathy	CMV (? MC) Cryptosporidium , Microsporidium, Isospora, Cyclospora (not given in S&F)
Acalculous cholecystitis in AIDS	CMV > micro/crypto/iso Again- cyclo isn't given in S&F
Biliary atresia	CMV, Rubella, Rota virus group C, Reovirus 3, HHV 6, HPV
Choledocal cyst	Reovirus
Colorectal adenomas	Inc. Dorea, fecalibacterium, Dec. Bacteroides, <i>S. Bovis</i> bacteremia, JC virus
Idiopathic gastroparesis	Norwalk, HSV, EBV
CD	Pseudomonas, Reovirus, Mycobacteria paratuberculosis , Listeria, Chlamydia
Colonic ischemia	<i>E. Coli</i> (O157:H7), Parasites – strongyloides, Viruses (HSV, HCV, CMV)
Ulcerative enteritis in compromised	CMV, Cryptosporidium, TB
Acute appendicitis	CMV
Eosinophilic esophagitis	HSV
Diverticulitis	CMV
Menetrier's disease in children	CMV, <i>H. pylori</i>
IBS	Increased Ruminococcus, Clostridium, Dorea Decreased Bacteroides, Bifidobacterium, Fecalibacterium

Diverticulitis	CMV infection
Cholangitis	E.Coli, Klebsiella, Pseudomonas, Proteus, Enterococci, Bacteroides fragilis, Clostridium perfringens
Menetrier's disease	Hp infection, CMV gastritis, HIV infection
Acute pancreatitis in children	Coxakievirus, Echo virus
Colorectal cancer	Fusobacterium species
Esophageal cancer (ESCC)	Fusarium verticilloides
Calcium activated chloride channels	Rotavirus infection in children
PTLD	EBV following liver transplantation
Esophageal cancer (ESCC)	HPV 16 & 18
Anal cancers	HPV 16 & 18
Anal warts	HPV 6 & 11
Malakoplakia (reduced cGMP in macrophages)	E.Coli >> Klebsiella, Proteus, MTB, Staph
Colonic adenomas	High dorea, faecalibacterium, fusobacterium Low bacteroides
Colonic adenomas and CRC	Streptococcus bovis bateremia, Streptococcus agalactiae, JC virus
Ulcerative enteritis	CMV, Cryptosporidium, TB
Infectious colitis in UC (or overall !!!)	Shigella, Salmonella, Campylobacter jejunii (requires no treatment)
Blastocystis hominis	IBS
Tropical enteropathy (not sprue)	Citrobacter rodentium, Hook worm
Persistant Strongyloides infection and malabsorption	HTLV -1 infection
Oral hairy leucoplakia	EBV in an HIV patient (poor prognosis) Associated with candidiasis in 50%
PUD	H pylori, HSV-1, CMV in HIV patients, H. Heilmanii
Unusual viral causes of ALF	HSV 1,2, & 6 (most important of all) VZV, EBV, CMV, Parvovirus B19
Alcohol liver disease	Reduced bifidobacterium, lactobacillus increased gram negative bacteria
Liver abscess	E . coli, Klebsiella, Proteus, Pseudomonas, Streptococcus milleri MC anaerobic are bacteroides, fusobacterium
Proteinaceous ascites	Chlamydia, TB, Coccidiomycosis
SBP & MNB	E. Coli, Pneumococci, Klebsiella

RISK FACTOR cancer

GB	PANC	GAST.	PROBABLE	CHO.
(TP53> Cholelithiasis (>1 cm) Porcelene gallbladder (type 2,3) Adenomatous sessile polyps Intrahepatic biliary dysplasia AUBPD PSC Cholangiocarcinoma Carriers of typhi and paratyphi Nitrosamines, methylchlorithan Mustard oil Secondary bile acids LYNCH syndrome (HNPCC) IBD Segmental adenomyomatosis First degree relative	PRSS-1 mutation (chr 7) max risk TP 17 STK/LKB- maximum RR MLH1 & MSH2 FANC-C & FANC-G (in young) Pallidin → family X FAMMM(TP-16) > kRAS BRCA-2>1 (MC mutation) First degree relative HNPPCC Smoking (deletion of GSST-1) Red / processed meat Alcohol ? Diabetes mellitus* & obesity Exenatide and Sitagliptin**	TP53 > APC > DCC, FHIT, p16 MAJOR Hp infection Chronic atrophic gastritis Cigarette smoking Intestinal metaplasia Dysplasia* Adenomatous polyps* Billroth II* Genetic factors: • Family history * • FAP fundic polyps* • HNPCC* • P-J syndrome* • Juvenile polyposis*	Hyperplastic polyps High nitrates High salt, obesity, Snuff tobacco H/O PUD Pernicious anemia* Alcohol, Fat, red meat Low SE status Menetrier's disease Aflatoxin PROTECTS: Green tea Aspirin / NSAID, Statins Vegetables, Vitamin C	(IL6 → PI3K, JAK/STAT, MAPK, EGFR COX-2, HGF/c-MET), polysomy ▲ Definitive PSC (5-15%) Opisthorchis Choledocal cyst 1,4,5 (todani class) Hepatolithiasis Thorotrust Probable Heavy Alcohol Chlonorchis sinensis Biliary drainage (recur. cholangitis) Toxins (Dioxins, PVC) HCV, cirrhosis in intrahepatic Cirrhosis (any cause) -> extrahepatic Possible: DHONI DM, Hepatitis, Obesity, NAFLD, IBD

ESCC	EAC	AMPUL	HCC	COLON
Smoking, Tobacco, Alcohol Vitamin A,C,E deficiency Folic acid, Zn, Se deficiency Hot herbal tea of south America Low socioeconomic status Nitroso compounds Fusarium verticilloides (maize) HPV 16,18 Achalasia (M>F) Lye ingestion Plummer winson syndrome Esophageal webs Ptylosis (AD; chr 17) Radiation for Ca breast T. crauzi infection Zenker's diverticula Inlet patch PROTECTS : NSAID Obesity Aspirin Zn,Se, Fruits, vegetables	Smoking Obesity Tobacco GERD High calorie diet Nitrates Male sex hormones PROTECTS : H.pylori Aspirin NSAID Fruits, vegetables Female sex hormones	FAP Gardner syndrome NF-1 Muirre-torre syndrome Chronic liver fluke infection (not associated with HNPCC) Annular pancreas ADENOMA Excess fat Alcohol Obesity Smoking Insulin C- Peptide	MAJOR : HBV, HCV, Cirrhosis, Aflatoxin OTHER : α-1 AT deficiency Hemochromatosis Membranous IVC bstruction NAFLD GSD 1 & 2 Hereditary tyrosinemia -1 Wilson's disease INHERITED : Ataxia telangiectasia Hypercitrullinemia OTHER : Smoking DM, OCP, Obesity Vinyl chloride, HIV infection ? PBC Low platelet count	(APC> High fat, low fibre diet Red meat consumption Beer / ale consumption (rectal) Smoking DM Carcinogens, radiation Heterocyclic amines (fried food) Low Se and Ca Microbial dysbiosis Familial syndromes IBD Acromegaly Renal transplant Urinary diversion Cholecystectomy Androgen deprivation Pelvic irradiation PROTECTS : Aspirin, Ca, Se, A, C, D, E Fish oil, statin, HRT, Low BMI, vigorous activity High fibre diet

Vitamin

Vitamin	Function	Sources	Deficiency	Toxicity
C (AA, DHAA) Distal SI 90-120 mg SVCT-1 & 2	Maintaining metal ions in their reduced forms Scavenging free radicals Synthesis of collagen Synthesis of catecholamines Helping in chloride secretion from CFTR Hydroxylation of proline and lysine Tryptophan → serotonin Interferes with testing of FOBT, cholesterol, glucose	Citrus fruits Broccoli Cabbage Mango Watermelon Strawberry Cantaloupe Cauliflowers Potatoes Tomatoes No endogenous sources Smoking ↓ levels	Scurvy Fatigue Depression Inflamed gingival, petechiae Perifollicular hge Poor wound healing Coiled hairs Hyperkeratosis Internal bleeding Defective ossification	Nausea & vomiting Nephrolithiasis Rebound scurvy
Biotin (vit. H) Proximal SI (J) 30 mcg SMVT (SLC5A6)	Maintains gut immunity by regulating NK cells Deficiency causes Growth delay, Congenital malformations, Seizures, vision problems, Skin issues, Hearing problem, Alopecia	Certain vegetables Egg yolk, liver, nuts, legumes intestinal flora	Myalgia Hyperesthesia Anorexia Seborrhic dermatitis Alopecia Lactic acidosis Organic aciduria	Not reported
B12 Ileum Adult-2.4 μ Preg-2.6 μ Lact.-2.8 μ Cubam MDR for exit	In its coenzyme form (Ado Cbl) in catabolism of FA Conversion of homocysteine to methionine (SAM)	Meat, Poultry, Egg, Dairy products, Nutritional yeast.		
Folate (B9)* Prox. SI 400 μ hPCFT(PSI) hRFC (DSI) MDR for exit	Synthesis of purine and pyrimidine One carbon metabolism of amino acids	Green vegetables Liver Bean lentils		
Niacin (B3) Stomach and SI 15 mg Ph dependent carrier (not Na ⁺)	Acts as precursor for NAD, NADP (deficiency causes pellagra)	Meat Fish Bread Yeast Endogenous		
Pantothenic acid (B5) ? 5 mg Na dep. SMVT	In coenzyme A In fat and protein metabolism	Wide distribution	Fatigue Abdominal pain Vomiting Insomnia Paresthesia	Diarrhea

Vitamin	Function	Sources	Deficiency	Toxicity
Pyridoxine (B6) SI & LI 1.5-2 mg Ph (not Na) dependent (amiloride suppressible)	Pyridoxal 5 phosphate In carbohydrate metabolism	Meat Fish Potatoes Non citrus fruits Endogenpus		
Riboflavin (B2) SI & LI 1.3-1.5 mg RFT-2 >> RFT -1 (amiloride and chlorpromazine suppressible)	Part of FMN & FAD	Dairy products Eggs Meat Green veggies Legumes		
Thiamine (B1) Free form in PSI & TPP form in LI 1.4 – male 1.1 – female 1.5–pregnancy 1.6- lactation Ph (not Na+) THTR1 & THTR2	TPP cofactor for multiple enzymes: <ul style="list-style-type: none"> • Transketolase • Pyruvate dehydrogenase • α ketoglutarate dehydrogenase • Branched chain keto acid dehydrogenase ATP production in mitochondria Maintaining normal cellular redox TTP in function of membrane chloride channels	Baker's yeast Whole grain cereal Rice bran Nuts Dried legumes Gut flora		

Vitamin	Function	Sources	Deficiency	Toxicity
A SI (retinol>carotene) 900 μ - males 700 μ - females (2-4 mg of carotene) As retinyl esters or free retinol	Differentiation of T cell immunity Maintaining intestinal mucosal integrity IgA production Important role in embryogenesis As macular pigment	Spinach Carrots Papaya Mango Green leafy veggies	Follicular hyperkeratosis Night blindness Xerosis, Retinal dysfunction Infection susceptibility	Raised ICT Skin exfoliation Hepatocellular injury Alopecia Ataxia Bone/muscle pain Dermatitis/chelitis Conjunctivitis Pseudotumor cerebri Hepatic fibrosis Hyperlipidemia Hyperostosis Teratogenic
D SI 10 μ Or 600 IU Simple diffusion	Calcium and phosphate homeostasis Cellular proliferation Diabetes Immunomodulation Has implications in <ul style="list-style-type: none"> • CV Disease, • Immune Deficiency • Diabetes • Arterial Hypertension • Cancer 	Salmon Tuna Mackerel Cod liver oil Eggs Liver Human breast milk (not cow)	Rickets Osteomalacia Splaying of bone Unmineralized bone matrix ↓ S. Ca ⁺⁺ & PO4 ⁻⁻⁻	↑ S. Ca ⁺⁺ & PO4 ⁻⁻⁻ Metastatic calcification Renal damage Altered mentation
E SI 22.4 IU (15 mg)	Transcriptional, translational, post translational effects. Antioxidant activity Inhibitory effect on clotting cascade. Inhibitory effects on cell cycle progression Antiproliferation effects	Lipid rich plant seeds, oils Wheat germ, Sunflower, Almond Hazelnuts Peanut Corn Soyabean Broccoli Tomato Spinach Margarine Breast milk	Seen in premature infant Haemolytic anemia Irreversible neurological Ds. Defective CMI Retrosternal fibroplasias	Decreased action of vit K Impaired leucocyte function Hemorrhagic stroke
K1 (phylllo) K2 (mena) SI 120 μ - M; 90 μ - F K1- carrier mediated K2- diffusion	Gamma carboxylation of <ul style="list-style-type: none"> • Factors 2,7,9,10 • Osteocalcin & matrix gla protein 	Broccoli, spinach, lettuce, herbs Kale Egg, meat, dairy products	In bottle fed babies causing Hgic. Ds of newborn Associated with warfarin, phenytoin, AB, Vit E	

Minerals

	Function	Sources	Deficiency	Toxicity
Cr 30 micg			Def in pts on TPN Hyperglycemia ↑ FFA Neuropathy, encephalopathy Abnormal nitrogen metabolism	Gastric irritation Contact dermatitis Eczema Skin ulcer Bronchogenic carcinoma
Cu Stomach, proximal D 1 mg hCtr1 (3 TMDs)	Highest level in liver, brain,kidney Found in : Vegetables, fish, dry fruits, Chocolate		In Bottle fed infants LBW babies TPN without copper Depigmentation of hair/skin Neurologic disturbances Leukopenia Hypo/micro anemia (↓ Fe abs.) Skeletal abnormalities Poor wound healing Leukopenia and anemia is not seen in menke's	Nausea, vomiting, pain, diarrhea Coma Hepatocellular injury
Fl 4 mg				Stat Fl >30mg/kg → death Mottling of teeth Calcification ligaments/tendons Exostoses Brittle bones
Iodine Stomach & SI 150 mcg Abs. as inorganic iodide		Seafood	Abortion Still birth Hypothyroidism Cretinism Dwarfism Permanent cognitive deficits	Hyperthyroidism (>100mcg/d) Hypothyroidism (> 2mg/day)
Iron Proximal Duodenum 10 mg (1 mg &1.5 mg) DMT-1 (Nramp-2)	Cofactor for heme and nonheme protein and enzymes Total body store = 3-5 gm Bile acid ↑ absorption BLM has hephestin & ferroportin		MC micronutrient deficiency Hookworm is MC cause Glossitis Koilonychia Easy fatiguability (earliest) Irritability Behaviora changes	Not much Iron accumulates in RES

	Function	Sources	Deficiency	Toxicity
Manganese 2 mg Molybdenum 45 mcg			Hypercholesterolemia Weight loss Hair and nail changes Dermatitis Impaired vit. K function Extremely rare By Molybdenum deficient TPN By parenteral sulphite administn Hyperoxypurinemia Hypourcemia Low urinary sulphate CNS disturbances	Hallucination Impaired mentation Extrapyramidal symptoms Hyperuremia Gout
Selenium Duodenum 55mcg AA associated absorption	60% of selenium absorbed		By TPN lacking Se Myalgia Cardiomyopathy Keshan's (china) → irreversible	Nausea, diarrhea Altered mentation Peripheral neuropathy Loss of hair and nails
Zinc 10 mg Distal SI	7 Zn molecules can bind MT	Meat Shell fish Cereals Legumes	Growth arrest Teratogenicity Hypogonadism Infertility Disguisea Poor wound healing Diarrhea Dermatitis Glossitis, stomatitis Alopecia Corneal clouding Loss of dark adaptation Behavioural changes Impaired CMI Acro. enteropathy (AR inherit) Cu and Zn compete for absn.	Epigasric pain Nausea, vomiting, Diarrhea Hyperapnea Weakness, diaphoresis Gastric erosions Low HDL Impaired CMI

Macronutrients

	Function	Sources	Deficiency	Toxicity
Ca	Active - D & proximal J Passive (@ high intake) - D, J& I	Milk Dairy products	Tetany Weakness	Calcification
Active - D & proximal J Passive (@ high intake) - D, J& I 1000 mg	But max. Abs. in Jej. & Ileum Jej. absorbs faster than Ileum Passive abs. is Vit D dependent Active Duo. Abs. ↑ in deficiency Calcium absorption ↓ with age Rate limiting step → calbindin	Fibres and lactose ↓ absorption		
Mg I > J&D in basal state 400 mg	Absn. In basal state Ileum > D&J Jej. is Vit. D dependent (not Ileum) Both para/transcellular in Ileum Ca affects paracellular pathway Mg flux across ileum > Ca flux Efficiency of Mg absn. 25 %		Impaired electrolyte regulation of Ca, K, Na	

LUMEN

3 Important Tumors

Carcinoid	Carcinoid	Carcinoid
MC SI malignancy MC site – ileum > appendix > rectum	MC site – stomach (worse prog) MC site in SI – J > I > D 5th decade; male > female	MC site – antrum of stomach 10-15% of all NHL, 30-40% of all non lymphoid NHL Types of intestinal lymphoma : PSIL & IPSID
Multicentric Highly vascular tumors Strong desmoplasia seen Midgut carcinoid: argyrophilic & argentaffin + Midgut carcinoids associated with carcinoid syndrome	Arise from Telocytes or ICC Spindle cell pattern Almost all GIST are malignant Malignant tumor grows extramurally LN mets is rare	10 SI lymphoma (PSIL) : I > J > D → pain & wt. loss <ul style="list-style-type: none"> All are B cell except EATL All localized to one segment except Mantle All involve regional LN (in 50%) except MALT (3 X) IPSID : J > I > D → diarrhea & wt loss
MC symptom – pain, diarrhea Bleeding is common Intussusception common Hepatomegaly without rise in AST/ALT	Symptomatic are > 5 cm Pain 40% have hemorrhage and rupture Functional hypothyroidism	IPSID : α heavy chain disease , medeterenian lymphoma Seen with tropical sprue, 2 nd -3 rd decade, male = female Associated with C.Jejuni, broad & stunted villi Short & small crypts, diffuse dilation of D, J & proximal I Impaired CMI & ABMI, ↓ lymphocyt, ↑ ESR, giardia infn, IgG & IgM may be ↑ or ↓ but , IgA is always ↓ Immune electrophoresis is best test Rx – trial of AB (tetra or ampi/metro) for 6 months If no response → give CHOP
EUS for > 1cm & type 3 carcinoids ↑ HIAA & 5-HT	CT is best and early choice PET/CT can detect upto 1 cm lesion Deep Bx is needed from submucosa Highly vascular – don't do Bx in all cases	FOLLICULAR: Bcl 2 + ; t (14; 18) MC symptom = obstruction, Cleaved or small cell lymphocytes seen
Sx if : <ul style="list-style-type: none"> Size > 2 cm , Reached MP or if Present in Jej. & ileum 	Malignant GIST if : <ul style="list-style-type: none"> Size 4 cm , Irregular border Echogenic Foci > 3 mm Cystic spaces > 4mm 	MANTLE: Widespread adenopathy , lymphomatous polyposis, MC in ileocecal junction, contain pan B cell marker along with cyclin D1 +, CD-5 +, CD 10-
Worse prognosis of p-NET or GI-NET if : ↑ ALP, CgA, Gastrin, HIAA Site of primary tumor is : <ul style="list-style-type: none"> Carcinoid : panc reatic > colorectal > SI > appendix Gastrinoma : pancreatic > duodenal NET : SI > pancreatic Aneuploidy, High Ki 67 index, Solid tumor	Prognosis depends on : <ul style="list-style-type: none"> Size Number of mitosis Rupture of tumor PMN/Lymphocyte ratio Exon 11 mutatn – CT responsive Rule of 5 is 5cm; 5 mitosis/hpf	BURKITT'S: t (2; 8), t (8;14), t (8;22), c-MYC, CD20+ Starry sky appearance, tumor lysis syndrome, Highly basophilic, brisk mitotic activity seen types → sporadic, endemic African , HIV associate

Carcinoid	Carcinoid	Carcinoid
<p>No role of Adjuvant CT in NET</p> <p>TACE beads used in Metastatic liver carcinoid :</p> <p>FU-Mi-Cis-Do-St along with gel foam or PVA</p> <p>PALLIATION :</p> <p>p-NET → FU-TESCa -Dox-St (temozol, everolimus, streptoz)</p> <p>GI-NET → use SST or IFN or ? everolimus/sunitinib</p> <p>Poorly differentiated – cisplatin + etoposide ± vincristine</p> <p>LTx can be done as palliation in liver mets</p>	<p>Main Rx is Sx</p> <p>Adjuvant – Imatinib</p> <p>No role of RT</p>	<p>DLBCL: high % of large cells , affect body and antrum</p> <p>60 yrs; male > female; pain, less multifocal than MALT</p> <p>More invasive , loss of p53 or p16; CD10+ CD45+ BCL2-</p> <p>Hp seen in only 35%, typically involves muscle layer</p> <p>Has immunoblast & centroblast</p> <p>PET scan is useful</p> <p>Rx is - CHOP + rituximab ± RT</p>
<p>GASTRIC : type I, II & III</p> <p>Type I - 70% of all, ECL cells +, Female, Small, Multiple , ↑ Gastrin & Histamine, ↑ Acid, Gastric Atrophy, Less Metastasis, ↓ Mortality, Associated pernicious anemia</p> <p>Type II - Associated ZES/MEN, hypergastrinemia</p> <p>Type III - 20%, large, aggressive, no hypergastrinemia</p> <p>ILEAL : Hannibal lecter:</p> <p>Single, small ,within 2 feet of ileum, highly malignant, well differentiated, from EC cell, carcinoid syndrome in 10%</p> <p>APPENDICIAL :</p> <p>4-5th decade, MC tumor of appendix, Present @ tip, present as a C/O appendicitis, IF SIZE < 1 CM → DO SIMPLE APPENDECTOMY</p> <p>RECTAL :</p> <p>Uncommon , small, ant. & lat. Wall, Well differentiated</p> <p>Rx as CRC if > 2 cm/ T3orT4/ G3 grade</p> <p>POORLY DIFFERENTIATED :</p> <p>G-3, Ki-67 index > 20%, necrosis, atypia, No SST receptors, no CGA, But Synaptophysin positive</p>	<p>Origin of B-cell lymphomas</p>	<p>MALT : GASTRIC MARGINAL ZONE TUMOR - antrum C in stomach, pain, associated with Hp in 98% cases, 80% disappears on eradication; Indolent, good prognosis</p> <p>LDH is normal, multifocal, PET scan not useful</p> <p>Cyclin D -; CD5/10 -, CD 19, 20, 43 + t(11;18) > t (14;18) > t (1;14) > t (3;14) t(11;18) → resistant to AB, responsive to cladribine</p> <p>Rx →</p> <p>T1 (mucosa/submucosa) → only AB T2 (MP or serosa) → CT or RT > Sx + AB Tx (N1-2 , M0-1) → CT > RT or Sx</p> <p>CT for MALT → cyclophosphamide or chlorambucil</p> <p>Fludarabine or cladribine if t(11;18) is positive combination of either with rituximab is better</p> <p>Poor Rx response is seen if:</p> <p>Hp negative, t(11;18), LN mets +, high % of large cells</p>
<p>Esophageal, colonic & pancreatic carcinoids are atypical large, difficult to Rx & argyrophilic but argentaffin negative</p> <p>Valvular fibrosis is caused by serotonin, on ventricular side</p> <p>Insulinoma has ↓ SSTR 2 & 5 but ↑ GLP-1R</p>		<p>SI MARGINAL ZONE LYMPHOMA:</p> <p>Similar to stomach but: Seen in old age pts, Not associated with Hp</p> <p>Single exophytic mass associated with bleed & malena</p> <p>Slow growing, indolent</p> <p>Uncurable mostly, main Rx is Sx resection</p>

Cancer Summary

Tumor	Genes	MC C/F	Diagnosis / role of PET	Treatment	Neo / Adjuvant
Esophagus 5 yr 20% <i>METS :</i> <i>To :</i> <i>4m: Breast/MM</i>	Ade –carc sequence in EAC Poor prognosis: <ul style="list-style-type: none">● High p⁵³ / Absent p¹⁶● EGF/Her2-neu / Cyclin D1 +● Bax/bcl2/bcl-x/ survivin● ↑ hTERT/VEGF/ COX2/FGF	Dysphagia Weight loss ↓ albumin ↑ PTHrP	Best investigation is endoscopy and biopsy Do Ba swallow before UGD if suspecting TEF Screen by lugol iodine – unstained area Staging by FDG-PET/EUS-FNA/ MDCT Mass hypoechoic on EUS EUS best for loco-regional spread	Best Rx is Sx even if goes to pleura (T4a) Surgery alone till T2 stage without nodes CT with curative intent can be given upto T4a Endoscopic(ESD >> EMR) – only for 1a Palliative Rx for 4b stage	Neo – FU+ Mitomycin/ cisplatin combined CT-RT is more effective Adjuvant – CT+RT > RT alone <i>T2 = muscularis propria</i> <i>T3 = adventitia/ no serosa in esophagus</i> <i>T4a = resectable spread to pleura, pericardia</i>
Gastric <i>EGC 5 yr- 90% Overall</i> 5 yr 27% <i>METS:</i> <i>To: liver/ perito 4m: breast</i>	Follow adeno → carcino ↓ TP53 is MC mutat ⁿ – 70% ↓ FHIT/APC/DCC ↓ p16/TFF1/p27/ MLH1 ↓ E-cadherin ↑ COX/HGF/VEGF/ EGFR	Wt loss > Pain Lesser trelat sign Shoulder hand S Krukenberg Sister joseph Virchow's	EGD is choice – 6-8 Bx from edge and base EUS for local staging & regional LN Early GC: not beyond SM- (only T1) PET/CT (PET not alone) reasonable for ≥ T2N0 Potential markers TGF-1; CA 72-4, HGF; M2-Pyru. Kinase	Sx is best Rx - D2 in japan/ D1 (15 LN) in USA EMR can be done upto 1.5-2.0 cm ESD if nonulcer, <3cm, <500 μm invasion SM Palliative Sx or stenting <i>T1b=SM; T2 =MP;</i> <i>T3=Subserosa;</i> <i>T4a=serosa</i>	Neo – FU+Epirubicin/ cisplatin Adjuvant – chemoradiation Peritoneal chemo - ↓ trial Palliation: <i>I line : trastu/pertuzumab (Do/Cis/Tra)</i> <i>II line : single agent doxorub/irinotecan</i>
GB 5 yr 10% <i>Median 6 mon</i> <i>Female</i> <i>7th decade</i> <i>Nevin moran</i>	Adenoma → carcinoma (15 yrs) TP53/MDM2 is MC mutatⁿ ↓ expression- p27 kip/p21cip k-ras highest in AUBPD increased p16 ^{INK4a}	Painful jaundice Wt loss Abd. Distension	Diagnosed incidentally in 50-80% CEA > CA 19-9 markers used , not confirmatory USG is 80% sensitive Doppler US to differentiate b/n benign-malignant MRI/CT if US isn't informative/ confirmatory PET has no role in GB cancer	Only 15-50% are surgically resectable Clean the LN till one level past the affected Spread to colon, liver , duodenum not a C/I Simple cholecystectomy in Tis/T1a 15% of T1b are LN positive → go for radical Sx	No neo / adjuvant therapy works For palliation = gemcitabin + cisplatin <i>T1a – invades LP;</i> <i>T1b – Invades MP</i> <i>T2- perimuscular;</i> <i>T3 – perforate serosa</i> <i>T4 – vascular invasion</i>

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Cho Ca 85% extrahepatic Median 2 yrs	IL-6 → PI3K → JAK/STAT MAPK → EGFR pathway HGF → c-MET receptor	Painless jaundice <i>Pain in intrahepatic</i>	PET is useful only for intrahepatic tumors, (Not much for extrahepatic, L N or metastasis) MRI is best imaging modality for diagnosis Δ - stricture with CA19-9 > 129 or cytology+	Only cure is Sx (LTx is C/I) except in : PSC + Perihilar Ca → go for LTx + neo-adjuvant	Neo / adjuvant Rx not recommended Palliation with gemcitabine / oxaliplatin <i>T2a- vascular invasion, T2b – multiple tumors</i> <i>T3 – perforates peritonem, T4 – periductal invn</i>
Ampullary Caucasian male	Adenoma → carcinoma (seen only in intestinal variant) Not in pancreaticobiliary or ulcerating type K-ras > p53 > p21, cip/kip	Painless jaundice Silver stools	Markers are CA 19-9 > CEA Diagnosis on UGIE with Bx Double duct sign on imaging – hypodense on T2 PET role isn't defined in ampullary ca	Pancreatobiliary has better prognosis Intestinal variant has intermediate prognosis Ulcerative variant has worst prognosis 80-90% are resectable @ Δ; 5 yr survival 70% Do a pancreatico-duodenectomy	Adjuvant CT/RT with 5-FU if LN mets + Neoadjuvant hasn't been studied <i>T2 invades duodenum;</i> <i>T3 invades pancreas</i>
Pancreas MC perampullary	Hereditary – PRSS > others Familial- SPINK > others Tropical – SPINK > others MC mutation	Painless jaundice	Most accurate/ most sensitive test - EUS Most preferred – CT (fails in respectability in 25%) MRI- hypointense in T1 PET/NCCT – for recurrence & Rx response FNA- always done if tumor is unresectable T4 (stage III & IV) – is unresectable	Main Rx is Sx (not in liver mets or aortic LN) Only 15-20% of candidates are operable Relative C/I – SMA or PV involvement Preop lap if :tumor > 2 cm or if tumor in body	Neoadjuvant in advanced Ds-investigational Adjuvant in all patients- 5-FU & gemcita For palliation: FOLFIRINOX or Gemcitabine + nab- paclitaxel or Gemcitabine alone <i>T2 = limited to pancreas; > 2cm</i> <i>T3 (stage II) = extend beyond the pancreas</i> <i>T4 (stage III, IV) = involves celiac axis / SMA</i>
HCC <i>Overall 5 yr 27%</i> METS : <i>To : lung > LN</i> <i>4m: panc > colon</i>	HBV accounts for 80% HCC CCC seen in upto 90% of HBV related cancers	Pain → MC & 1 st Hepatomegaly	Screening with USG (< 5 cm are hypoechoic) AFP > 10,000 in clinical setting is Astic Confirm with Triphasic CECT TPCT & MRI is more sensitive than PET PET have a role in tumor outside milan criteria Angiography → blush of delayed capillary emptying Gold standard is Histology	Management as per Milan BCLC and milan CTPS > A or if PHTN is + → don't do resection Stage B (PST = 1) is TACE (palliative) Stage C (M1, N1, PST = 1-2) is Sorafenib Stage D → PST>2 ; CTPS – C → symptomatic Doxorubicin is used in TACE No survival advantage of CT	AFP is not a part of standard screening TACE considered if LTx waiting > 6 mo

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Colon <i>Overall 5 yr 64%</i> <i>METS : To : liver 4m: br, ov, lu, pr,st</i>	MC in sporadic TP53>APC HNPCC(6%) > APC (1%) <i>CIN seen in 80-85%</i> CRC <i>MC MSI seen =</i> <i>TGFβ2R</i>	Anemia - left Constipation - R Diarrhea	<p>Do colonoscopy on suspect with Bx</p> <p><i>Tumor limited till muscularis propria is stage I (Duke A)</i></p> <p><i>Any depth without distant deposit - stage II (B) ; T4 = worse</i></p> <p><i>Any node positive is stage III (C) ; >3 nodes is N2 = worse</i></p> <p><i>Any distant mets is stage IV</i></p> <ul style="list-style-type: none"> ● <i>PET is not used routinely ; done if CEA isn't helping</i> ● <i>Done in potentially resectable Ds not in routine staging</i> 	<p>Before Sx give trial CT in case of hepatic mets</p> <p>Up to 4 liver/3 lung mets can be operated</p> <p>Transanal Sx if - < 3cm ; <30% circumference</p> <p>5cm margin needed on either side in Sx</p> <p>For rectal tumors – trans-anal/LAR/APR</p> <p>For upper rectal/sigmoid – LAR</p> <p>RT given in only rectal cancer not in colon</p>	<p>Colon cancer : For stage II- controversial role Stage III – adj – mFOLFOX / CapeOx / capecitabine Stage IV - neo + adj - 6 months total</p> <p>Advanced : FOLFOX or FOLFIRI → FOLFIRINOX</p> <ul style="list-style-type: none"> ● Cetuxi/panitumumab if pt is k-RAS + ● Nd-YAG/APC/snare/ PDT/fulguration <p>For rectal : stage II/III Preop = RT + 5FU or capacitabine (no oxaliplatin) Post op = CT & FOLFOX or capacitabine</p>

Caustic Ingestions / Corrosive Injury

Burn α Quantity Majority: intentional	Alkali pH > 7 More common	Acid pH < 7
Caustic Agents	Cleaning/draining agent, button battery	Swimming pool cleaners, battery fluid
Characteristics	Tasteless, dourless, colorless more amount ingested	Pungent odour, unpleasant taste. Smaller amount ingested
Pathogenesis	Liquefactive necrosis Transmural damage in esophagus Gastric acid neutralises – limits the damage	Coagulative necrosis Coagulum → limits full thickness injury
Axiom	Bites the esophagus & licks the stomach Esophagus >> Button battery- burn in 4Hr; perforates in 6 Hr	Licks the esophagus & bites the stomach. Stomach >> Upper airway injuries more common
Presentation	Early symptoms – no correlation with extent or severity of burn	
Symptoms	Initial: Oropharyngeal/retrosternal pain; Dysphagia/odynophagia; Hypersalivation Persistent pain, fever, shock, tachycardia, rebound tenderness → perforation	
Bleeding	3%; usually 3 weeks after ingestion	
Fistulisation	3% tracheoesophageal fistula - Cough on swallowing liquids; pneumonia 0.02% aortoenteric fistula- GI bleed	
Stricture	MC complication; 1/3rd develop strictures; α depth of injury Esophageal: 3 weeks/years to develop; dysphagia; Manometry → low amplitude, long duration waves Stomach: Less common; acid ingestion; Antrum- MC affected; Symps s/o GOO Cicatrization and pseudodiverticulae noted on barium	
Esophageal Squamous cell carcinoma (SCC)	30%; after 30 years of ingestion Better prognosis than other forms of SCC → early presentation; less lymphatic/direct spread; better response to surgery/RT in view of scar tissue	
Examination	Corrosive Type, Time, Together with food/other drugs, tongue burn Oropharynx: edema, erosions, burn Neck, chest, abdomen: respiratory distress, perforation	
Labs	High TC/CRP/lactic acidosis/creat → poor prognosis	
Imaging	CXR: perforation, foreign body,pneumonia CT - depth of necrosis; optional	
Management	Respiratory- ? intubation; airway support; supplemental oxygen Fluids - NPO No Ryles tube- Can cause retching → worsens injuries Pain control IV PPI- prevents stress ulcers Broad spectrum Antibiotics - ? perforation Emetics, neutralising agents, NG tube- contraindicated Steroids- ? role Emergency surgery- in perforation; resect necrotic tissues; Feeding Jejunostomy	
Endoscopy after ingestion	< 24 Hr → extent of gastro-esophageal injury; Endoscopic vacuum therapy with sponges - can maintain patency; > 48hr - endoscopic grading not correct due to submucosal edema	

ZARGAR et al. GASTROINTESTINAL ENDOSCOPY 1991

ZARGAR	DESCRIPTION	MANAGEMENT	SEQUALAE
GRADE 0 No	No Visible Damage	Pain control	NO SEQUALAE
GRADE 1 Edema	EDEMA, HYPEREMIA	Liquid diet → regular diet in 48 hours	
GRADE 2A Ulcers	TRANSMURAL INJURY, SUPERFICIAL / Focal ULCERS		
GRADE 2B Ulcers	CIRCUMFERENTIAL INJURY, DEEP/ Extensive ULCERS	Monitor for 1 week Watch for perforation signs; if + needs CT	Stricture in 70-100% of cases
GRADE 3A Necrosis	Focal Necrosis AND ESCHAR	Swallowing saliva → liquids; Not tolerate → NG/NJ tube	
GRADE 3B Necrosis	Extensive Necrosis	TPN/FJ	
GRADE 4 Perf	Perforation	Surgery	

Stricture:

Endoscopy: 3-6 weeks later for fibrosis to set in; Perforation rate is higher and success rate for dilation is lower than other strictures; Multiple sessions needed.

No preventive measures; ? low rate in people received steroids;

Reconstructive surgery after 6 months; Gastric pull up- transhiatal esophagectomy with cervical anastomosis

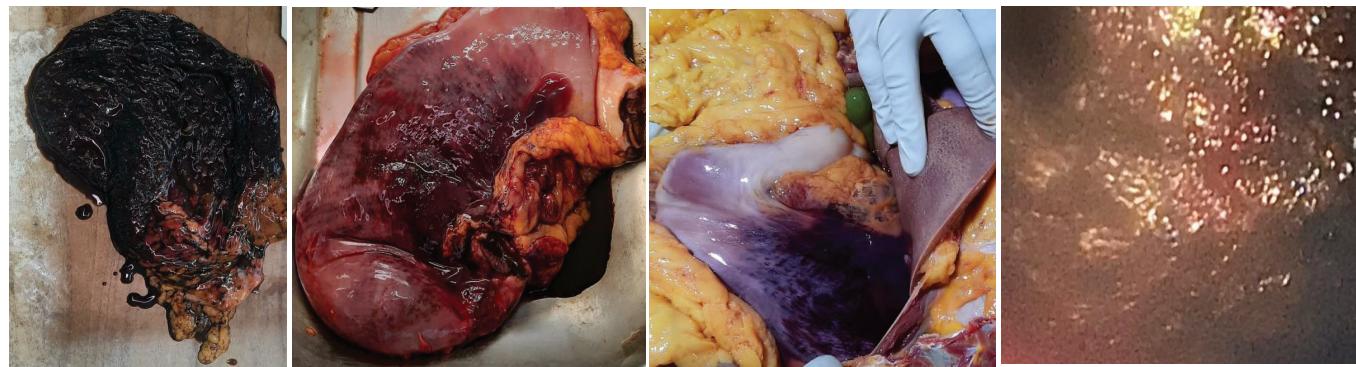
If stomach is involved- colonic transposition; either right or left colon can be used; retrosternal esophagocoloplasty

Native esophagus → risk of cancer and mucocele of retained esophagus

Endoscopic surveillance every two to three years beginning 10 to 20 years after the caustic ingestion due to the increased risk of esophageal cancer (ASGE)

Esophagus: Endoscopy and autopsy:



Esophagus: Endoscopy and autopsy:**Kidneys: Gross and Cut: Autopsy**

CD Vs UC

Crohn's disease	Ulcerative colitis
NOD2/CARD15: chromosome 16 Chromosome 8, 13, 21	Chromosome 11, 20
Female: Male = 1.3:1 but not in children	1:1 ; slight male predominance
Later age of onset	Earlier (2nd - 3rd decade)
Second peak (@60-70 yrs) more pronounced	Second peak less pronounced
Prior misdiagnosis of IBS is common	Rare
Prodromal period seen	Not seen
Diagnosis delayed	Earlier diagnosis
Fecal occult blood in 50%	Frank blood is common
Pain more common (MC symptom diarrhoea)	Less common than in CD
Constitutional symptoms present	Absent
Tenismus less common if associated with colitis (because of rectal sparing)	More common
Right sided disease	Left sided
SI disease present	Absent
Fistulization seen (except ?)	Fistulisation not seen
Major perianal granulomas	?
Panmural disease	Not
ASCA ALCA/ACCA	pANCA in 40-70%
NOD-2 & ATLG-1 present	Absent
Predominant IgG2	IgG1 > IgG3
TH1 response	TH2 response
Pseudopolyps rarely seen	Characteristic
TPN and bowel rest help in management	Of no help
Pseudopolyps less common	More common
Malignancy is less common	Malignancy more common
Smoking is a risk factor	Smoking & appendectomy is protective

Celiac Vs Tropical Vs Whipples

FEATURE	CELIAC DISEASE	TROPICAL SPRUE	WHIPPLE'S DISEASE
Age	Infants – 3 months, around weaning Mean age of presentation now is 45 yrs 25% diagnosed in age > 60 yrs Prevalence 1%	Adults (typical) Children (sometimes, no epidemic form in children)	<u>Not</u> found in children White adults (55 yrs) Very rare disease, 2000 cases Wrongly named intestinal lipodystrophy
Causative factors	Barley, Rye, Oat, Wheat CMI and ABMI both play important role (Gluten = prolamine + glutenin-insoluble) 31-49 aa of α -gliadine (QQQPF) High glutamine & prolamine content in gliadine tTG deamidates glutamine into -ve epitopes HLA-DQ2 ($\alpha 1^*02 < \alpha 1^*05 + \beta 1^*02$) > DQ8 Gliadine's glutamine → -ve glutamic acid IL-4, IL-15 & IFN gamma play important role IL15 is a mediator, regulates IEL homeostasis IL15 triggers adaptive immune response in LP No peripheral lymphadenopathy Associated with Down's syndrome Gamma-delta lymphocytes # increased	Post infection Malabsorption <ul style="list-style-type: none">● EPEC● Giardia● Cyclospora Bacterial and mycotoxins involved Damage to stem cells Exaggeration of ILEAL BREAK SI transit time is increased SIBO (E.coli, klebsiella) Increased IEL (nonspecific) Functional pancreatic insufficiency But stool contains FFA	T. whipplei (fastidious); doubles in 1-4 day Gram positive bacilli (actinomycetes) Commensal bacteria, only humans Relatively small genome = 9,26,000 bp 0.25 by 2.5 μ m (electron dense outer layer) Variation is due to WiSP (VNTR sequences) Slightly more common in farm workers -10% HLA DRB1*13 & DQB1*06 Reduced CD4/CD8 ratio in LP & circulation Reduced CMI & ABMI, CD11b, IL-12 (But ↑ IgG response in asymptomatic carriers) Increased IL-16 & nucleosomes → apoptosis TH1 → TH2 Defective monocyte / macrophage function Defective chemotaxis of cells M2 / alternative activation phenotype Intracellular glycoprotein deposits
Sex	F > M, slight (except in DH)	No sex predilection	M > F ; 3:1
Symptoms	Most are asymptomatic Diarrhea, steatorrhea (in extensive disease), Vague Abdominal pain/ Discomfort, Bloating (severe nausea, vomiting and pain not seen)	Borborygmi, Sore Tongue, Leukonychia, Aguesia Nocturia !!!	Arthralgia usually precede abdo symptom Abdominal pain is the dominant symptom Low grade fever, wt loss, diarrhea Giardia infection seen in 10%
Diarrhoea	Episodic (nocturnal, early morning, postprandial)	Cronic watery/rare bloody diarrhoea Steatorrhoea in 90% Stool fat is largely free fatty acid	+ may be associated with occult bleeding Sometimes gross GI bleeding can occur
Fever	-	+ (in 25 %)	+ (chronic low grade intermittent fever)
Dementia	-	-	+ (CNS manifestations) – 10-40% of GI pts More common in refractory clinical relapse
CNS manifestations	Seizures B/L cerebroparieto occipital calcification		Oculomasticatory myorhythmia Oculofacial skeletal myorhythmia
Clubbing	+ Similar to in UC	- (present in IPSID)	+

FEATURE	CELIAC DISEASE	TROPICAL SPRUE	WHIPPLE'S DISEASE
Dental enamel defects	Commonly seen with chelitis & glossitis	Stomatitis, chelitis, glossitis	-
Peripheral neuropathy	+ (no improvement on therapy)	+	-
SACD	+ (celiac ataxia present) Do not respond to therapy	Not seen now a days B12 deficiency is seen in 60-90%	
Sprue coma	- (celiac crisis is seen)	+ (listlessness, apathy due to Mg++)	
Ogilivie syndrome	-	+ (exaggerated bowel sounds) Colonic pseudo-obstruction +	-
Cognitive	-	+	+
Atrophic gastritis	-	Gastric hyposecretion in 50%	-
Aphthous ulcers	Recurrent aphthii + other oral lesions	Not common	-
Skin pigmentation	+	+ (buccal mucosa , palms, knuckles) Due to vitamin B 12 deficiency	+ (in light exposed areas, unrelated to adrenal function and hyperbilirubinemia)
Fertility	Amenorroea in a third patients Menarche delayed by 1 year		
Catch up growth	Very well seen	Disease seen in adults mainly	
Biopsy	2 nd – 3 rd part of Duodenum (6-8 biopsies)	3 rd & 4 th part	Distal Duodenum and Jejunum (5 biopsy) Go as far distal as possible
Histopathology	<p>Affects only mucosa</p> <p>Villous atrophy due to premature shedding</p> <p>Total thickness of mucosa doesn't change</p> <p>Cuboidal or squamoid epithelial cells</p> <p>Short and fused microvilli</p> <p>Complete villous atrophy seen*</p> <p>Marked compensatory crypt elongation</p> <p>Inc cytoplasmic basophilia - free ribosom</p> <p>Cytoplasmic and mitochondrial vacuolization</p> <p>Large lysosomes, Sparse ER</p> <p>Abnormal tight junctions</p> <p>Mitosis in crypts increased (6 times)</p> <p>IEL increased – CD8 T cells in surface</p> <p>Lamina propria cellularity is increased - CD4</p> <p>IgA, IgM, IgG producing B cells increased</p> <p>Marsh sequential progression (0-4)</p>	<p>Also affects ? submucosa</p> <p>Villous atrophy = scalloping</p> <p>Thickness of mucosa reduced</p> <p>Blunting and fusion of villi</p> <p>Variable degree of villous atrophy</p> <p>Complete flat atrophy never seen*</p> <p>Elongation of crypts seen</p> <p>Damage to stem cell</p> <p>Villous crypt ratio ↓ to 2:1 to 1:1</p> <p>Intestinal stem cell defect</p> <p>Increase IEL (not characteristic)</p> <p>Defective stem cell signalling</p> <p>Degenerating cells in crypts (on EM)</p> <p>Baker and mathan grading (0-III)</p> <p>IEL is more in crypts than surface</p> <p>Infiltration of colonic mucosa seen</p> <p>Reduction in total absorptive surface</p>	Whitish , yellow plaque like patches- in 75% Thick plica circularis,Abnormal villous structure Reduced CD4/CD8 ratio in LP Decreased proliferation peripheral T cells Lipid deposits – actually glycoproteins Mild mucosal flattening due to macrophages H&E stained foamy macrophages in LP PAS positive phagolysosome in macrophages Single bacilli are not seen in light microscopy YO-PRO nucleic acid dye - Small rods in chains (with high resolution) In villous tip below basement memb. in LP Fibroblast cell culture- doubling time 1-4 days Bacteria prefers extracellular media Mucosal infiltration shifts on treatment (from upper part to lower part of villi) Type 3 macrophages → long remission

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Gross GI bleed	-	Rare (but bloody diarrhea seen)	Can occur (mainly occult GI bleed)
Lymphadenopathy	(mesenteric LN with central necrosis common, but not peripheral LN)	Uncommon (seen in IPSID) (mesenteric nodes only involved)	Common (abdominal and peripheral) Lymph nodes have granulomas
Specific clinical features	<p>Hypokalemia & Hypocalcemia Combine Fe & FA deficiency-characteristic Normal B-12, decreased serum FA ALT/AST increase by 1.5 - 2 times ULN</p> <p>Endoscopic findings :</p> <ul style="list-style-type: none"> • Scalloping • Flattening of duodenal folds • Multiple fissures • Mosaic like appearance <p>Jejunum resembles ileum on Ba study: With flocculation, clumping & segmentation</p>	<p>B-12, serum FA both decrease Functional pancreatic insufficiency</p> <ul style="list-style-type: none"> • Abnormal pancreolauryl test in 50% • Normal secretin response ↓ Zn⁺⁺, K⁺, Ca²⁺, Mg²⁺, PO₄ <p>Defective D-xylose test 99% Statorrhea : 90% B-12 malabsorption 60-90%</p> <p>On Ba study :</p> <ul style="list-style-type: none"> • Thickening jejunal mucosal folds • Decreased feathering mucosa • Moulage sign – atony of Jejunum 	Decreased serum carotene, serum iron Increased CRP and ESR, stool fat Proteinuria is seen Granulomas on biopsy Peripheral LN don't have lipid but do have epithiloid macrophages Mediastinal nodes have sarcoid like granuloma Ba study : <ul style="list-style-type: none"> • Prominent duodenal and jejunum folds • Thickening of plica circularis • Loss of mucosal relief pattern • Intestinal dilatation
Site	Proximal SI- Duodenum, Jejunum , Ileum	Distal SI and terminal Ileum	Distal Duodenum , Jejunum
Diagnosis	Biopsy and serology(both for diagnosis) Anti tTG2 – IgA or IgG (best antibody test) Anti endomysium – IgA or IgG Anti DGP – IgA or IgG HLA testing to rule out disease IgA tTG2 is single best test Best test in IgA def. → IgG DGP	Van de Kramer, sudan staining Xylose test – 5 gm in tropics (1&5 hr) Increased S.Methylmalonic acid Dilated featureless atonic loops of J & Mucosal thickening (monilage sign) Magnification endoscopy / NBI Use of 3% acetic acid	Primary diagnosis : UGIE and mucosal biopsy with PAS staining Confirmatory test : PCR is gold standard now-a-days CSF analysis of centrifuge & PCR analysis Fibroblast culture : Only used in labs
Treatment	Pretreatment AB level should be determined Level comes to normal in 3-12 months Steroids in celiac crisis Nonresponsive is treated as UC	Tetracycline 250mg QID (6 month) Doxycycline 100mg BD (6 months) Low fat, high calorie & high protein MCFA rich diet IV metoclopramide in pseudo-obstrn	Duke's regimen : pen G +strepto □ tetra Salvage : IV cephalosporins , rifampin Induction phase : 2 wks (IV drugs) Oral treatment : 1 year (drugs crossing BBB)

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Extraintestinal manifestations	Ecchymosis, Edema Dermatitis herpetiformis (anti tTG3) Follicular hyperkeratosis and dermatitis Amenorrhoea in one third Menarche delayed by one yr Infertility & Impotence (androgen resistance) Secondary hyperparathyroidism Anemia Hemorrhage		Compromised states don't precipitate Ds" Arthralgia & carditis precede GI symptoms Obstruction of mesenteric lymph nodes CNS features present with relapse CNS relapses are ominous & refractory Oculomasticatory myorhythmia (1/sec) Occulofacial skeletal myorhythmia CSF pleocytosis with PCR positivity Pancarditis (culture -ve) = no duke's criteria Most common are aortic and mitral valve Most symptomatic is aortic valve Murmur from pulmonary valve
Extraintestinal manifestations	Thrombocytosis Hyposplenism in 50%- not seen in children Howell jolly bodies Elevated LFTs (lyphocytic hepatitis) Autoimmune hepatitis Muscular atrophy Tetany Peripheral neuropathy (not respond to GFD) Ataxia –cerebellum,SC,Post. column,Per.nerve CNS demyelination Seizures (MC is CPS) Osteopenia-75% / malacia / porosis-25% Osteoarthropathy Pathologic fractures		Oligo/polyarthritis (RF negative) Destructive joint changes are rare Sacroileitis and spondylitis can occur (not AS) Prosthetic joint infection, Spondylodiscitis Uveitis, viteitis, retinitis, pappiloedema Granulomatous pulmonary disease Pulmonary effusion T.whipelli in BAL fluid of HIV patients Abdominal node have foreign body reaction Peripheral LN do not contain lipids But do contain epithiloid macrophages Mediastenal nodes have sarcoid ganuloma

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Associated disorders	<p>Definite :</p> <p>DM1 (celiac in DM = 5%)</p> <p>Hypo > hyperthyroidism</p> <p>Down syndrome</p> <p>Epilepsy cerebral calcification</p> <p>Bird's fancier's disease</p> <p>Pulmonary hemosiderosis</p> <p>Fibrosing alveolitis</p> <p>Sarcoidosis</p> <p>Recurrent pericarditis</p> <p>RA</p> <p>IgA deficiency (2%)</p> <p>IgA mesangial nephropathy</p> <p>Dermatitis herpetiformis</p> <p>IBD</p> <p>Microscopic colitis (share HLA-try GFD Rx)</p> <p>Possible :</p> <p>Addison's disease</p> <p>Myasthenia gravis</p> <p>AIHA</p> <p>AIH</p> <p>Sjogren's disease</p> <p>Cavitary lung Ds</p> <p>Cystic fibrosis</p> <p>Congenital heart disease</p> <p>ITP</p> <p>Iridocyclitis or choroiditis</p> <p>Macroamylasemia</p> <p>Polymyositis</p> <p>Schizophrenia</p> <p>Systemic & cutaneous vasculitis</p> <p>SLE</p>		<p>CNS lesions :</p> <p>Perivascular infiltrates of PAS + cells</p> <p>Granuloma of variable size with glial cells</p> <p>Granuloma in ventricles → obs. hydrocephalus</p> <p>Changes after treatment :</p> <p>Diarrhea : several days</p> <p>Arthralgia : few weeks</p> <p>Weight gain : in few months</p> <p>Macroscopic : in months</p> <p>Histologic : in several months</p> <p>PCR on gut Bx : 1 – 12 months</p> <p>Lymph node regression with fibrosis : > 1 year</p> <p>Type 3 macrophages in 6-15 months for 10 yrs</p> <p>Follow up with CSF should be done</p> <p>IRIS seen in compromised, Rx with steroids</p> <p>Drugs in induction : 2 wks Rx</p> <ul style="list-style-type: none"> • Penicillin G + streptomycin • Carbapenems • III generation cephalosporins(salvage Rx) <p>Long term therapy for 1 yr : (oral)</p> <ul style="list-style-type: none"> • TMP/SMX- no THFR for trimethoprim !!! • Sulfadiazine(better) • Penicillin VK • Doxycycline + HCQ (\downarrow intracellular pH) • Minocycline (penetrates CNS) + HCQ • Cefixime • Rifampine • Chloramphenicol <p>"Resistant to FQ"</p>
Associated malignancy	<p>EATL</p> <p>Oropharynx</p> <p>Esophagus</p> <p>SI</p>	<p>IPSID = mediterranean lymphoma</p> <p>Alpha heavy chain disease</p> <p>(Relapse should raise a suspicion)</p>	Malignant lymphoma (seen only rarely)

Chemo and IBD Drugs

CANCER AND TYPE OF THERAPY	COMPONENTS
Colonic cancer: For stage III and stage II with risk factors	Only adjuvant therapy : mFOLFOX(Leucovorin/5-FU/Oxaliplatin) bolus FLOX (5-FU/Leucovorin/Oxaliplatin) Cape-Ox (Capecitabin/Oxaliplatin) Single agent Capacitabin 5-FU/LV
Rectal cancer : (high rate of locoregional spread) Stage II & III	Preop chemo-radiation : Infusional 5-FU/RT or oral Capacitabine/RT Post – op, only chemo : 6 months total FOLFOX or Oral Capacitabine
Locoregionally advanced or metastatic CRC	Cetuximab and panitumumab (in k-RAS + pts) IFL (irinotecan/5FU/Leucovorin)- not recommended now FOLFIRI along with mFOLFOX6 is first line Rx FOLFOXIRI CapeOx Infusional 5-FU/LV or capacitabine Bevacizumab in combination with IV 5-FU Ziv-aflibercept in conjunction with FOLFIRI Cetuximab in combo with Irinotecan Regorafenib
Ana canal cancer	Mitomycin C + 5-FU APR on recurrence
Palliation in gastric cancer	Do CisTra <ul style="list-style-type: none"> ● Docitaxel ● Cisplatin ● Trastuzumab EOX ECF or DCF
Gastric epithelial lymphoma / MALTOMA	T1(mucosa and submucosa) → only antibiotic T2 (muscle layer and serosa) → RT > CT/Sx T3 → CT > RT / Sx Cyclophosphamide 65 or chlorambucil Purin analogue (fludarabin/cladribin) effective in t(11:18) Chemo-immuno Rx : chemo(above) + rituximab Radio-immuno : rituximab + 90 Y-ibritumumab tiuxitan
Gastric DLBCL	CHOP {3-4 cycles(6-8 in stage IV)} + rituximab ± XRT
IPSID	Tetracycline or ampicillin/metrogyl combo for 6 months. If no response in 6 month Or no complete remission in 12 months start CHOP. Doubtful role of radiotherapy.

CANCER AND TYPE OF THERAPY	COMPONENTS
EATL	CHOP; Alemtuzumab (anti CD-25) Brentuximab (anti CD-30 + auristatin E)
GIST	No chemo Imatinib for adjuvant and neo-adjuvant
Esophageal cancer	Neo-adjuvant is MC approach Cisplatin or mitomycin + 5-FU + RT
Cholangio carcinoma	Modest effect of chemo & radio therapy □ as in HCC Cisplatin & gemcitabin Conventional and drug eluting TACE Trans-arterial radioembolization
Hepatoblastoma	Give Cisplatin + doxorubicin prior to surgery
HCC	Sorafenib
Pancreatic cancer	Gemcitabine + 5-FU ± FOLFIRINOX
GB cancer	Gemcitabine

EMERGING DRUGS IN IBS

DRUG	MOA
Pregabalin / gabapentin	CCB
LX-1031	Tryptophan hydroxylase inhibitor
Asimadolin	Peripheral Kappa antagonist
Dexloxioglumde	CCK-1 antagonist
Pexacerfont Velucetrag Prucalopride	CRF antagonist
Naronapride	5HT4 antagonist
Ketotifen	Mast cell stabilizer
Mesalazine	5-ASA
Dextofesopam	BDZ receptor modulator
Cholesevlam	Bile acid sequesterant
A-3309	Bile acid transporter inhibitor
Chenodeoxycholate	Bile acid

TREATMENT OF IBD (CD)

DRUG	MOA	USE	SIDE EFFECTS
Antibiotics			
5-ASA			Headache Diarrhoea Abdominal pain Nausea Fatigue
Steroids			
Azathioprine (TG) <i>(converts to 6-MP)</i>	Serum T $\frac{1}{2}$ = 0.2-0.5 hrs Biologic T $\frac{1}{2}$ = 24 hrs	Used successfully in CD for: <ul style="list-style-type: none">- For remission in steroid refractory- Maintenance of remission- As a steroid sparing agent- Fistulizing disease	Nausea Drug fever/rash Arthralgias Marrow suppression Pancreatitis Hepatitis Infection Lipoma
Methotrexate	Structural analogue of folic acid Enhances extracellular adenosine Inhibits methylation reaction		Nausea/vomiting Hepatotoxicity Hepatic fibrosis Neuropathy Alopecia Infections Marrow suppression Interstitial pneumonia
Cyclosporine		May have a role only in fistulising disease	Renal dysfunction Hypertension Tremor Headache Paresthesia Seizure Gingival hyperplasia Hypertrichosis Hepatotoxicity Lymphoma infection
Tacrolimus (FK506)	100 fold more potent to cyclosporin		
Sirolimus			
Everolimus			

DRUG	MOA	USE	SIDE EFFECTS
Anti TNF alpha: Infliximab Adalimumab Certolizumab pegol Eternacept		Eternacept and certolizumab do not induce apoptosis	
Thalidomide	Down regulation of TNF-alpha Inhibition of NF-KB activity		
Natalizumab	IgG4 against $\alpha 4\beta 1$ & $\alpha 4\beta 7$		
Vedolizumab	IgG1 against $\alpha 4\beta 7$		
Ustekinumab	AB against P40 of IL-12 & IL-23		
Tofacitinib	Oral JAK inhibitors		Rise in LDL & HDL Neutropenia Raised liver enzymes Raised creatinine anemia
Probiotics			
Porcine whipworm (trichuris suis)			

THERAPY FOR ULCERATIVE COLITIS

TREATMENT	MOA	NOTE
Antibiotics (cipro+metro)		Only for suppurative complications
Steroids		
Azathioprine		
6-MP		
Cyclosporine		
Tacrolimus	Not recommended at present	
Methotrexate		
Anti TNF antibody	Steroid sparing and mucosal healing	
Natalizumab		
Vedolizumab		
Tofacitinib		
Daclizumab	AB against IL-2R (CD25)	Hawabaazi
Basiliximab	Chimeric AB against IL-2R	Hawabaazi
Visilizumab	AB to CD-3	Hawabaazi
Abatacept	Recombinant Fc portion of IgG1 & HTLA-4 ; inhibits costimulation of T cells	Hawabaazi
EGF enemas		
Repifermin	Keratinocyte growth factor 2	Hawabaazi
Probiotics	VSL#3 lactobacillus + bifidobacterium + streptococcus	No strong recommendation
Fecal microbiota transplant		Investigational
Butyrate enemas		
LMWH	Anti inflammatory	Hawabaazi
PPAR agonist (Rosiglitazone)	Immunomodulatory antiinflammatory	Restricted to those who can't tolerate standard treatment
Ada-column apheresis		Not recommended at present

- Sulfasalazine is a sulfa (sulfapyridine) derivative of mesalazine or mesalamine

ASA PREPERATIONS

DRUG	FORMULATION	SITE OF DELIVERY
PRODRUGS		
Sulfasalazine	Sulfapyridine + 5-ASA	Colon
Olsalazine	5-ASA dimer	Colon
Balsalazide	4-aminobenzoyl alanine + 5-ASA	Colon
MESALAMINE PREPERATIONS		
Asacol, claversal, apriso, delzicol	pH sensitive resin coated delayed release	Distal ileum & colon
Rowasa	Enema	Distal colon
Canasa	Suppository	Rectum
Pentasa	Ethylcellulose coated microgranules; controlled release	Duodenum to colon
Lialda	pH sensitive multimatrix (MMX) and Polymethacrylate coated	
Delayed and slow release	Distal ileum & colon	

Larazotde acetate: Inhibitor of paracellular permeability thus decreases gluten entry (resemblance with ZOT toxin)

DOC for acute biliary colicky: Meperidine

Teduglutide: GLP2 analogue: Used in short bowel syndrome

Adenomatous Polyps Syndromes → All are APC mutations

Synrome	Gene Mutation	Polyps	Extraintestinal Abnormalities	Screening & Notes
Classical FAP After 10 yrs of age Gastric polyp: fundus & adenoma: antrum Duodenum: 60-90% Jejunum: 40 % Ileum: 20 %	APC (truncated) 1244 aa protein 25 yrs: onset 35: symptoms 36: diagnosis 39: cancer 42: death	Colonic adenoma (1000) Duodenal & periampullary adenomas (80%) Jejunal & ileal adenomas (40 & 20%) Gastric fundic polyp (30-100%) Adenomas (5%, antrum) Microcarcinomas Ileal lymphoid polyps 1000 polyps in intestine	Mandibular osteomas (90%)- no mal.potential Dental abnormalities Most other tumors seen in Gardner's 4-12 % lifetime risk of periampullary cancer, major cause of death after polypectomy	Colon cancer: 10-12 yrs / 1 yrly Duodenal : 25-30 / 0, 1, 3, 5 Spigelman classification of duodenal adenomas Jejuna and ileal adenoma are rarely malignant in FAP 25% will have cancer @ diagnosis Cancer develops 10-15 yrs after presentation
Gardner	APC	Same as FAP CHRPE has most accurate genotype phenotype correlation when APC mutation is distal to exon 9	Osteomas of mandible (90%, multiple), skull, long bones Exostoses Mandibular cyst, impacted teeth CHRPE (90%) → asymptomatic, most accurate correlation Desmoids tumors (4-32%) → familial aggregation Epidermoid cyst (inclusion cyst), multiple Fibroms Lipomas Adrenal tumors Hepatoblastoma in very young children Papillary ca of thyroid mainly in females (1%)	Desmoids tumors : <ul style="list-style-type: none">Young operated femalesFamily history is important10-50% mortality, radioresponsiveAPC mutation distal to codon 1444Rx → sulindac, estrogen antagonist, tamoxifen, radiationNo role of surgery. CHRPE are seen mutation distal to exon 9 Maximum polyps seen if mutation is b/n 1250-1450 PCT seen in mutation proximal to cluster region
Turcot (AD/AR) aka glioma-polyposis	APC APC DNA MMR	Colonic adenomas – sometimes fewer (single to multiple) than in classic FAP	Medulloblastoma (APC)-more common form Glioblastoma multiforme (MMR) CHRPE	
Attenuated FAP	APC 5' & 3' regions	Colonic adenomas (<100; proximal colon) Duodenal & periampullary adenoma Gastric fundic polyps	Mandibular osteoms	CRC arise later → 55 yrs of age Colonoscopy start @ 18-20 yrs / 2 yrly Extreme 5' and 3' are affected Mainly flat lesions in proximal colon
Familial tooth agenesis	Axin- 2 (APC pathway)	Colonic adenomas Hyperplastic polyps	Agenesis of teeth	

Synrome	Gene Mutation	Polyps	Extraintestinal Abnormalities	Screening & Notes
Bloom's syndrome	BLM	Colonic adenomas	Small stature Facial erythema / Ectropion Male sterility Adenocarcinomas Leukemia Lymphoma	
MUTYH polyposis (AR) Y179C; G396D G:C→T: A transition	MUTYH (MYH)	Colonic adenomas (5-100) Duodenal polyposis Gastric cancer Some hyperplastic polyps	CHRPE Osteomas Gastric cancer & duodenal adenomas No microsatellite instability.	Colonoscopy start @ 18-20 yrs / 2 yrly
GAPPS	Gastric adenocarcinoma with proximal polyposis of stomach			Numerous fundic gland polyps High risk of gastric adenocarcinoma No duodenal polyps Few colonic adenomas

Muir torre syndrome: subtype of HNPCC; colonic adenomas/carcinoma, sebaceous adenoma/carcinoma, basal cell and SCC.

Classification of GI polyposis syndromes :

Inherited polyposis syndromes :

Adenomatous Polyposis Syndromes : APC TAG To Bloo Tooth Muth

- Familial adenomatous polyposis
- Variants of familial adenomatous polyposis
 - ▶ Gardner's syndrome
 - ▶ Turcot's syndrome
 - ▶ Attenuated adenomatous polyposis coli
- Familial tooth agenesis syndrome
- Bloom's syndrome
- MUTYH polyposis (MYH polyposis)

Hamartomatous Polyposis Syndromes: PIyush Ji BHID PTEN -BC

- Peutz-Jeghers syndrome
- Juvenile polyposis
- PTEN hamartoma tumor syndromes
 - ▶ Cowden's disease
 - ▶ Bannayan-Ruvalcaba-Riley syndrome

- Rare hamartomatous polyposis syndromes
 - ▶ Hereditary mixed polyposis syndrome
 - ▶ Intestinal ganglioneuromatosis and neurofibromatosis
 - ▶ Devon family syndrome
 - ▶ Basal cell nevus syndrome

Noninherited Polyposis Syndromes:

- Cronkhite-Canada syndrome → diffuse GI polyposis, diarrhoea, wt.loss, integumentary changes, carcinoma colon risk
- Serrated polyposis syndrome → atleast 5 polyps with 2 > 10mm; any no. proximal to sigmoid with first degree; >20 anywhere
- Lymphomatous polyposis
- Nodular lymphoid hyperplasia

Familial hamartomatous polyposis syndrome (all are AD)

Syndrome	Mutated gene	Polyps	Location of GI polyps	Other features
PJ syndrome <i>Surveillance UGIE and colonoscopy starts at 8 yrs, every 2 yrly</i>	STK11/LKB1 (19p)	Hamartomatous with band of smooth muscle in lamina propria	Small intestine (MC) Stomach Colon	Pigmented lesions (mouth, hands, feet) Ovarian sex cord tumors Sertoli tumors of the testes Airway polyps (54%) Cancer : Breast > Colon > Pancreas > SI
Juvenile polyposis S. (diagnosis of exclusion) Screening begins at 15 yrs of age	MADH4 → TGF-B signal BMPR1A → TGF-B ENG → early onset & associated with HHT <i>MADH4 = SMAD4</i>	Juvenile polyps Adenomas & Hyperplastic polyps	Colon Small intestine Stomach	Colon cancer in some families Congenital abnormalities : <ul style="list-style-type: none">● Craniofacial (macrocephaly)● CVS(COA, ASD, TOF)● Urogenital● GIT (meckle's, malrotation)
Cowden's syndrome <i>(polyps are due to muscularis mucosa; epithelium is normal)</i>	PTEN (10)	Hamartomas with disorganised muscularis mucosa	Stomach Colon	Trichilemmomas (eyes, nose & mouth) <ul style="list-style-type: none">● Papillomas● Oroticaneous hamartomas● Benign and malignant breast disease● Benign and malignant thyroid disease● Uterine cancer CRC is uncommon (so no screening) Ganglioneuromatosis of colon Glycogenic acanthosis of esophagus

Syndrome	Mutated gene	Polyps	Location of GI polyps	Other features
Banayan-ruvalcaba-riley syndrome	PTEN	Juvenile polyps	Colon	Macrocephaly Developmental delay Pigmented spots on penis Thyroiditis
Neurofibromatosis	NF-1, RET	Neurofibromatosis	Small intestine Stomach Colon	Von recklinghausen's disease MEN-IIB
Hereditary mixed polyposis syndrome	CRAC1(15q) GERM 1 expression	Polyps of mixed histology in colon	Colon	Atypical juvenile polyp
Tuberous sclerosis			Distal colon	
Devon family syndrome	Multiple and recurrent inflammatory fibroid polyp	Fibroid polyps	Stomach & intestine	Stomach & intestine
Basal cell nevus syndrome		Hamartomatous	Gastric	

Esophageal Motility Disorder

	ZENKER'S	ACHALASIA	DES	JACK-HAMMER
Sex	Males > females	Male = females		
Age	7th – 9t decade	25 – 60		
Genetics		Familial clustering Genetic achalasia syndrome : ALADIN protein : AAAS gene (adrenal insufficiency, ANS dysfunction, delayed gastric emptying & alacrima)		
Pathogen	<p>False diverticula Pulsion diverticula Cricopharyngeal bar Midline disease Fibroadipose replace. Muscle degeneration Dec. Compliance</p> <p>Norml LES relaxation</p>	<p>Impaired LES relaxation Cistant symptoms Aperistalsis in SMC Absent tLESR Nonperistaltic contrn in type III Resting LES pressure inc. Loss of ganglion in MY plexus Degeneration of vagus nerve HSV – 1 implicated CTL and IgM antibodies DQA1*0103 & B1*0603 Ass. With PD & lewy bodies Inh dysfn > excit dysfn Lack of NO synthase CCK paradoxically inc. Pressure</p>	Only SMC affected Disorder of peristalsis but Retains normal peristalsis SMC hypertrophy distal 3rd MY plexus dysfunctn Absent progressive delay No deglutitive inhibition No LES involvement Intermittent disease	Only SMC affected Disorder of peristalsis but Retains normal peristalsis As a result of mech. Obstruction or cholinergic hyperactivity Normal propagation latency Spontaneous distal contractn longer and greater amplitude Asynchrony b/n LSM & CSM Prolonged repetitive contraction Nutcracker @ 180 mmHg Pain, dysphagia @ 260 mmHg DCI > 8000 mmHg/cm/s
		Weight loss Dysphagia for both Regurgitation Chest pain an early complaint Hiccups Halitosis Aspiration pneumonia Esophageal dilation Saliva regurgitation	No weight loss Episodic dysphagia present Chest pain (same as angina) Swallowing not always impaired Pain due to longitudinal muscle	
Comments	MC anatomic cause of dysphagia in old age			
D/D		DES (normal LES relaxation) Chagas disease Pseudoachalasia (malignancy etc) Resistance on passing endoscope with pseudoachalasia Postsurgical : amyl nitrate test	Angina pectoris	

GERD usually have no weight loss, mild weight loss MAY be present in cases with dysphagia

Candidal ulcer	? proximal – mid esophagus, linear plaques, linear filling defects, black esophagus may be seen
HSV ulcer	Mid-distal esophagus , 1-3 mm vesicles, ulcers with raised edges, volcano like lesions on Ba study, MNGC, ballooning degeneration, ground glass intranuclear cowdry A inclusions
HPV ulcer	Mid-distal esophagus , erythematous macules, white plaques, nodules or exuberant frond like lesions, koilocytes, giant cells risk factor for carcinoma esophagus
TB	Shallow ulcers, mucosal plaques, heaped up lesions mimicking neoplasia, perforation, bleeding, fistula
CMV	Distal esophagus , large (like HIV) or giant, solitary, discrete ulcers
Causes of black esophagus : <ul style="list-style-type: none"> • Ischemia • Impaired mucosal barrier • HSV • Candida • CMV • Severe reflux • DM • Hematologic • Solid organ malignancy • Malnutrition • Renal insufficiency 	Causes of upper esophageal ulcers : <ul style="list-style-type: none"> • Candida • Drug induced • Crohn's disease

Gastritis

Infectious :			
CMV	Pain, fever, atypical lymphocytosis Antral edema (GOO) Underlying ulcers CMV inclusion : owl eye		IV gancyclovir or foscarnet
HHV-1 & HHV-3 (VZV)	Cobblestone pattern, Shallow multiple ulcerations Eosinophilic intracellular inclusions		Acyclovir
HHV-4 (EBV)	Gastritis cystic profunda Gastric cancer IMN (gastric lymphoid hyperplasia)		
Measles	Morbilliform Giant cells (warthin finkeldey type)		
Mycobacterial	GOO, Enlarged stomach & prepyloric ulcers Hemorrhage from ulcer		
MAC (very rare)	Foamy histiocytes		
Actinomycosis (gram +, aerobic, filamentous)	Multiple abscess Draining sinuses Abundant granulations dense fibrous tissue Prediction for terminal ileum, cecum, appendix Gastric site is rare		6-12 month of amoxicillin or penicillin
Syphilis	Present as PUD / UGI bleed Nonspecific gastritis Hourglass stomach Numerous shallow irregular small serpigenous ulcers Granulomatous gastritis Warthin starry gastritis or modified steiner silver impregnation		
Helicobacter heilmanni (longer than Hp)	MALTOMA		
Candida albicans	Very large ulcers Easily confused with malignancy Early stage - aphthoid ulcers on radiologic ulcers		Treatment is not indicated (<i>fluconazole in systemic infections</i>)
Histoplasmosis	Extreme of ages Hypertrophic gastric folds Plenty of mucosal macrophages		IV amphotericin B Or itraconazole
Mucormycosis	As gastric ulcer or PUD Lethal Risk: compromised, DM, DKA , acidosis Nonseptate hyphae branching at right angle Invasive form is always fatal		Gastric resection

Aspergillosis & Monascus ruber	Invasive disease	
Giardiasis	Cotton like antral lesions	
Strongyloides	In immunocompromised raised eosinophilic counts	
Anisakidosis	From raw marine fish Invasive gastric wall Chronic infection can cause perforation Can present with UGIB Mild peripheral eosinophilia , eosinophilic granulomatous condition Firm yellowish submucosal masses Intramural abscess can contain larva (0.3mm) 5-10 mm erosive gastric lesions	Removal of larvae Wood cresolate
Ascariasis	UGIB	Endoscopic removal Albendazole
Capillariasis	Eosinophilic gastritis from eating fish	
Sarcoidosis	Affects antrum Severe UGIB Mimic linitis plastic and menetrier's disease Prepyloric ulcers and erosions (as in TB) Multiple noncaseating granulomas (may be necrotic though)	GC Subtotal resection
Xanthogranulomatous	Foamy histiocytes MNGC Coexist with neoplasm	
Collagenous	Young pts : anemia, epigastric pain Older adults : diarrhoea Affects body along greater curvature Collagen in subepithelial submucosa. Muscularis propria hypertrophy	
Lymphocytic gastritis or Varioliform	Most commonly with Hp Precursor of MALTOMA Loss of apical mucin secretion Other conditions <ul style="list-style-type: none"> • CeD • CD • HIV • CVID 	
Lymphomatoiid gastropathy	NK cells with CD56+ infiltrate the stomach Simulates gastric lymphoma 1 cm raised nodules Seen in japan No need of treatment	
Eosinophilic gastritis	Mucosal : pain, weight loss, anemia, protein losing enteropathy. Thickened mucosal folds, ulceration >20 eosinophils/hpf	GC

CD	Bamboo joint like gastric mucosal fissures MC lesions in antral region GOO because of antral thickness Focally enhanced gastritis seen in isolated terminal ileitis cases Marked submucosal fibrosis	PPI is first line Infliximab is useful
UC	Lesser prevalence than in CD	Not responsive to PPI Rx as for typical UC
Gastritis cystic profunda	Ass. with menetrier's disease, gastric cancer, EBV infection Dilated cystic gastric glands upto muscuaris propria Strong association with gastric cancer Removed by snares	Removed by snares
GVHD	Acute 21-1000 days Chronic > 100 days Most commonly seen with bone marrow transplantation Rectosigmoid biopsy is diagnostic (not gastric) Apoptotic bodies in neck region of glands	
Allergic gastritis	In young children with milk allergy	
Reactive/ acute erosive	Paucity of inflammatory cells Rapid epithelial restitution Foveolar hyperplasia Ocuurs in about 15% of normal people Incidence increases with age Associated with inflammation elsewhere in GI tract	
Bile reflux gastropathy	Following peptic Sx, cholecystectomy, sphincterotomy Foveolar hyperplasia, dilated cystic glands, atypical glands Paucity of inflammation Eventually intestinal metaplasia	PPI Antacid hydrotalcite Sucralfate ? UDCA
Cocaine	Pyloric or prepyloric ulceration, hemorrhage, perforation	
Radiation	Acute < 6 months Chronic > 12 months Solitary 0.5- 2 cm ulcers located in the antrum Tolerance : 5 Gy	
Hyperplastic gastropathy	Menetrie's : <i>Typical Menetrier's</i> : protein loss, hypochlorhydria <i>Hyperplastic hypersecretory variant</i> : Increased or normal acid, parietal and chief cell hyperplasia, with or without excessive gastric protein loss <i>Fibrosing variant</i> : Mimics linitis plastic <i>Polypoid variant</i> : Multiple hyperplastic polyps	Gancyclovir in children with CMV Cetuximab?

Squamous cell Ca Vs Adeno

	ESCC	EAC	Cholangiocarcinoma	Gallbladder
AGE/SEX		8M>F	M>F	F>M
RISK FACTORS	Smoking Tobacco Alcohol Vitamin A,C,E deficiency Folic acid, Zn, Se deficiency Hot herbal tea of south America Nitroso compounds Fusarium verticilloides (maize) HPV 16,18 Achalasia (M>F) Lye ingestion Plummer winson syndrome Ptylosis (AD; schr 17) (obesity, NSAIDS protects)	Obesity Tobacco Alcohol (doubtful) GERD Male sex hormones (? H.pylori protects)	PSC (5-15%) Opisthorchis Choledocal cyst 1,4,5 Hepatolithiasis Alcohol HBV, HCV, cirrhosis in intrahepatic Cirrhosis for extrahepatic	Cholelithiasis (>1 cm) Porcelene gallbladder (type 2,3) Adenomatous sessile polyps AUBPD PSC Cholangiocarcinoma Carriers of salmonella typhi and paratyphi Nitrosamines Mustard oil Secondary bile acids LYNCH syndrome IBD Segmental adenomyomatosis
Pathogenesis			Il-6 is signalling axis, JAK-STAT, MAPK, EGFR, COX2 90% adenocarcinoma	TP53, MDM2, KRAS, p16
CLINICAL FEATURES			Pain (intra), jaundice (extra)	Mainly asymptomatic Pain/jaundice
Diagnosis				
Tumor markers			CA 19-9	CEA, CA19-9
Screening protocol				
Scoring systems/ names			Bismuth collate Memorials slon kettring AJCC/UICC	Nevin moran classification
	Ampullary carcinoma	Pancreatic cancer	Gastric carcinoma	Colon cancer
AGE/SEX				Above 40 yrs

	ESCC	EAC	Cholangiocarcinoma	Gallbladder
RISK FACTORS	FAP NF-1 Muirre-torre syndrome Chronic liver fluke infection (not associated with HNPCC)	PRSS-1 mutation (chr 7) TP 17 STK/LKB-maximum RR MLH1 & MSH2 FANC-C & FANC-G (in young) Pallidin PJ syndrome (STK11) FAMMM(TP-16) BRCA-2>1 First degree relative HNPCC Smoking(deletion of GSST-1) Red / processed meat ?? Alcohol Diabetes mellitus* Exenatide and Sitagliptin**	Hp infection Chronic atrophic gastritis Intestinal metaplasia Dysplasia* Adenomatous gastric polyps* Cigarette smoking History of Billroth II* Genetic factors: <ul style="list-style-type: none"> • Family history • FAP fundic gland polyps • HNPCC • P-J syndrome* • Juvenile polyposis* 	HNPCC APC Other familial syndrome History of adenoma / cancer IBD Acromegaly DM/obesity Renal transplant Urinary diversion Red meat Tobacco/Alcohol Cholecystectomy Androgen deprivation
Pathogenesis				Adenoma – carcinoma sequence
CLINICAL FEATURES				Anaemia, constipation
Diagnosis		CA 19-9		Colonoscopy
Tumor markers				CEA,
Screening protocol				Colonoscopy best tool; 10yrly
Scoring systems/ names				
Protective factors				Fiber, resistant starch, folic acid Pyridoxine, calcium, vitamin D, Magnesium, garlic, fish Aspirin, DFMO, HRT, statins, Antioxidants, bisphosphonates, ACEI
Chemotherapy regimen		FOLFIRINOX		

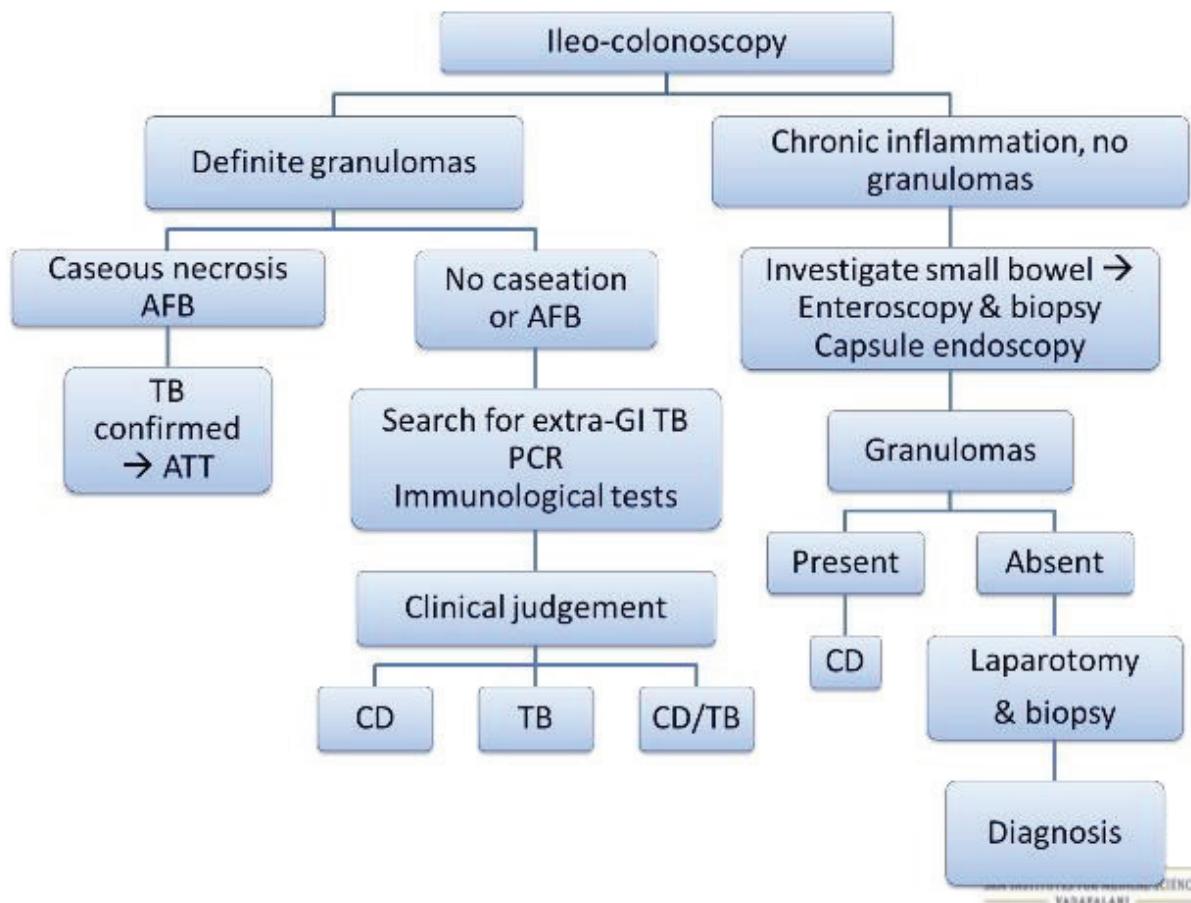
UCTBCD

Tuberculosis Vs Crohns disease

	TB	CD
Duration of illness	<12 months	>12 months
Fever	Evening rise with night sweats - 40-70%	No specific pattern
Family history	TB	CD
Recurrence of disease after surgery	Unlikely	Yes
Peri anal disease	Unlikely	Often present- fissure (25%), fistula (15-35)
Ascites	Exudate, common	Rare, transudate
Extra intestinal Features	Lungs Nodes	Arthropathy PSC
Other clinical	Abdominal pain – MC- 80%- RIF Dull ache/SAIO pain Diarrhea-20%- MAS secondary to ulceration/obstruction/bacterial overgrowth Weight loss	MAS Knee/ankle arthritis
Examination	Lymphadenopathy Cutaneous markers of TB/HIV RIF mass - 25-50% Doughy abdomen - 6-10%	Pyoderma/erythema nodosum/sweet syndrome/Polyarteritis nodosa Episcleritis/scleritis
ASCA	35.2%	45%
Radiology- Barium	Straightening of IC Jn Narrow cecum Nodules Transverse ulcers Fleischners sign: Thick IC valve Sterling sign: rapid transit in ileum String sign: narrow segment before IC valve	Omega sign Longitudinal ulcers Shortening of mesenteric border
Radiology- CECT	Bowel displacement due to nodes Nodes with central necrosis (30%) Absent or asymmetric bowel thickening	Bowel displacement due to fibrofatty change No central necrosis in nodes Concentric bowel wall thickening Comb sign

	TB	CD
Colonoscopy	Superficial well defined ulcers with irregular borders Nodular mucosa Deformed IC valve with ulcers Ileocecal involvement <ul style="list-style-type: none"> ● Skip lesions (10%) ● Segmental (26%) ● Pancolitis (4%) 	Aphthous ulcers Irregular ulcers Longitudinal ulcers Cobblestoning Pseudopolyps Mucosal bridgeing Skip lesions/Strictures Fistulas Spares rectum Predilection of anti mesenteric border
Pathology	AFB smear on Bx - 5-10% AFB culture on Bx - 7-40% AFB culture on surgical Bx - 70% Caseation - 36% >4 granulomas/site - 45% > 400µm size - 51% Confluent granulomas - 42% Band of epitheloid histiocytes - 61%	Single small non caseating granulomas - 26% Mucosal changes distant to granulomas - 65% Endoscopic biopsy - Focal duodenal cryptitis, focal enhanced gastritis
Miscellaneous	Montoux test Concomitant pulmonary lesion-24-28% Plain X Ray Abd-SAIO/calcified node Low SAAG, high protein and pleocytic ascites ADA in Ascitic fluid > 40U/L Laparoscopy- Tubercles all over peritoneum	Vit B12 deficiency Folate def.- drugs Iron def.- ulceration
Organisms	Mycobacterium tuberculosis Mycobacterium bovis MAIC- HIV	Genetic-NOD2- chromosome 16 Immunological Environmental Microbial
Pathogenesis	Swallowing infected sputum Ingestion of infected milk Hematogenous spread from active TB Direct extension from adjacent organ	
Types	<ul style="list-style-type: none"> ● Ulcerative - 20%: Adult, malnourished. Diarrhea MC; Multiple/single transverse ulcers- strictures with healing- adhesion prevent free perforation ● Hypertrophic -10%: Young, well nourished. Mass and dull pain MC; cecum MC site; low virulence of organism and high immunity- no granulomas on Bx ● Ulcerohypertrophic - 70%: MC 	Diarrhea - Mucosal inflammation/SIBO Pain - dull aching/SAIO Weight loss MAS Anorexia

	TB	CD
Points	<p>IC: MC- lymphoid tissue - physiological stasis- fluid absorption - greater contact time</p> <p>Obstruction: inflammatory thickening of bowel with healing fibrosis of transverse ulcers, adhesions and nodal compression</p>	<p>Vienna: Age of diagnosis - A1<40 yr; A2>40 yr</p> <p>Location - L1-ileal, L2- colon, L3-ileocolic (40%), L4- Upper GI</p> <p>Behaviour - B1-not cicatrising/non fistulising B2- stricturing B3- penetrating</p>
Site	Small, Small and large intestine	Small, small and large intestine, mouth in 9%, perianal in 3-36%
DDs	Crohns, Yersinia, Amoebiasis, Carcinoma	
Treatment	ATT Surgery - stricturoplasty/resection - obstruction (20%), perforation (5%), abscess, fistula	Depending on severity 5-ASA Antibiotics- metro/cipro Steroids MTX/AZA/6-MP Biologicals



LIVER

ALD vs NAFLD

■ ALD:

- ▶ Fatty liver seen in 90% heavy drinkers
- ▶ Risk drinking is > 5 drinks/day in males, > 4 drinks / day in females
- ▶ MC physical finding is hepatomegaly in 75%--> jaundice /ascites in 60%
- ▶ Only 1/3rd of fatty liver patients will have LFT abnormalities; AST almost always less than 300-500
- ▶ ALT doesn't rise much coz of deficiency of pridoxal- 5 – phosphate
- ▶ Anemia, thrombocytopenia and leucocytosis ; S.bilirubn is b/n 20-40 mg%
- ▶ S. Albumin is as low as 1.0-1.5 gm, S. ALP range from normal to 1000
- ▶ Oriental flush syndrome → asia → ALDH 22 allele
- ▶ Activation of ADH (main), CYP2E1 (at high doses > 10mM), catalase
- ▶ Adduct MAA (malonaldehyde &acetaldehyde) is unique to alcohol exposure
- ▶ Most specific for ALD → carbohydrate deficient transferring (CDT)
- ▶ **Even more specific is CDT + MCV + GGTP COMBINATION**
- ▶ Binge alcohol alters type I, II, IV histone deacytelase (AADACs) → epigenetics
- ▶ MiRNA 155 modulate LPS induces TNF alpha production
- ▶ CB1, cannabinoid may be involved
- ▶ Increased NADH/NAD + ratio i.e. in reduced state → superoxide generation
- ▶ Hepatic mitochondria lacks catalase (imported glutathione is main antioxidant)
- ▶ ↓ glutathione in liver mitochondria → TNF mediated injury
- ▶ Alcohol cause closure of VDAC, voltage dependent anion channels in mitochondria
- ▶ Megamitochondria as in NAFLD, increase in PAI → microclots → hypoxic injury
- ▶ Endotoxin → TLR 4 → TRIF → priming → TNF - α , IL-6 → inflammation → fibrosis
- ▶ Mi-RNA 212 is increased → decreased ZO-1 protein level → ↑ permeability
- ▶ Increased serum and urine neopterin denotes priming of macrophages, monocyte
- ▶ ↑ **4-hydroxy-nonyal** → ↑ **procollagen & TIMP**
- ▶ Chronic alcohol intake leads to increase in lobular oxygen gradient
- ▶ Zone 3 steatosis, ballooning degeneration, PMN infiltrates, sclerosing hyaline
- ▶ ↑ in hypoxia inducible factor in liver, ↓ in intestine
- ▶ Impaired 26S ubiquitin proteasome pathway → Mallory denk bodies
- ▶ IL8 & IL-18 involved, IL-10 also increased
- ▶ **Around 20-30% remain abstinent @ yr after Rx of addiction**
- ▶ **Specific Rx is needed if → MELD > 18 ; DF>32 ; glassgow score > 9**
- ▶ **Pentoxifylline or better GC given for 4 wks**
- ▶ NAC is of no use, if patient is taking enteral nutrition
- ▶ **Basiliximab & theophylline can overcome steroid resistance (seen in 25%)**
- ▶ Co-factors in progression of ALD → HCV, obesity, smoking
- ▶ Poor outcome of LTx in ALD if → HCV infection +, Smoking ,Redrinking

- ▶ 5 yr mortality in alcoholic cirrhosis → 60-85%
- ▶ 1 yr mortality → 15% no complication, 20% bleed, 30% ascites, 50% both, 60% HE
- ▶ 1 month mortality with DF > 32 is 35-50%
- ▶ MC histological D/D → **Hereditary Hemochromatosis, BCS, NAFLD**

■ **NAFLD:**

- ▶ For diagnosis → alcohol less than 20-40 gm (<3 drinks/day in men 2 in women)
- ▶ Centrilobular steatosis in zone 3
- ▶ Chicken wire fibrosis in zone-3 (pericellular)
- ▶ Portal based inflammation in pediatric NAFLD
- ▶ Megamitochondria , PAS diastase resistant kupffer cells
- ▶ Vaculated nucei in zone 3 hepatocytes seen
- ▶ Activation of CYP2E1 in NAFLD (as in ALD) → oxidative stress
- ▶ Reduced synthesis of Apo-B100 in liver
- ▶ EMT – epithelial mesenchymal transition → ductular reaction & fibrosis
- ▶ Hedgehog activation → fibrosis
- ▶ Defective unfolded protein response → induction of autophagy
- ▶ Endotoxin & LPS → TLR-4 → JNK/NF-kB → TNF-alpha, IL-6, IL-8
- ▶ Elevated ferritin in 20-50% → indicates poor prognosis
- ▶ Bilirubin, PT, Albumin is normal in most patients
- ▶ ↑ LCFA → destabilized lysosomes & ↑ TNF- α →↑PPAR α
- ▶ Biomarkers = CK18, soluble Fas, M65-ELISA, procollagen III,
- ▶ Main cause of death – CVS
- ▶ NAFLD associated with vit D deficiency, colonic adenoma and dysplasia
- ▶ OSAS in NAFLD → in 50%
- ▶ NAFLD in OSAS → 90% of OSAS have NAFLD
- ▶ 2 point improvement in histology is positive Rx response
- ▶ Rx of NAFLD doses :
- ▶ Restrict calories by 500-700
- ▶ Wt loss by 7-10%
- ▶ Vit E – 800-1000 IU
- ▶ Omega 3 fatty acid – 1 gm daily = 10 gm walnut
- ▶ Exercise – aerobic 30-45 min daily for 5 days+ wt. Training 45 min in 3 days
- ▶ 2-3 cups of coffee daily
- ▶ Pioglitazone 30-45mg
- ▶ Pentoxifylline 400 mg daily
- ▶ LTx → donor liver should have < 30% steatosis ; < 60% at worst scenario

■ **NASH** 4th-6th decade, more common in males, late peaking in females

■ Genes with NAFLD:

- ▶ PLPLA-3 → isoleucine to methionine
- ▶ APOC-3 → regulate TG concentration
- ▶ MTP, SOD-2, TNF- alpha, TGF beta
- ▶ LPPR-4 → in adolescents
- ▶ SLC38A8 → in adolescents

Amoebic vs Pyrogenic

Sl. No.	Variable	Amoebic liver Abscess	Pyogenic Liver Abscess
1	Epidemiology	MC extraintestinal manifestation of amoebiasis Travel to endemic/resident of endemic region	MC setting in peritonitis MC visceral abscess
2	Spread	Ascending the portal vein	Ascending the portal vein or direct spread by biliary obstruction or hematogenous spread
3	Age, Gender	40-50 years Men X 7 times > women	Older adults Men = women
4	Predisposing conditions	Alcohol Immunocompromised state Oral-anal sex ASD- Lt → Rt shunt- risk of pulmonary complications	DM/ Prior gall stones/biliary obstruction Prior Hepatobiliary surgery PPI intake/Chronic granulomatous disease Monomicrobial Culture consider: Colon cancer- Klebsiella; Infective endocarditis
5	Incubation period	Median 12 weeks	Depends
6	Clinical Features	2 weeks- RUQ abdominal pain + fever Kehrs sign ± Cough/hiccough Inflammatory Diarrhea - 30% Jaundice - < 10% Tender hepatomegaly - 50%	Fever - 90% Abdominal pain - 75% Jaundice Tender hepatomegaly + Absence does not exclude abscess
7	Complications	Rupture- into chest (30%), peritonitis (7%) IVC/PV thrombosis	Rupture into perihepatic space or into pleural space
8	Labs	Leucocytosis No eosinophilia Elevated SAP in LFT (80%) Abnormal CXR- elevated Rt hemidiaphragm (50%); sympathetic pleural effusion; amoebic empyema Colonoscopy - amoebic ulcers/amoeboma	Leucocytosis - more common LFT Bilirubinemia + Transaminitis Elevated SAP
9	Imaging	USG- cystic intrahepatic cavity MC in right posterior lobe 80% as solitary sub-capsular location Ct- hypoechoic centre with peripheral enhancing rim	USG- hypo/hyperechoic cystic areas with septations/debris CT- PVT/Biliary pathology/ Alternate diagnosis Peripheral rim enhancement- not common MC in Rt lobe - Larger; greater blood flow than left/caudate lobe

Sl. No.	Variable	Amoebic liver Abscess	Pyogenic Liver Abscess
10	Serology + Stool	Positive in 35% in endemic zone Takes 7 days' time for detection Cannot distinguish acute and previous infection Stool - Hemophagocytosis	
11	Drainage	Needle aspiration/pig tail insertion Cyst > 10cm Imminent risk of rupture Left Lobe lesions Lack of response to empiric medicines To exclude alternate diagnosis	Standard of treatment USG/CT/ERCP/Surgical Risk of rupture: Size > 6cm and co - existent cirrhosis Aspirate- purulent confirms diagnosis; Not purulent- cytology for r/o malignancy Pig tail catheter (up to 7 days/minimal drainage)- better than repeated aspiration-unilocular
12	Content	Brown acellular proteinaceous anchovy sauce (necrotic hepatocytes) Microscopy- Trophozoites in < 20% Aspirate- send for grams stain and culture & sensitivity	Microscopy-Grams stain readily diagnose bacterial organisms and PMNs Diagnosis by aspiration and culture (polymicrobial) Blood C/s before antibiotics – 50% Pig tail C/s- Not reliable for choosing antibiotic
13	DDs	1. Echinococcal disease; Multicystic/ daughter cysts + Aspiration not done 2. Malignancy: Usually asymptomatic/Assn with CLD 3. IBD Assn	1. Mycobacterium: Miliary TB/culture is negative- consider atypical 2. <i>Burkholderia/Candida: Neutropenic/ Hematological malignancies</i>
14	Treatment	Tissue agent + Luminal agent (to eliminate cysts) Metro - 500-750mg - TID X 10 days or Tini - 2gm - OD X 5 days + Diloxanide Furoate - 20mg/kg- TID X 10 days	Multiple/ loculated abscesses → percutaneous drainage No response in 7 days/viscous contents/ underlying condition → surgery Ceftriaxone 2g OD + Metro 500mg TID → change by C/s
15	Pregnancy	Chloroquine 600mg BD X 2 days; 300mg OD X 3 weeks + Paromomycin- 30mg/kg X 7 days Caution: Severe amoebic colitis	Antibiotics for 6 weeks Oral tabs- Co-Amoxclav TID/Cipro 500mg BD X 6 weeks + Metro total of 2 weeks
16	Follow up	Serial imaging - not helpful As the lesions can increase in size/number with treatment Antiboma/calcified/anechoic cyst Clinically well/ no scan	Pain Temperature Labs: TC & CRP Serial imaging- If Symps+
17	Mortality-predictors	< 1 % Bilirubin > 3.5mg/dL Albumin < 2 g/dL Encephalopathy Large volume and multiple abscesses	2-12% Need for open surgical drainage Malignancy Anaerobic infection
18	Others	Perineal ulceration- rare- Infants with diapers/ Homosexuality Cerebral amoebiasis - Hematogenous spread	Giant Abscesses - Size > 10cm Mean time for USG resolution of abscess < 10 cm is 16 weeks and > 10cm is 22 weeks after drainage

Embryo Relavent

- Hepatic development = 3-4 wks (FGF and BMP involved) → from endodermal cells of ventral foregut
- Extrahepatic biliary : at the end of 5 wks
- Intrahepatic biliary development - 6 wks, peripheral small portal tracts require an additional 4 wks for developing
- Centrilobular vein and Artery : 8 wks (@ 10th wk first artery in centre is seen ; reach periphery of liver by 15 wks)
- Sinusoids : 5-12 wks of development (cells lose CD 31, CD 34 ; becomes rich in perisinusoidal tenacin)
- Bile canaliculi develop in perinatal and early postnatal period
- Abundant RER and golgi complex forming albumin is earliest marker of nascent hepatocytes
- Developing ducts **in ductal plate produce VEGF, while hepatoblast produce angiopoitin for vessel development**
- Kupffer cells from yolk sac adlater on from bone marrow
- Stellate cells from mesothilia / submesothilial cells from surface ; mesenchymal cells of septum transversum

Hemochromatosis Vs Wilson's Disease

HEMOCHROMATOSIS	WILSON'S DISEASE
HFE on 6p , (HJV gene on 1q) ; AR	13q14; AR
Main defect: Reduced hepcidin function Increased gut iron absorption	Main defect: due to malfunction of ATB7B Copper is not excreted in bile Ceruloplasmin is not synthesized
Pearl's Prussian blue	Timms Sulphide, Rhodamine, Orcein Blue, Victoria Blue, Acid Rubenic <i>Orcein stains/binds copper binding protein</i>
Iron accumulates in zone 1 hepatocytes Sparing of kupffer's cells ; except in : <ul style="list-style-type: none"> ● African iron overload ● Ferroportin - loss of function mutation ● Late stage HFE related HH ● Parenteral iron Rx 	Copper deposits in lysosomes of hepatocytes Kupffer's cells involved in fumant WD
40-50 yrs, male; Variable penetrance in females	3-55 yrs (5- 25 yrs) Classic patient is 6-40 yrs of age
Symptom: Asymptomatic (73%) > Lethargy (25%) > Joint Pain (13%) Sign : Enzymes (33%) > Hepatomegaly (13%) > Pigmentation (5%) Liver, Heart, Joints (II & III MCP involved), Endocrine (except adrenal), Hypogonadism, Hypopituitarism Bronze skin → melanin; grey skin → iron in basal layer Predisposition for LYV bacteria	Hepatic presentation Most commonly in children → hepatomegaly, steatosis, raised enzymes May present as FHF (in 25%) or CLD or isolate splenomegaly , may resemble AIH Acute intravascular hemolysis, renal failure, abdominal malignancies , GB stones In wilsonian ALF→ low AST, ALP normal, S.bilirubin is disproportionately ↑ Neurologic manifestation: 2nd – 3rd decade , most will have hepatic disease and KF ring in 98% 2 patterns are movement disorder comes earlier and rigid dystonia later MC manifestation is dysarthria > tremor, dyscoordination, pseudobulbar, gait Peripheral neuropathy and dysautonomia is rare Seizure is uncommon and intellect isn't impaired Severe neyrologic disese may not resolve after Rx
Does not reverse with treatment: <ul style="list-style-type: none"> ● Advanced cirrhosis ● Arthritis ● Hypogonadism ● DM (but insulin resistance improves) MCC of death : Infection > CVS >HCC	Others: More than 20% of WD patients are purely psychiatric, depression is common KF ring → superior and inferior pole, disappear with Rx like sunflower cataract Fanconi Syndrome : Microscopic Hematuria, Aminoaciduria, Proteinuria Phosphateuria, ↓ H ⁺ Excretion, Nephrolithiasis, Vitamin D Resistant Rickets Rhabdomyolysis Large Jt Arthritis, Osteoporosis, Osteochondroitis Dessicans Osseomuscular Wilson's Common In India Cardiomyopathy, Cardiac Arrhythmias, Sudden Cardiac Death Hypoparathyroidism, Amenorrhea, Testicular Problem Infertility, Repeated Spontaneous Abortions, Pancreatitis

HYPOTHYROIDISM	HYPOPARTHYROIDISM
C282Y, H63D (& other HFE mutations)	ATP7B; R778L, H1069Q (MC; missense mutation)
HFE-HH = TFR1 (type 1) → C282Y/H63D HJV(2A), HAMP(2B), TFR2(3), SLC40A1(4)	D13S314, D13S301, D13S316 → these 3 are sufficient for diagnosis D13S133, D13S137, WND
Mildly elevated transaminases	Disproportionately low levels
HCC increased risk in cirrhotics with HFE-HH	Rare HCC; increased risk of intraabdominal malignancies
Micronodular cirrhosis	Macronodular cirrhosis; steatosis; malory bodies Mitochondrial involvement (tennis racket, increase dense bodies)
Most commonly detected incidentally	Most commonly present with liver symptoms
First test in a patient is transferring saturation f/b genotype	ALP/bilirubin <4 ; AST/ALT > 2.2, transferees are only moderately raised
Iron ↑ 60-180 (180-300) Transferrin saturation ↑ 20-45 (45-100) Ferritin ↑ 20-200 (300-3000 in males) TIBC ↑ 300-360 Marrow sideroblasts ↑ 40-60% RBC protoporphyrin ↑ 30-50 Marrow iron stores ↑ 3+/4+ with typical symptoms is ▲tic Hepatic Iron concentration ↑ 300-1500 (3,000 - 30,000) • Symptomatic = > 10,000 • Fibrosis/ cirrhosis = > 20,000 Hepatic iron index = HIC/Age ↑ Normal = < 1.1 • < 1.9 = secondary overload • >.1.9 = HH	S. ceruloplasmin ↓ 200-350 (0-200; classic is < 50) Total S.copper ↓ 700-1520 (190-640) Basal 24 hrs urinary protein (3 sample) ↑ < 40 (40-10,000; usually ▲ > 100) Liver copper ↑ 20-50 (usually >250; start suspecting @ >70) Non ceruloplasmin copper ↑ < 150 micg/L (>200 micg/L) D-penicillamine urine Cu excretion ↑ to > 1600 micg (but low sensitivity)
Rx : Best is phlebotomy 500 ml blood (200-250 mg iron), Initially once a wk till transf. Saturatn is < 45% & ferritin 50-100 Then once every 2-3 months Alternative is deferoxamine (s/c infusion, 5 days a wk)	CNS manifestations → tetrathiomolybdate + Zn Hepatitis or cirrhosis with mild/ moderate decompensation → trientene + Zn Severe decompensation or ALF/FLF → LTx (chelation not useful) Hepatitis or cirrhosis (without decompensation) → Zn Maintenance, pregnancy, paediatrics, presymptomatics → Zn In pregnancy → Rx is given throughout pregnancy, else decompensation occurs A-tocopherol can be given in severe hepatic decompensation

Copper is bound to metallochaperones inside a cell. In plasma it's bound to albumin and histidine & ceruloplasmin (alpha 2 glycoprotein)

Copper is required for function of :

- Lysyl oxidase
- SOD
- Cytochrome oxidase
- Tyrosinase
- Dopamine beta mono-oxygenase

ATP7B gene : p type ATPase

- 550 types of mutations seen → **most patients are compound heterozygotes**; documentation of one mutation is enough
- Two mutations can be seen in 95%; **MC mutation is missense mutation** (large gene deletions seen with menke's disease)
- H1069Q seen in 35-75% associated with neurological disease and late onset; R778L mutation seen in Chinese
- High throughput sequencing & multiple ligation dependent probe amplification is used
- Sorting intolerant from tolerant score → SIFT to check whether aa substitution affects function
- **Wilson ATPase gene 4.1 kb , mRNA is 8 kb, protein is 1443 aa, 160 kd mass, 6 binding sites, 8 Transmembrane domains**
- **Wilson ATPase found in liver , kidney, brain , lungs, placenta**
- **ATP7B synthesizes ceruloplasmin of blood & helps excreting copper via COMMD1**

Ceruloplasmin : 132 kd, α2- glycoprotein synthesized by ATP7B gene is an acute phase reactant and act as ferroxidase

- Can be falsely high in
 - ▶ Inflammation / ALF
 - ▶ Pregnancy,
 - ▶ Estrogen,
 - ▶ Children,
 - ▶ Assessment By Immunologic Method (Apo + Holo)
- Can be falsely low in :
 - ▶ CLD
 - ▶ Intestinal malabsorption
 - ▶ Nephrotic syndrome
 - ▶ Malnutrition
 - ▶ In 10% of heterozygotes for WD

KF ring (golden brown or greenish yellow) can also be seen in :

- Wilson disease
- PBC / PSC
- Cholestatic syndromes

Non ceruloplasmin bound copper = {Total Serum Copper – Copper Bound to Ceruloplasmin (S. Ceruloplasmin X 3.15)}

- Value in normal person = 15 micg/dL (for copper 1 gm = 63 mols)
- In WD it is > 20 micg/dL = > 200 micg/L

Urinary copper reflects **non ceruloplasmin** bound copper in plasma; thus is increased despite decreased **total** serum copper.

In both HH & WD screening of **all first degree relatives** should be done.

In WD if genetic analysis is not available, **do all other tests** annually starting @ 6 yr of age for next 5-10 yrs

Copper Rich Food : Organ Meat, Shell Fish, Nuts, Chocolates, Mushroom

D-penicillamine mobilizes copper from lysosomes & loosening bound proteins (**not from metallothioneine**); increase urinary copper, D-penicillamine is more potent than trientine & has more toxicity.

Trentene increases urinary copper and also decreases absorption from gut.

Zn increases metallothioneine within enterocytes which permanently bind to Cu and shed with enterocytes, Zn also decreases absorption of Cu from gut .nocupropresis with Zn. Zn is more effective in neurological disease than in liver disease. Zn taken 1 hr before meals.

Tetrathiomolybdate binds serum copper and also decreases its absorption, **removes strongly bound copper from metallothioneine**, its side effects are bone marrow toxicity and hepatotoxicity, can even cause copper deficiency.

Zn may deteriorate hepatic Wilson while **D-Penicillamine** may deteriorate CNS Wilson disease.

Rapid progression of hepatic disease is seen if treatment if WD is stopped, disease also become refractory now.

Hepatitis Virus

	HAV (MCC of viral hepatitis worldwide)	HBV MCC of cirrhosis world wide Prevalence in india à 4%	HCV (20% of all cases of acute hepatitis) MCC of HCC in USA MCC of cirrhosis in USA Prevalence in india à 2%	HDV Satellite virus	HEV MCC of acute viral hepatitis in india MCC of acute liver failure in India
Family/Genus	Picornaviridae/ Hepadnavirus (old enterovirus) ? heparnavirus genus	Hepadnaviridae/ Orthohepadnavirus	Flaviviridae family Hepacivirus genus	Deltaviridae Deltavirus	Hepeviridae
Morphology	27 nm Non enveloped Icosahedral Acid resistant Heat labile Enterohepatic circulation Buoyancy → 1.33-1.34 Sediment coeff – 160 S Dry feces → 4 wks	42 nm (dane particle) Enveloped Icosahedral 22 nm subviral particles 3200 bp in length	50 nm diameter Enveloped E1, E2 form tetramer Fishbone/ Icosahedral	36 nm Nonenveloped Spherical	34 nm Icosahedral
Surface receptor	HAVcr-1 on monkey		E1 , E2 binding on CD 81 NPC1L1 → ezetimib drug CD81/ SR-B1 / CLDN/ occludin		
RNA/DNA	SS linear + sense RNA 7.84 kb RNA	Circular partially dsDNA 3.2 kb	SS linear +strand RNA 9.6 kb	SS circular RNA Negative polarity 1.7 kb	SS linear RNA Positive polarity 7.2 kb
Protein	2227 aa P1- structural; VP 1,2,3,4 P2- A,B,C P3- A, B, C, D		3200 aa		
Reservoir	Bats Rodents Hedgehog Shrews	Ross Goose, Woodchuck, Squirrel, Wooley Monkey, Crane, Heron, Duck Adrenal, testis, colon, ganglia, skin	Chimpanzee	Woodchuck	Deer meat → in japan Wild boar Pigs • Rat, Shrew, Cow, sheep, goat • Swine HEV in India • Shell fish
Epidemiology	Max in children 5-14 yrs Main risk is travel				Max in 15-40 yrs
Total Patients		40 crores	20 crores	5 crore	Population prevalence in india 40%
Cytopathic/Not	Non cytopathic	Non cytopathic	Non cytopathic	Non cytopathic	Non cytopathic
Transmission	Feco-oral → primary route Parenteral Non injection illicit drug MSM & PWID No transplacental spread	Parental Injection Saliva MSM & PWID Transplacental Not seen in stool	Parental Injection Saliva MSM & PWID Transplacental (only 5-6% rate)	Blood Percutaneous Sexual	Feco-oral Not by blood
IP	15-45 days	30-180 days	15-150 days	30-180 days	15-60 days
Chronicity	No chronicity But prolonged or recurrent course in 15%	In 3-5 %	+	+ in 50-90%	Rarely chronic

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Genotype	Human : I, II ,III, VII (4) (AVIAN : IV , V , VI)	A-J (10)	1,2,3,4,5,6 (6) MC in India is 3 MC in Asia is 6	(8)	(4) 1 = Asia, Africa 2 = Mexico, West Africa 3 = Europe, USA 4 = China, Japan
ORF	1	4	1	6	3
Gene Products	P1 + P2 + P3 = 2227 aa P1 → VP1, VP2, VP3, VP4 (VP1 , VP2A & VP2C are responsible for virulence)	HBsAg (PreS1/ PreS2,S) Core & HBeAg X protein Polymerase	C, E1, E2, P7, NS2, NS3, NS4A, NS4B, NS5A, NS5B		
Mutations	In 5' UTR influence severity	Precore → 1896 stop codon Core promoter - 70% (1762 – 1764) Vaccine mutant → 2-3% of vaccines Mutation in HBIG → 50% 'a' epitope → 124-147 10^{13} – 1015 mutations /day 10 million base pair error /day Genetic diversion in genotypes → 8%	5' (mainly) & 3' UTR no mutn E1 & E2 max mutn 1 error for every 10^4 – 10^5 nucleotides Sequence divergence in genotype → 40%		
Pathogenesis		CMI & ABMI CD8 cell mediated lysis			
Acute attack	Depends on age	Mild or severe Only 1/3 rd are symptomatic in acute Ds 1% go for FHF	Mild Very often asymptomatic	Mild or severe	Mild
Peak ALT	800-1000	1000-1500	300-800 (raised in chronic asymptomatic patients) Raised in 50% infected @ any given time	1000-1500 Double peak in AST	800-1000 Associated with marked elevations of AST/ALT/GGTP/ALP
Histo		Ground glass hepatocytes	Steatosis	Can be used in diagnosis HDAG detected on immunohisto staining	

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Diagnosis	IgM anti HAV upto 4 months IgG for lifetime HAV RNA upto 21 days	HBsAg, IgM Anti HBC	Anti HCV → if + do HCV RNA to confirm HCV RNA → if + confirms infection	HD Ag – confused by AB IgM anti HDV (1st test) HDV RNA(earliest) RT-PCR is most sensitive Multimeric IgM persists in chronic Ds - indicates severe disease	IgM anti HEV → last for 4-5 months HEV RNA in stool / serum by RTPCR Demo of virus specific host response
Treatment	Symptomatic <i>Ig for PEP (0.02 mL/kg) in 2 wks</i>	IFN, Lami/telbivudine, entecavir tenofovir, adefovir	Pro – PEG – Ri Previrs, Asvirs , Buvirs (HCV polymerase inhibitor) <i>Only IFN in acute HCV</i>	Cure > 90% can be achieved IFN-α (clearance is 20% in 1 yr) Lorafarnib	Symptomatic Ribavirin & PEG interferon α2a,α2b for 3-12 months can be tried in chronic HEV infection
Vaccines	HM175- HAVRIX for > 1yr age CR326- VAQTA for > 1 yr age Formaline inactivated Alum adjunct 2 doses ; 6 months apart TWINRIX – for age > 18 yrs PEP → single dose within 2 wks MC S/E of vaccine → soreness HAV vaccine for : LTx, HIV, CLD, MSM, PWID, clotting factor disorders	Engerix B Thiomersal preservative Aluminium hydroxide adj. I/M deltoid or anterior thigh Doses 0,1,6 Passive : Ig – 0.06 ml/kg	No vaccine No PEP But post exposure Rx can be given*	Vaccination against HBV confers protection against HDV Simultaneous infection with woodchuck hepatitis virus (WHV) can prevent	Used for : <ul style="list-style-type: none">• Travellers to endemic• Pregnant in endemics• CLD in endemic areas Vaccine do not decrease shedding ORF2 vaccine in Nepal : <ul style="list-style-type: none">• Alum adjunct used• 0, 1, 6 months• 95.5% efficacy Chinese vaccine using ORF-2 : <ul style="list-style-type: none">• In E.Coli• 23 nm VLPs• Efficacy 100%

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Extraintestinal Manifestations	Evanescence Rash → 14% Arthralgia → lower limb Glomerulonephritis Arthritis Leukocytoclastic Vasculitis Seen in legs & butts Cryoglobulinemia (IgM HAV) Necrolysis Fatal Myocarditis Renal Failure Optic Neuritis/ Polyneuritis Transverse Myelitis Cholecystitis Aplastic Anemia Pure Red Cell Aplasia Thrombocytopenia	Arthritis/dermatitis / vasculitis Polyarteritis nodosa(1&30%) Glomerulonephritis • Membranous > MPGN • MC mode : nephritic Cryoglobulinemia II → PM III → PP	Proved: Autoimmune thyroiditis B cell NHL LP Mixed cryoglobulinemia (PM/PP) Monoclonal gammopathy PCT Possible: Chronic polyarthritis DM Idiopathic pulmonary fibrosis Non cryoglobulinemic nephropathies Sicca syndrome Thyroid cancer RCC Vitiligo Fatigue / Arthralgia Arthritis (RF positive) Purpura Raynaud's Phenomenon , Vasculitis (low complement levels) Peripheral Neuropathy, Nephropathy		

	HAV (MCC of viral hepatitis worldwide)	HBV MCC of cirrhosis world wide Prevalence in india à 4%	HCV (20% of all cases of acute hepatitis) MCC of HCC in USA MCC of cirrhosis in USA Prevalence in india à 2%	HDV Satellite virus	HEV MCC of acute viral hepatitis in india MCC of acute liver failure in India
Notes	<p>10-20% require hospitalization Occasional profound cholestasis seen Morbidity higher in adults Liver dysfn in adults MC symp → jaundice 68 In prodrome → fever 85% Dark urine precede in 90% < 2 yr → asymptomatic > 5 yr → 80% symptomatic 10-15% have relapsing Disease RUQ tender in 85% Spleen in 15% Compleat recovery by 6 mo Mortality → ABC <ul style="list-style-type: none"> • Albumin < 2.5 • Bilirubin > 9.6 • Creat > 2 – best predictor Mortality high in > 75 male FHF rarely occur after 4 wk HAV is 10% of FHF india If low RNA level is found → LTx</p> <p>Increased mortality in:</p> <ul style="list-style-type: none"> • Males • >.75 yrs age • Non white • CLD • HIV • Albumin < 2.5 • Bilirubin > 9.6 • Creatinine > 2 	<p>Breast feeding is safe But breastfeeding on Rx → avoided 15-40% carriers will have sequelae Indian risk 20-60% Infectivity : HBV>HCV>HIV HBV not seen in stool Survival in ALF → 20% ALF survival with LTx → 50-60%</p>	<p>Breast feeding is safe Virus bind to VLDL, LDL, Ig, free virions 5' UTR is internal ribosomal entry site allows cap independent translation First 21 aa of E2 form HVR E1, E2 attach CD81 for early entry E2 also bind SRB-1 for entry in cells Claudin / occludin needed for later entry Heparin sulphated proteoglycan needed T1/2 of virus is 45 mins Daily 1011 viruses are produced MC in india is genotype 3, in asia is 6 Highest prevalence in 55-64 age grp Prevalence of HCv in PWID → 60-90% Anti HCV seroconversion rate is 0.3-4% 1/1,90,000 sexual contacts Maternal antibodies persist for 18 months Fibrosing cholestatic hepatitis (30 million) RNA detectable in 7-21 days ALT rises in 4-12 wks Majority are asymptomatic Symptoms if at all arise in 2-12 wks MC symptom is jaundice in 50-80% Anti HCV takes 5-20 yrs to disapear Real time HCV RNA test detect 10 IU For genotype PCR for NS5B & E1 is done Cirrhosis @ 65 yrs irrespective if infn age Survival in compensated cirrhosis : <ul style="list-style-type: none"> • 5 yr → 80-90% • 10 yr → 80% SVR is end point of Rx RVR is associated with 80-90% SVR Rx in acute HCV infection → after 4-8 wks</p>	<p>Is a satellite virus Least common cause of chronic hepatitis but most severe form of hepatitis Intra-RNA basepairing Autocatalytic RNA seen RNA editing seen-unique Smallest genome Help by HBV is HBsAg Host's DNA dependent RNA polymerase is used HDAgL need prenylation to bind HBsAg HDAg-L inhibits replication HDAg-S increases replien HDV-3 + HBV-F is bad Autoantibodies – <ul style="list-style-type: none"> • Anti-LKM • Thymocyte • Nuclear laminin C 70% chronicity in supinfn HDV inhibits HBV & HCV</p>	<p>Prolong cholestasis seen in 60% Secondary attack rate = 0.7% In stool → from 1 wk before, till 2 wk after Prevalence in india = 40% Viremia = 2 wks Fecal shedding = 4 wks HBeAg within 7 days Case fatality → 0.07-0.6 % Case fatality in pregnancy → 25% Cholestatic picture Mild leukopenia Relative lymphocytosis Hepatosplenomegaly GB wall edema + Anicteric hepatitis common in children Mortality in pregnancy → 5-25% FHF in pregnancy → 22%</p>

	HAV (MCC of viral hepatitis worldwide)	HBV MCC of cirrhosis world wide Prevalence in india à 4%	HCV (20% of all cases of acute hepatitis) MCC of HCC in USA MCC of cirrhosis in USA Prevalence in india à 2%	HDV Satellite virus	HEV MCC of acute viral hepatitis in india MCC of acute liver failure in India
		IFN response → A>B≥C>D HBeAg seroconversion → B>C Core mutation & HCC → C IFN induced flares → C Highest mortality → F	Best response to Rx → 2 Response → 2 ≥ 3 > 4 > 1b > 1a Accelerated Ds progression → genotype 3 Increased mortality → genotype 3 Steatosis & NASH → genotype 3 Increased flares → genotype 2 DM & insulin resistance → genotype 1&4 Best SVR-RVR > cEVR > pEVR > no EVR		Most common form → 1&2 Autochthonous transmission → 3 (rarely 4) India → 1 & 4 Rainy season & epidemic → 1 & 2 Spring/ Summer & sporadic → 3 & 4 Healthy, young males → 1,2 Old, comorbid males → 3, 4 Alcoholics → 3 Chronicity → 3 & compromised Cirrhosis → 3 Severe Ds during pregnancy → 1&2 Zoonotic transmission in 3 & 4 From pigs to humans → 3&4 Subclinical infection → 3 Neurological manifestations → 3

PANCREAS

DRUGS CAUSING ACUTE PANCREATITIS

A	Acetaminophen, Alpha Methldopa, 5-ASA, Azathioprine, L-Asparginine
B	Benazepril, Benzafibrate
C	Cannabis, Captopril, Carbimazole, Cimetidine, Clozapine, Codeine, Cytosine Arabinoside
D	Dapsone, Didanosine, Dexamethasone
E	Enalapril, Erythromycin, Estrogen
F	Fluvastatin, Furosemide
G	Glucocorticoides
H	Hydrochlorthiazide, Hydrocortisone
I	Ifosfamide, INF-Alpha, Isoniazide
L	Lamivudine, Lisinopril, Losartan
M	Meglumine, 6-MP, Methimazole, Metronidazole
N	Nelfinavir, Norethindrone
P	Pentamidine, Procainamide, Pravastatin
R	Rifampin
S	Simvastatin, Sulfa Drugs, Stibogluconate, Sulindac
T	Tetracycline, Trimethoprim(Co-Trimox)
V	Valproate
Z	Zalcitabine

PANCREATITIS DUE TO HYPERSENSITIVITY (MAT)	
M	Metronidazole, 6-MP
A	Azathioprine, ASA
T	Tetracyclin
DUE TO TOXIC METABOLIC ACCUMULATION (DiVa TITs)	
Di	Didanosine
Va	Valproate
T	Thiazide
I	Isotretinoin
Ts	Tamoxifen

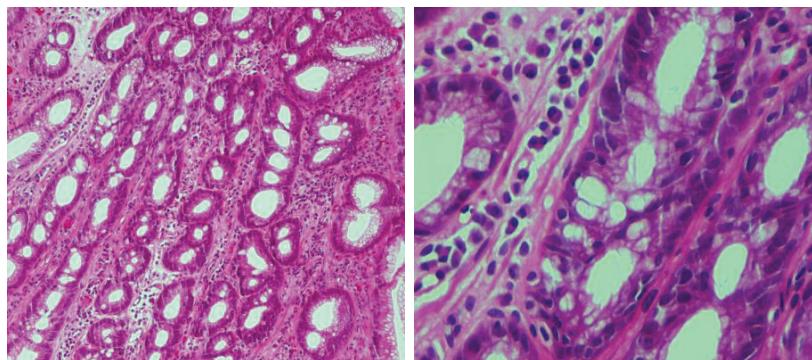
Small Cell Tumors

	Insulinoma	Gastrinoma ZES by ectopic secretion	Glucagonoma	VIPoma	Somatostatinoma	GRFoma	PPoma
Age	20-75 yrs Rare in adolescents	41 yrs	50-70 yrs Rare in adolescents	40-50 yrs	40-60 yrs	40 yrs	40-60 yrs
Sex	Female	Male	Female	Female	Female or equal	Female	Equal
Location	98 % in pancreas 1:01:01 D1>D2>D3>D4 Pancreas 1:1:2 60-90% in triangle	MC site: duodenum D1>D2>D3>D4 Pancreas 1:1:2 60-90% in triangle	97% in pancreas Mostly in tail	80-90% in pancreas Mostly in tail	45-75% in pancreas 14:02:05 MC- panc. Head II MC- D2	50% in lung 30 % in pancreas Mostly in tail Pancreatic tumors are multiple	60% in pancreatic head
Numbers	Solitary	Duodenal – multiple Pancreatic – single	Solitary	Solitary	Solitary	Solitary (70%)	Solitary
Size	Small	Duodenal – small Pancreatic – large	Large (5-10 cm)	Large	1.5 – 10 cm Pancreatic → larger Duodenal → small	Large (>6 cm)	Large
Character	Encapsulated Firm Highly vascular	Mets MC in pancreatic Increased MAO & BAO Large gastric folds Aggressive (25%) Non aggressive (75%) P.Ulcers are Hp negative P.Ulcers are Hp negative	No ketonemia Food aversion (GLP1) No mitotic figure No nuclear atypia 50-90% mets @ Δ	Mets @ Δ mitosis uncommon ganglioneuroma and ganglioneuroblastoma in children and 5% adults (less malignant)	Mets MC in pancreatic Well differentiated Fibrous septation Duod. → psammoma Duod. → pure Pancreas → mixed S-28 form mainly	Mets to LN in 50% (no relation with size) Releases GH-RH, GH, IGF-1	
Nature	Benign (5-16% malignant)	Malignant in 60-90% (mets to liver/ L.N.)	Malignant (50-80%) (mets to liver/ L.N.)	Malignant (30-80%)	Malignant (45-90%) (mets to liver/ L.N.)	30% malignant	60% malignant
Features	Hypoglycaemia during fasting & exertion, Neuroglycopenia (MC) Obesity Whipple's triad	Pain > diarrhoea > GERD Duodenal ulcer in 80% Ulcer complicatn in 30% 25% associated - MEN1 10-50% ass. H.Pylori	Migratory Nec. Eryt.* Dermatitis I to come DM Weight loss Diarrhoea (12%) V. Thromboembolism Hypoaminoacidemia Hypocholesterolemia Anaemia (↓ synthesis) EFA deficiency Glossitis, Stomatitis Dystrophic nails	Watery diarrhoea (MC) (episodic, > 3L) Hypokalemia (<2.5) Hyochlorhydria Achlorhdria Hypercalcemia Hypomagnesemia Hypoglycaemia Wt. Loss is common Flushing No steatorrhea	DM (MC in pancreatic) GB disease (MC in D) Steatorrhoea Diarrhea Weight loss Hypochlorhydria >98% asymptomatic Duodenal ass. NF-1	Acromegaly Hyperprolactemia 33% hv MEN-1 40% hv cushing 40% hv ZES Feature due to other hormones seen	Abdominal pain (MC) Jaundice Wt. Loss Mass 20% asymptomatic
Diagnosis	Whipple's triad 72 hr fasting test Insulin:glucose > 0.3 Proinsulin > 22%	Fasting S. Gastrin (1-10X) Secretin test >120 pg/ml ↑ BAO > 15 meq/L or > 5 Glucagon provocation !!!	P.Glucagon >1000pg (mean = 2100)	Fasting VIP levels (while having diarrhea) Intestinal perfusion studies !!!	Incidental ↑ somatostatin EUS with Bx		

	Insulinoma	Gastrinoma ZES by ectopic secretion	Glucagonoma	VIPoma	Somatostatinoma	GRFoma	PPoma
Treatment	Diazoxide Octreotide (LAR) Everolimus (mTOR) Sx resection if possible	PPI (reduce BAO to < 10) Sx if no* mets /no* MEN1 Sx in MEN1 if > 2cm	Octreotide (DM doesn't respond) Sx resection Debulking if mets +	5 L fluid 350 mEq K+ / day Mostly surgical, Octreotide	OHA Octreotide !!!! Surgery Endoscopic if <1 cm Laparotomy : 1-2 cm Whipple's : >2 cm	Octreotide	
Notes	Less SST receptors Malignant are larger Mets to liver,nodes Proinsulin # is 90%	Hypergastrinemia also seen in ovarian cancer ; Pancreatic tumor (> 3 cm) metastasize to liver; MEN1 has multiple small (< 2 cm) duodenal tumors ; Duodenal tumors are smaller Monitoring B12 during Rx	Mahvash disease : → Multiple tumors → P86S mutation	VIP is exclusively found in VIPoma	# of somatostatinoma in GI-NET is more than in p-NET DM is mild in most Somatostatinomas in: → NF-1 → MEN-1 → VHL		

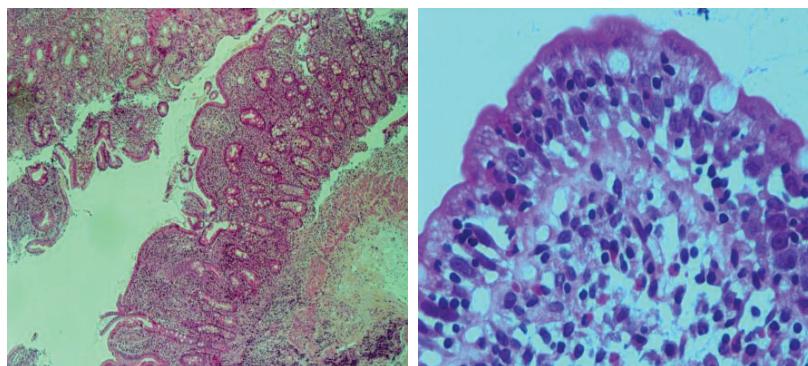
PATHOLOGY

Case 1: 48 year female, chronic history of heartburn, Endoscopy : salmon colored mucosal extension proximal to GE junction.

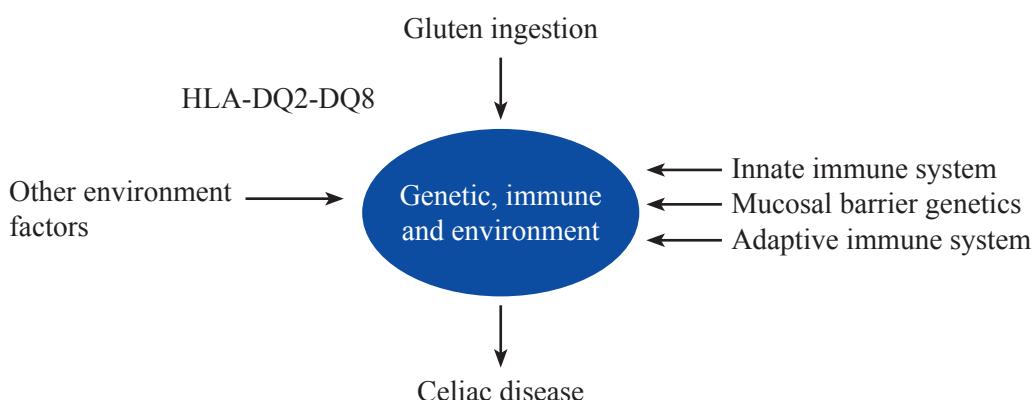


- Barretts esophagus is characterised by intestinal metaplasia where esophageal squamous epithelium is replaced by intestinal type columnar cells. The gastro esophageal junction is junction of squamous and glandular mucosa. Chronic irritation causes metaplasia into a more robust mucosa to deal with the injury. Presence of goblet cells at the junction is pathognomonic, see arrow. Diagnosis requires both endoscopic and biopsy confirmation.
- Barretts esophagus columnar epithelium has goblet cells which secrete acidic mucus with pH<2.5 and alcian blue positive.

Case 2: 26 year male, on and off diarrhea with weight loss for three months. Labs- low iron, Vitamin B12. Deficient. Endoscopy- scalloping of duodenal folds.



- Gluten sensitive enteropathy/celiac sprue: Immune mediated- triggered by gluten containing foods (BROW- barley, rye, oat, wheat) in genetically predisposed individuals.



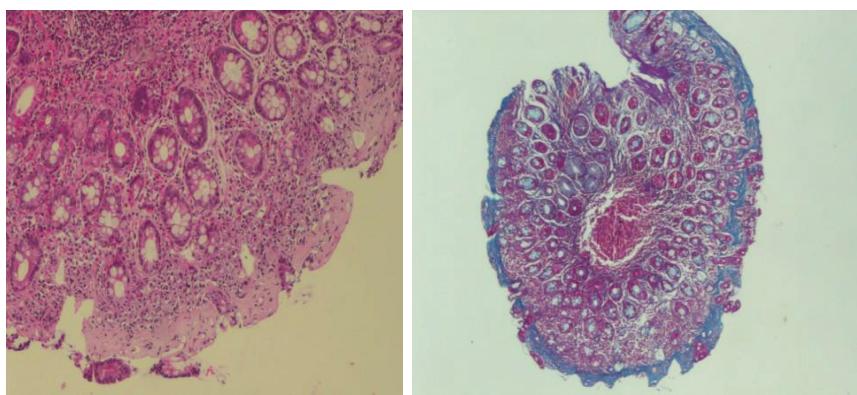
- Celiac disease is associated with T1DM, thyroiditis, sjogrens syndrome, IgA nephropathy and neurological disorders. Dermatitis herpetiformis, lymphocytic gastritis/colitis, increased risk of enteropathy associated t cell lymphoma, small bowel adenocarcinoma.

- Morphology:** Modified marsh categorisation

Marsh Type	IEL / 100 enterocytes - duodenum	Crypt hyperplasia	Villi
0	<30	Normal	Normal
1	>40	Normal	Normal
2	>30	Increased	Normal
3a	>30	Increased	Mild atrophy
3b	<30	Increased	Marked atrophy
3c	>30	Increased	Complete atrophy

- Atrophic villi, crypt hyperplasia, overall mucosal thickness remains the same, associated with intra epithelial CD8 T cells, chronic inflammation in lamina propria, severity is greatest in proximal intestine.
- Cryptitis is not seen in celiac disease. Cryptitis is seen in IBD, infectious colitis, diverticular disease and radiation colitis.
- Most sensitive and most specific serologic test for diagnosis is IgA.

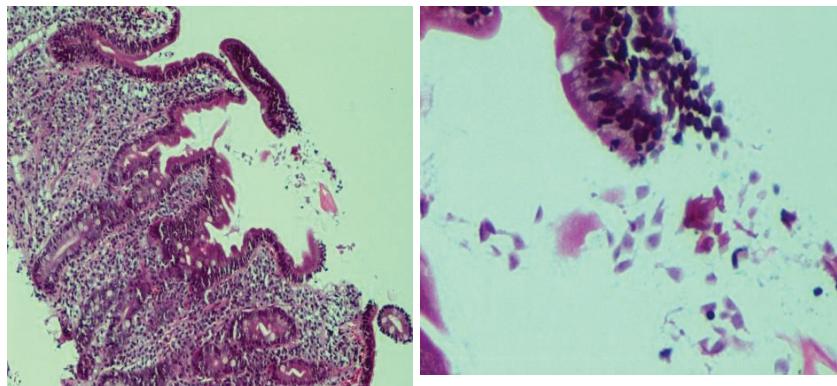
Case 3: 70 year male with massive watery diarrhea and weight loss for 6months. Labs: Microcytic anemia. Endoscopy: diffuse edema of duodenal folds with granularity



Collagenous sprue: Loss of villi with a pink band below the mucosa. Stains blue with confirmatory histochemical stains

Lymphocytic colitis is characterised by prominent IELs without band like collagen and associated with autoimmune diseases and celiac sprue

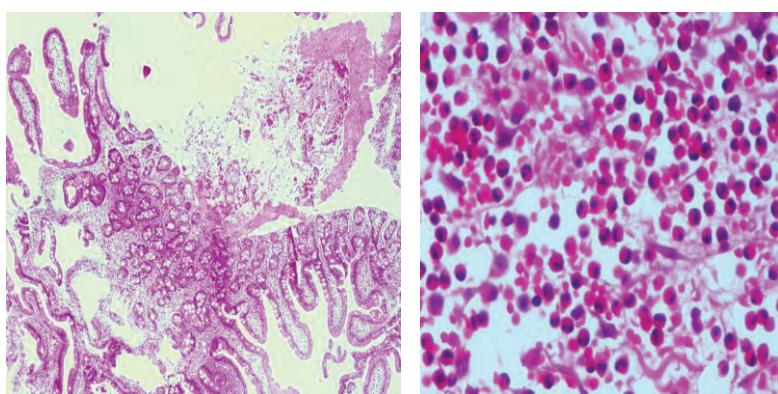
Case 4: 28 male, nausea and vomiting. Labs normal. Endoscopy normal



Giardiasis:

- Flagellated protozoan.
- MC pathogenic parasitic infection in humans.
- Giardia cysts are ingested from fecal contaminated water or food.
- Duodenal trophozoites shows characteristic pear/sickle shaped and binucleated morphology.
- There is no tissue invasion but secretes products that damage the microvillus brush border and causes malabsorption.
- Secretory IgA and mucosal IL-6 are important for clearance- immunocompromised individuals are severely affected

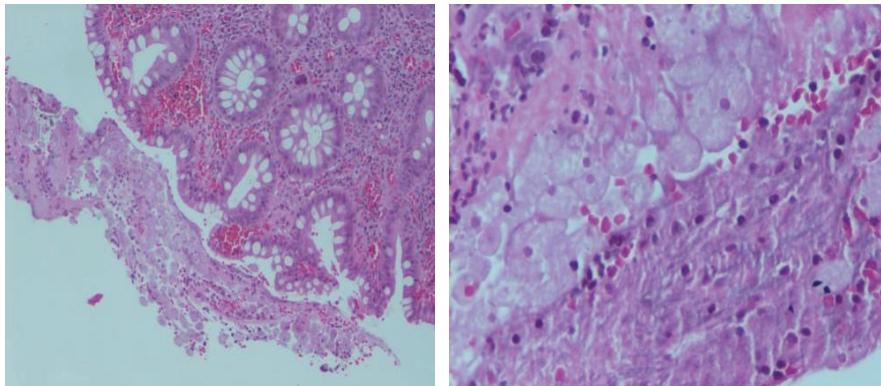
Case 5: 37 year male with pain abdomen. Endoscopy showed erosions in D2



Eosinophilic enteritis:

- Infiltration by eosinophils, clusters of more than 50 cells per HPF.
- Recognized by its bright orange color

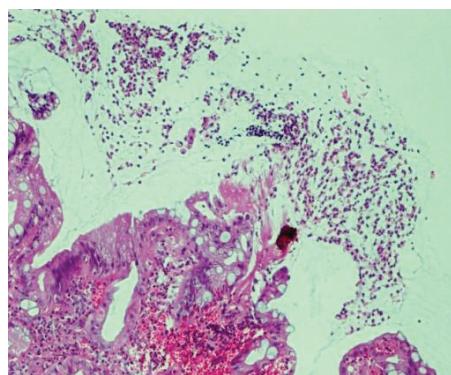
Case 6: 38 year female, abdominal cramping pain, bloody diarrhea for 4 weeks. Labs- leucocytosis. Colonoscopy- ulcers in ascending colon.



Amoebiasis:

- Pale ovoid organisms, stick on to mucosa in sheets
- Recognized by engulfed RBC, the orange dot within
- *E. histolytica*. MC site- cecum
- Ulcers are seen upto mucosa and submucosa only. It never reaches M.propria.
- Flask shaped ulcers- narrow neck and broad base- characteristic
- Mixture of hemorrhage and necrotic debris → anchovy sauce pus is noted in amoebic liver abscess.

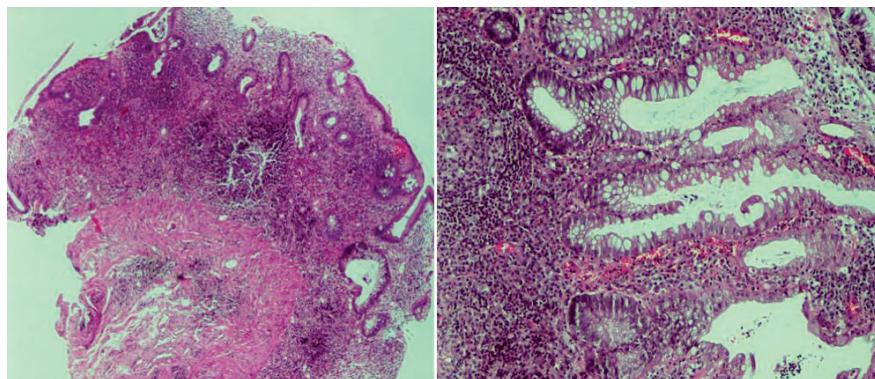
Case 7: 60 y female. Long standing ingestion of antibiotics presented with watery diarrhea and cramps. Labs leucocytosis. Colonoscopy showed white exudate over rectal mucosa.



Pseudomembranous colitis:

- Mushroom shaped or volcano shaped ulcers (bit of imagination needed)
- History is helpful to look for the peculiar shaped ulcers
- Antibiotic associated diarrhea
- Characterised by formation of adherent inflammatory pseudomembranes over mucosal injury sites
- Toxin production by *C.difficile*
- Can be caused by *salmonella*, *C.perfringens*, *S.aureus*
- Pseudomembrane is not specific and can be seen in severe mucosal injury- ischemia/necrotising infections.

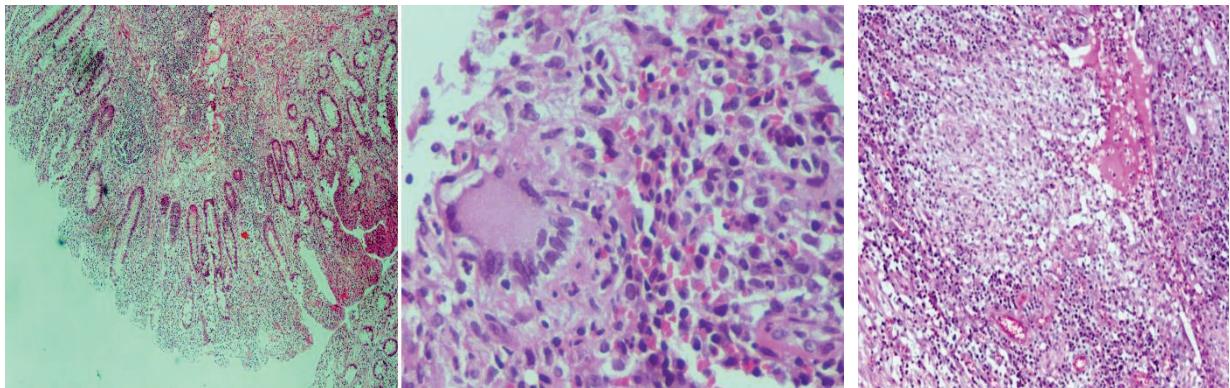
Case 8: 31 year male, bloody diarrhea. Colonoscopy diffuse ulceration and loss of normal vascular pattern in rectum



Ulcerative colitis:

- Note loss of glands, most of the biopsy composed of inflammatory cells
- Crypt distortion, see arrow
- Mucosal or submucosal involvement
- Crypt abscess with non specific acute and chronic inflammatory cells

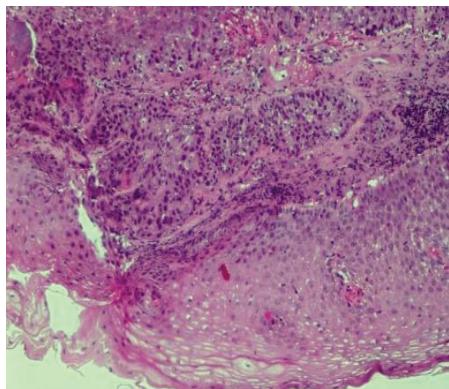
Case 9: 42 year male, Perianal pain and bleeding PR, Anal complex fistula present, Colonoscopy : deep ulcers and pseudopolyps more prominent in right colon, biopsy from IC valve



Crohns disease:

- IBD, with classical loss of architecture and if lucky granulomas
- Isolated IC region involvement, difficult to distinguish from TB, in absence of microbiological studies
- Mucosal inflammation and ulceration with intraepithelial neutrophils and crypt abscesses
- Transmural non caseating granuloma

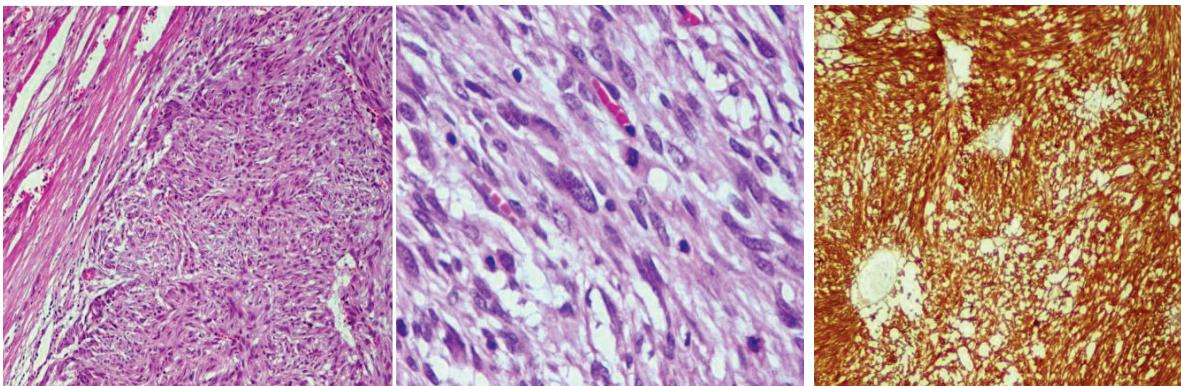
Case 10: 48 year female, Gradual dysphagia, Endoscopy- Circumferential growth, scope not negotiable



Squamous cell carcinoma:

- Atypical (more blue than pink) with irregular patterns infiltrating below the mucosal surface

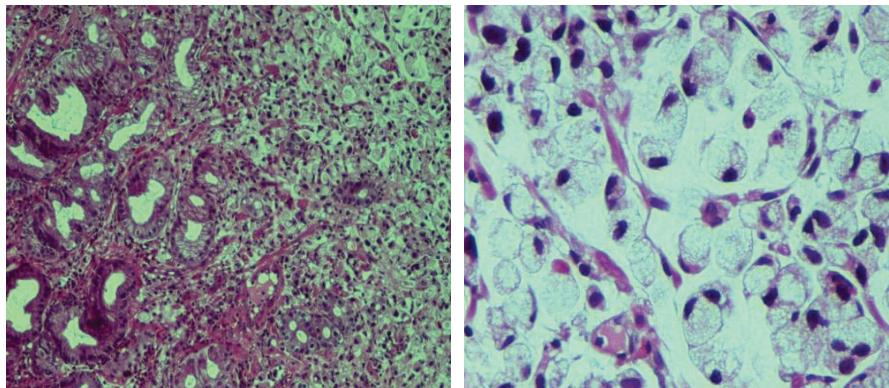
Case 11: 54 year male history of abdominal pain for few months. Endoscopy umblicated sub mucosal lesion in stomach



Gastrointestinal stromal tumour:

- Spindle cell lesion
- Prognosis: Tumor size (recurrence or metastasis are rare when tumors are <5cm and common when more than 10cm), Mitotic index (more than 10 per high power field), location (gastric GIST are less aggressive than other GIST), increased number of chromosomal alterations like loss/deletion of chromosome 9,14 and 22
- Confirmatory CD117 IHC
- GISTs arise from interstitial cells of cajal- pacemakers of gut peristalsis in muscularis propria
- App. 80% of GISTs contain c-KIT oncogenic mutation. 8% have platelet derived growth factor receptor α mutation.
- Best and most specific marker for GIST is DOG-1 (designed only for GIST). DOG-1 can detect metastasis also.
- Tumors are classified as : Epitheloid- MC type of GIST in stomach and spindle cell type- over all MC type of GIST

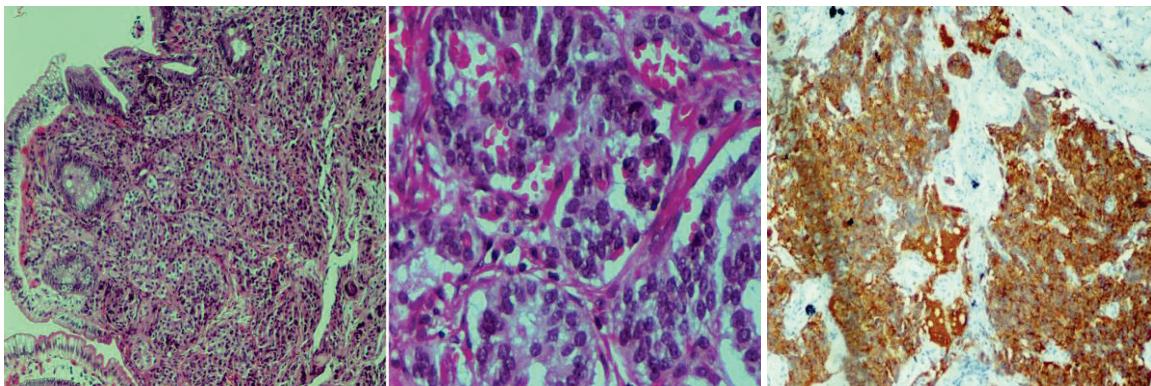
Case 12: 26 year male with anemia and weight loss. Endoscopy showed ulcerated lesion in antrum



Signet ring adenocarcinoma:

- Diffuse population of pale cells with eccentrically placed nuclei due to large mucin filled vacuoles
- Most easily missed cancer in pathology

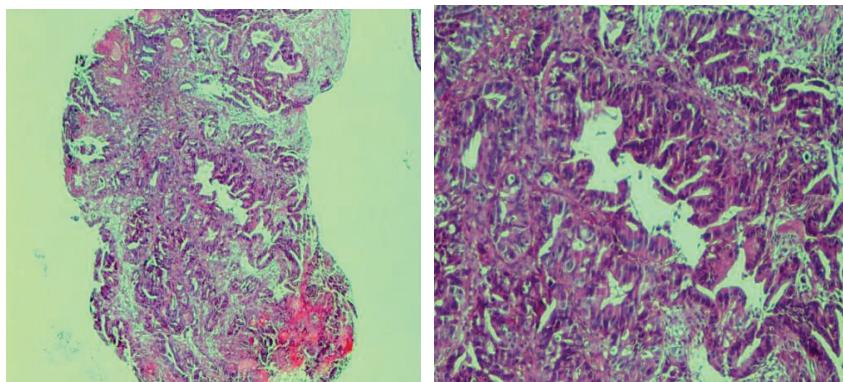
Case 13: 40 year male with abdominal pain and diarrhea. Endoscopy showed a sub mucosal lesion in the D1



Neuroendocrine tumor:

- Packets of small cell in the mucosa or sub mucosa
- Prognosticated by size, mitosis and KI67
- Confirmed by positive synaptophysin, chromogranin
- Most important: is the primary site of the tumor
- Foregut carcinoid: Esophagus, stomach and duodenum- rarely metastatize. Cured by resection
- Mid gut carcinoid: Jejunum and ileum- multiple and aggressive
- Hind gut tumors: appendix and colon- only found incidentally

Case 14: 65 Male, bleeding PR. Colonoscopy showed circumferential growth in sigmoid colon



Adenocarcinoma:

- Haphazard proliferation of glands, more blue than pink
- APC- key negative regulator of β catenin pathway
- Microsatellite instability (MSI) is associated with defects in DNA mismatch repair
- Late K RAS and p 53 mutations promote growth and prevent apoptosis

STAINS USED

Hepatitis B → OVA	Orcein Victoria blue Aldehyde fuscin
Cu ⁺⁺ → TROVA	Timms sulphide Rhodamine Orcein Victoria blue Acid (rubenic)
Glycogen (diastase breaks down glycogen)	PAS
Neutral gastric mucin	PAS
Acidic goblet mucin	Methylene blue Alcian blue
Fe ⁺⁺	Pearl's Prussian blue
Collagen	Masson's trichrome – blue colour Reticulin – gray colour Aniline blue Sirius red
Reticulin (collagen 3)	Masson's trichrome – blue colour Reticulin – gray colour Sirius red
Liver	Masson's trichrome
Collagen for fibrosis (quantitive)	Suramine red Acridine blue
Lipid	Oil red O Sudan fat II, III, IV, Black
Hp	Giemsa Silver Genta H/E Warthin starry stains Specific immune stains
Fungal stains	Gomori methamine silver PAS / diastase stain H&E stain
Treponema	Warthin starry Modified steiner silver impregnation
Nissl's granules of neurons	Cresyl violet
Masson's trichrome (for collagen 1)	Most commonly used for liver fibrosis Collagen is blue, hepatocyte is red
Reticulin (for collagen 3)	Stains reticulin (collagen 3) as gray

RADIOLOGY

AIDS Cholangiopathy

- The organism most closely associated with AIDS cholangiopathy is *Cryptosporidium parvum*; other pathogens that have been identified include *Microsporidium*, *cytomegalovirus (CMV)*, and *Cyclospora cayetanensis*.
- Involvement of the large intrahepatic ducts is usually associated with *C. parvum* and CMV infection
- AIDS cholangiopathy is usually seen in patients with a CD4 count well below 100/mm³
- Affected patients typically present with right upper quadrant and epigastric pain and diarrhea; fever and jaundice are less common, occurring in 10 to 20 percent of patients.
- The severity of the abdominal pain varies with the biliary tract lesion. Severe abdominal pain is indicative of papillary stenosis
- The diarrhea in AIDS cholangiopathy is due to small bowel involvement with the infectious agent and may be the initial presenting feature.

Laboratory studies: Liver function tests in AIDS cholangiopathy are usually indicative of cholestasis.

- Serum gammaglutamyl transpeptidase was persistently elevated in over 90 percent
- Serum alkaline phosphatase was elevated in 75 percent with a mean level of 700 to 800 int. unit/L
- Mild increases in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were common
- Jaundice, when present, was usually mild, with total bilirubin less than twice the upper limit of normal

DIAGNOSIS : The diagnosis of AIDS cholangiopathy is usually made by endoscopic retrograde cholangiopancreatography (ERCP).

- Ultrasound is the most cost-effective initial study, with a sensitivity for cholangitis ranging from 75 to 97 percent and specificity of up to 100 percent
- Thus, ERCP is the recommended procedure in the patient with suspected AIDS cholangiopathy and a positive ultrasound. It allows confirmation of the diagnosis and the performance of therapeutic procedures, if indicated.
- Likelihood of finding anatomic abnormalities at ERCP in the patient with a negative ultrasound is small
- Cholangiography reveals one of four patterns :
 - Combined papillary stenosis and sclerosing cholangitis – 50 to 60 percent
 - Combined intrahepatic and extrahepatic sclerosing cholangitis without papillary stenosis – 20 percent or less
 - Papillary stenosis alone – 10 percent
 - Long extrahepatic bile duct stricture with or without intrahepatic sclerosing cholangitis is unusual
- The combination of papillary stenosis and intrahepatic ductal strictures appears relatively unique to AIDS cholangiopathy

TREATMENT—Although infection is the most common cause of AIDS cholangiopathy, medical treatment directed against *C. parvum*, Microsporidium, or CMV does not influence symptoms or cholangiographic abnormalities. The therapy of AIDS cholangiopathy is primarily endoscopic, and the approach varies with the anatomic abnormality.

- In patients who have abdominal pain, cholangitis, or jaundice associated with papillary stenosis, we suggest sphincterotomy. Sphincterotomy does not help patients with sclerosing cholangitis in the absence of papillary stenosis.
- In patients with an isolated or dominant common bile duct stricture we suggest endoscopic stenting.
- Treatment options for patients with intrahepatic or extrahepatic sclerosing cholangitis are limited. We suggest giving ursodeoxycholic acid (UDCA) in a dose 300 mg three times daily, primarily in patients who have intrahepatic ductal disease and markedly elevated liver function tests.
- Because cholangiopathy typically occurs in patients with advanced AIDS (CD4 cell count below 100/mm³) the mean survival has been only 7 to 12 months. The survival of patients is not affected by cholangiopathy, since the mortality rate is primarily determined by the natural history of AIDS.

PTBD

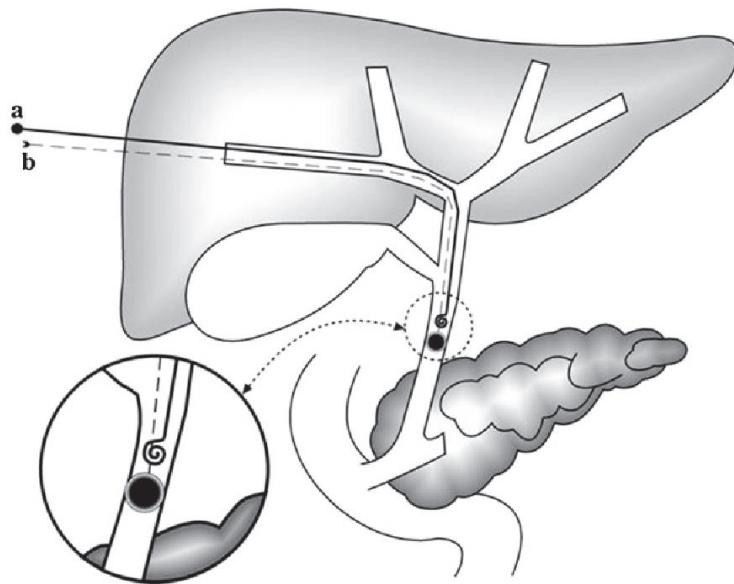
	CONTENT
PTBD Vs ERC	Relieves biliary obstruction in failed ERCP biliary drainage- which happens in 8%; Hilar stricture; More chances of pain, bile leak & external bag+
Steps Volume of lobe Status of portal vein Cholangitis	Ultrasound → initial access site chosen; Right sided access (more segments drained; more chance of slippage; shorter segmental ducts) – 11th intercostal/subcostal space in the midaxillary line / Left sided (easier; better compliance; preferred in pts with ascites): three fingers - subxiphoid - 10 → 1 % lidocaine as local anesthesia; under aseptic precautions → 22/ 21 G double-walled Chiba needle → peripheral segment duct punctured → USG/ Fluoro help Removal of stylet → bile outflow + → bile duct is opacified by contrast a 0.018" GW (22G needle)/ 0.035" (18G needle) wire is advanced into the duct → attempt to cross the obstruction into D2 → 8.5Fr ring biliary catheter & internal external catheter placement done by seldinger technique. Failure to cross obstruction → external drainage catheter is placed.
Indications	Benign/malignant biliary obstruction/Strictures Post operative → S/p cholecystectomy; Post transplant; Bilioenteric anastomosis Inflammatory → Chronic pancreatitis/sclerosing/pyogenic cholangitis/ Mirrizzi syndrome/ portal biliopathy Plz put the table of strictures in PSC chapter
Relative contraincn	Perihepatic fluid/ascites → pericatheter bile leak → biliary peritonitis
Pre –	CT/MRCP - identifying the level & cause of obstruction; biliary anatomy
Procedure care	INR < 1.4; Plt count > 70000/cmm Antibiotics – 3rd generation cephalosporins – routinely Piperacillin tazobactam for biliary sepsis Can be done under local anesthesia – 2% lidocaine with pre- procedural analgesia – paracetamol 1g i.v or Fentanyl 25 to 50 ug Or Conscious sedation (midazolam); NPO X 4 Hrs
COMPLICATIONS	Bleeding (portal tract- HA, PV, CBD); HV is rarely injured Antiplatelet intake: Aspirin/Clopidogrel- stopped 5 days prior-? Plt transfusion/use of desmopressin Central biliary access (HA & PV are larger)/Use of 18G needle/Left sided drain/Multiple passes/undilated biliary system/cirrhosis/renal insufficiency/advanced age Venous bleed → blood in bag / melena; Arterial bleed → 1-2 weeks after PTBD; Pulsatile & due to pseudoaneurysm of HA → angiogram & coil Bile leak – biliary peritonitis Pancreatitis/ cholecystitis Cholangitis:use minimal contrast & wire manipulations; Antibiotics Pericatheter leak: Catheter side holes outside bile duct/ascites → reposition with upsized catheter Catheter dislodgement: more common with external drain than internoexternal; Better anchorage

	CONTENT
Post procedure care	<p>Pulse, BP, abdominal distension → monitor for 24 hours</p> <p>Paracetomol for pain</p> <p>IV cephalosporin → followed by oral for a week</p> <p>IV fluids for 2 days to counter the choleresis</p> <p>After 24 hours → cap the external drainage catheter to allow the bile to drain inside</p> <p>Monthly follow-up → LFT, TC & bile output/color & USG abdomen</p> <p>10mL saline flush the catheter → if tubal block</p> <p>Skin changes & pericatheter leakage → might be noted</p> <p>Interno-external biliary drainage catheters → exchanged every 2 to 3 months or earlier if jaundice or cholangitis recurs or</p> <p>Good distal outflow & length of stricture on cholangiogram → Over a stiff wire, stent deployed either single/staged procedure</p> <p>Bismuth Type I,II → single stent; III → Double; IV → Multiple stents (Y preferred/T)</p>

Site of obstruction: Proximal → At confluence; Distal → below the insertion of cystic duct.

Selection of duct: Selected duct should drain at least 1/6th of liver; Distal obstruction → single puncture, single drain is sufficient.

Caution: No atrophy or portal vein involvement of the selected liver.



Radiology

Fluoroscopy: Real time X-ray imaging

Conventional fluoroscopy: Material used: Silver activated zinc cadmium sulfide

Image Intensifier: Cesium Iodide

Ultrasound: Ultrasound image is based on mechanical oscillations of the crystals (Zirconate titanate) in the transducer excited by electrical pulses (Piezo electric effect).

Acoustic shadowing: Dense material completely reflecting sound waves and shadow+. Noted behind a bone/GB or renal calculi

Acoustic Enhancement: No echoes as no difference in acoustic density. Noted in cysts, ascites, pleural effusions- echo free structures with posterior acoustic enhancement

3-5MHz - routine abdominal Ultrasound. For superficial ultrasound- 7-10MHz is used. Higher frequency for superficial parts.

Modes: A mode - Amplitude; B mode- gray scale for routine applications; M mode

Adv: No radiation and portable. Can use doppler for direction of flow- Blue is away from transducer and red is towards the transducer.

CT: Attenuation of X ray beam- Hounsfield units

Multislice CT: Multiple and thinner detector rows with faster tube rotation speed

High resolution CT: HRCT: 1-2 mm thin collimation scans for ILD/Bronchiectasis

CECT: Usually iodinated contrast is used

MRI: Proton acts as a dipole- principle is gyromagnetic

Clinical imaging: magnetic field strengths- 0.2-7 tesla- MC 1.5tesla

World War II: water is white in T2

Fat is white in T1

No contrast is used for MRCP - Heavy T2 weighted sequences

Contrast is Gadolinium - reduces T1 relaxation time.

Bone METs - bone scan is better except for spine- MRI is better

For lung METs - CT is preferred except pancoasts tumor and posterior mediastinal masses where MRI is better

Barium: Where not to use:

Tracheo esophageal fistula-use dianosil - water soluble non ionic contrast

Perforation peritonitis - Gastrograffin- water soluble ionic contrast

Single contrast - Barium alone

Double contrast - Barium + Air- better to delineate mucosal lesion

Barium swallow: Barium paste is used- for esophagus

Barium meal: 95% Ba SO₄ – for stomach and duodenum

Barium meal follow through: 50% BaSO₄- for small bowel

Barium enema: 25% BaSO₄ – for large bowel

Investigation of choice for small bowel lesions- enteroclysis

Biliary imaging:

Oral cholecystography/Graham cole test: Dye: Iopaonic acid/calcium ipodate

Most gall bladder pathologies - USG is the investigation of choice except acute cholecystitis- Tc99 HIDA scan is the gold standard and IOC is still USG.

Nuclear Medicine:

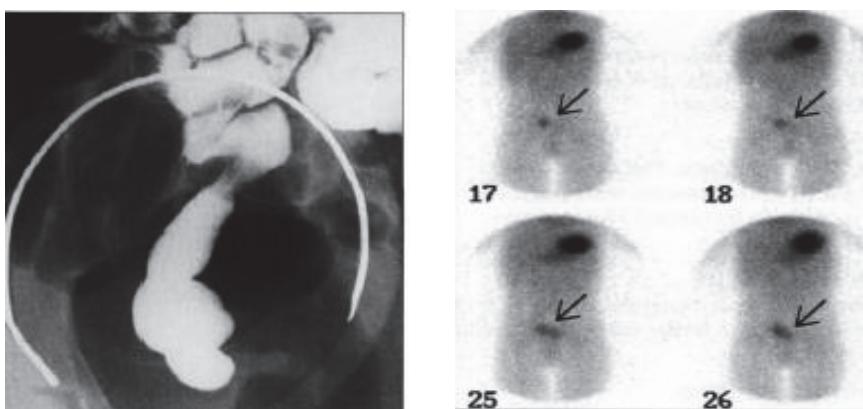
Tc99- MC used

T1/2: 6 hours

Tc99 RBC can detect as low as 0.1mL/min of bleeding as opposed to 0.5mL/min by angiography

Tc99 sulfur colloid scanning - Kupffer cells take up- focal nodular hyperplasia is kupffer cell rich vascular tumor- noted as hot nodule

Tc99 pertechnate - meckels diverticulum



In 111-DTPA or C14 labelled substrates- Gastric/duodenal emptying

PET scan:

Fluoro-2- deoxy glucose- F18- Glucose analogue- uptake by GLUT 1 receptors

False negative FDG: Mucinous adenocarcinomas/ low grade lymphomas/hepatocellular carcinomas

Radiation Effects:

Cell cycle: 4 phases- M: Mitosis → G1 → S: DNA synthesis → G2 → followed by M

Cells are most radiosensitive in G2-M phase and most radioresistant in late S phase (sulphydryls are natural radioprotectors- highest in S and lowest before M phase)

Maximum permissible dose of occupational exposure: 20mSv/year

Mediastinum:

Anterior mediastinal lesions: 9Ts

Thyroid, Teratoma, Thymic tumor, thoracic aorta, Tissue tumor(bronchogenic cyst/fibroma), T cell lymphoma, Parathyroid tumor, metastasis, transdiaphragmatic lesions

Middle Mediastinal lesions: ABCDE

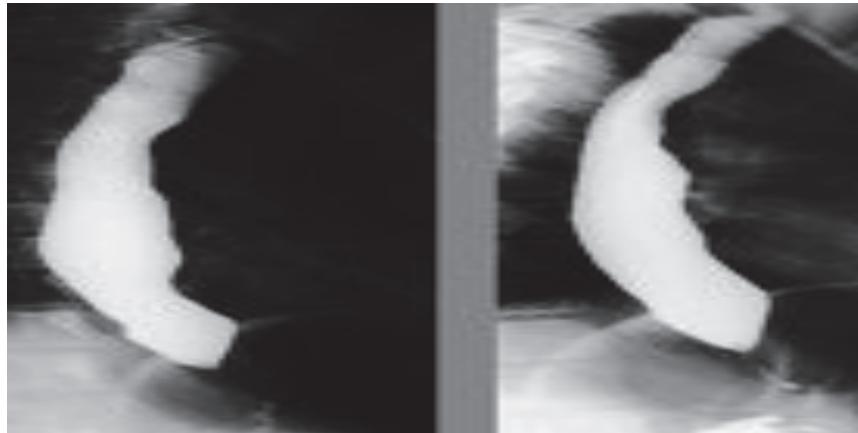
Aneurysm of aorta, Bronchogenic cyst, carcinoma of bronchus, distant METs, Enteric cyst

Posterior Mediastinal lesions:

Neurogenic tumor, paravertebral abscess, Paravertebral lymphoma/METs, hiatus hernia

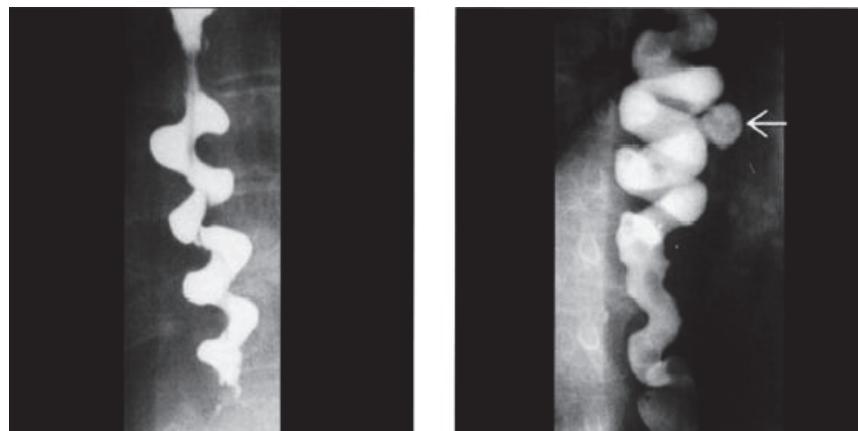
Systemic Radiology:

Achalasia cardia: Dilated Esophagus, Rat Tail/bird beak tapering, precipitated by methychochine, obstructed relieved by amyl nitrate and hot water, pre malignant condition



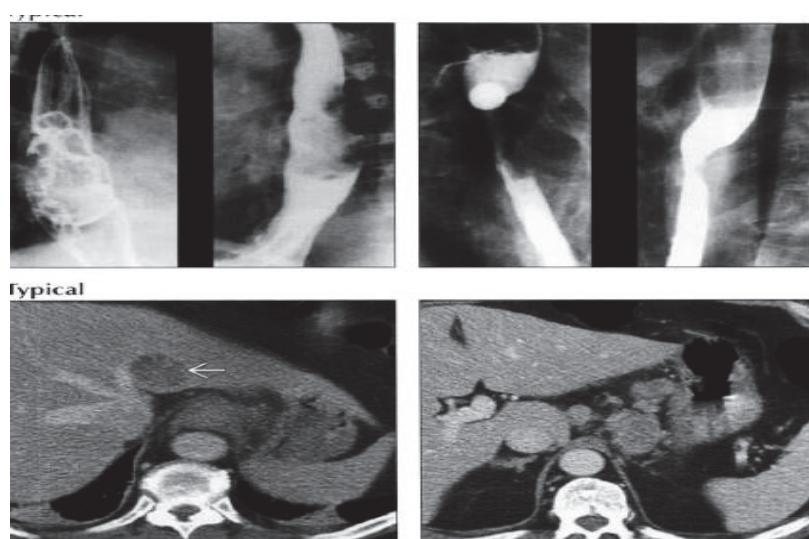
Barium is better for evaluation of motility disorders and for cricopharyngeal dysphagia

Diffuse Esophageal spasm: Corkscrew esophagus



Carcinoma Esophagus: Irregular narrowing, mucosal destruction, shouldered margins

Endoscopy and biopsy can confirm the malignancy and staging can be by CECT



Hiatus Hernia:

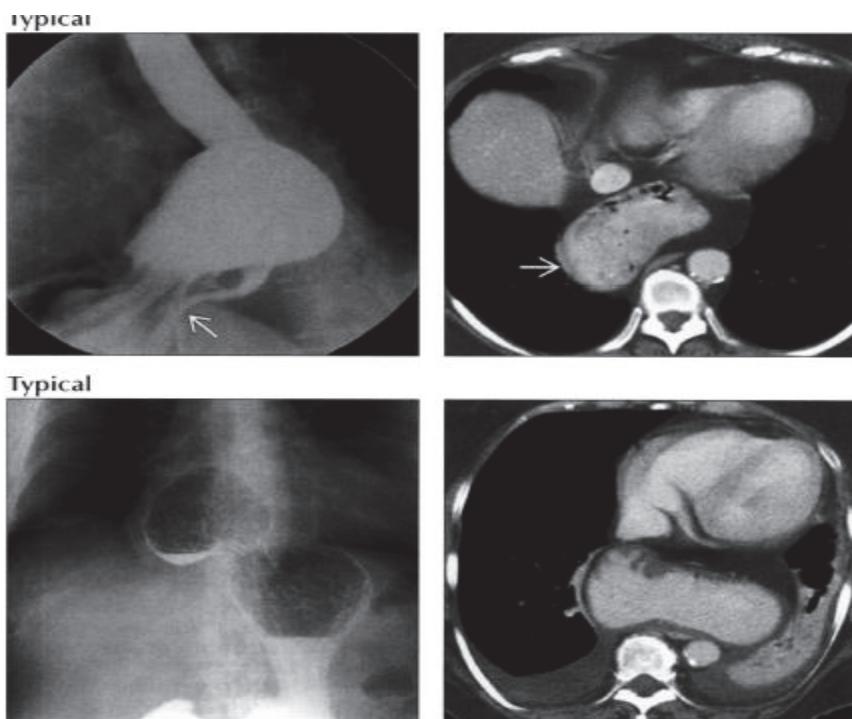
MC diaphragmatic hernia-Hiatus hernia

Bochdaleks: left sided; patent pleuro-peritoneal canals

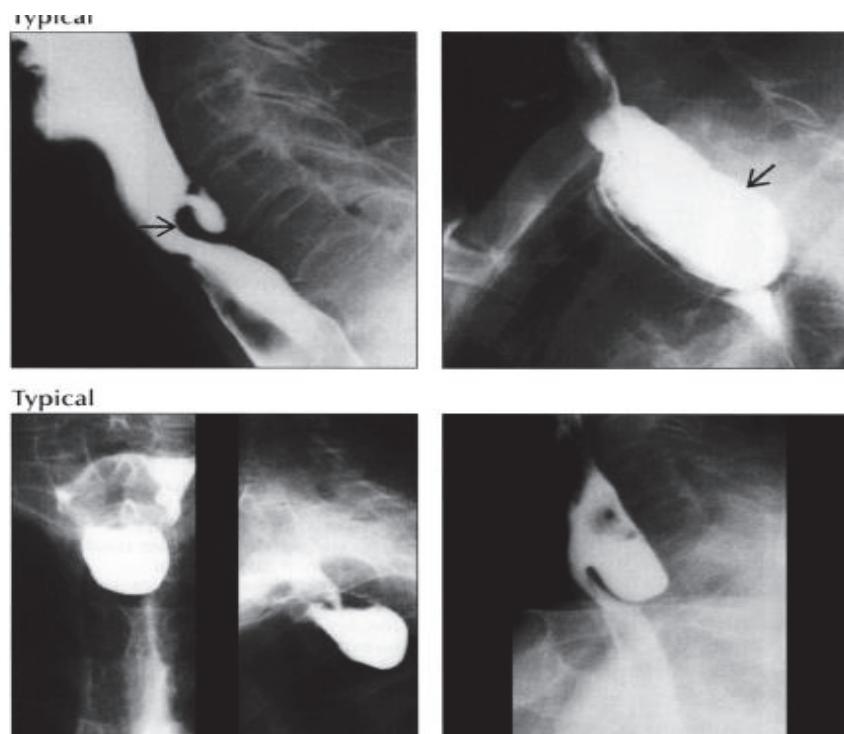
Morgagnis: right sided; Anterior; Sterno costal defect

Diagnosis of Hiatus hernia: GEJ: > 2cm above hiatus; Hiatus > 2.5cm; More than 3 gastric folds above the hiatus

GE Jn normal in rolling and paraesophageal hernias



Zenkers diverticulum: Pulsion diverticulum with mucosa and submucosa protruding through Killians dehiscence. Position: mid line,posterior, just above cricopharyngeus, protruding laterally and usually to left.



Stomach: Lymphoma more likely than carcinoma when extensive wall thickening, circumferential involvement of stomach, transpyloric spread, presence of lymph nodes above and below the renal hilum, splenomegaly

Bulls eye lesion in stomach:

- Submucosal METs: MC- melanoma
- Lymphoma
- Carcinoma breast, bronchus, pancreas
- Carcinoid
- Leiomyoma
- Pancreatic rest, neurofibroma

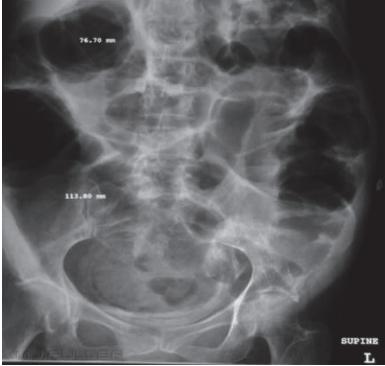


Double bubble appearance: Duodenal atresia/annular pancreas- one bubble stomach and another duodenum-D1.



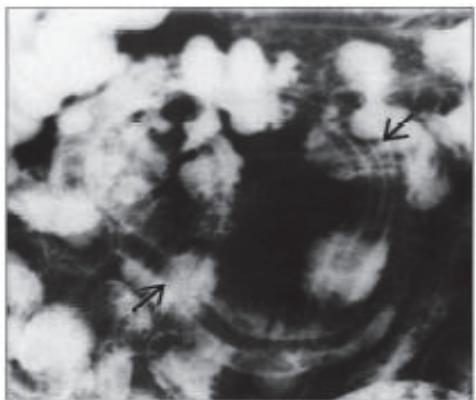
Triple bubble: Jejunal atresia

Obstruction:

Large bowel	Small bowel
Peripheral, few loops	Central, multiple loops
Presence of haustration- diameter- >8cm Haustra: Thickened, blunt and do not traverse completely	Jejunal → valvulae connivantes- traverse the complete length → ribbed appearance String of beads- air trapped in valvulae and rest of loop filled with fluid
Distended cecum → rounded gas shadow in RIF diameter >9cm	Ileum → featureless
3,6,9 rule: Maximum normal diameter of: Small bowel - 3cm Large bowel - 6cm Cecum - 9cm	Diameter 3-5cm
Air in rectum: Implies paralytic ileus than mechanical obstruction	No gas in colon
	 

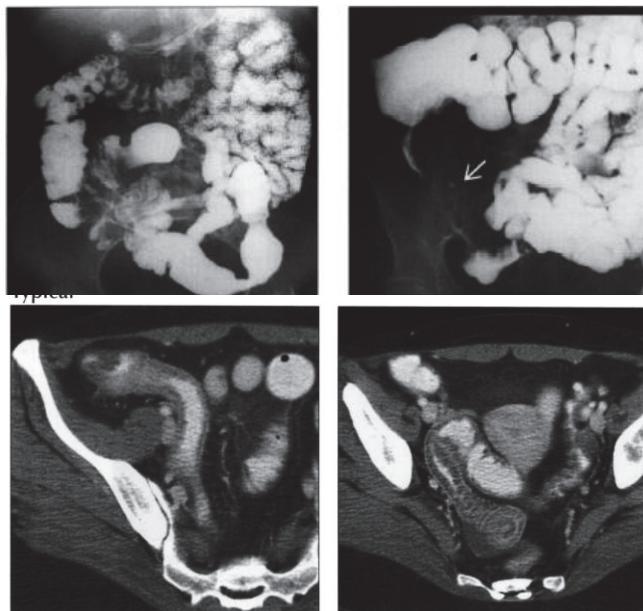
Malabsorption: Bowel loop dilation, intestinal hurry, flocculation of contrast, segmentation, fold thickening, excessive dilution of contrast, moulage sign- tube like appearance of bowel.

Ascariasis: Sphagetti appearance, bulls eye sign, impacted worm sign.



Crohns disease: Skip lesions, Transmural involvement, HALO sign on CT, String sign of kantor, cobble stoning, rose thorn appearance, pseudosacculations

Earliest sign- Aphthoid ulcers

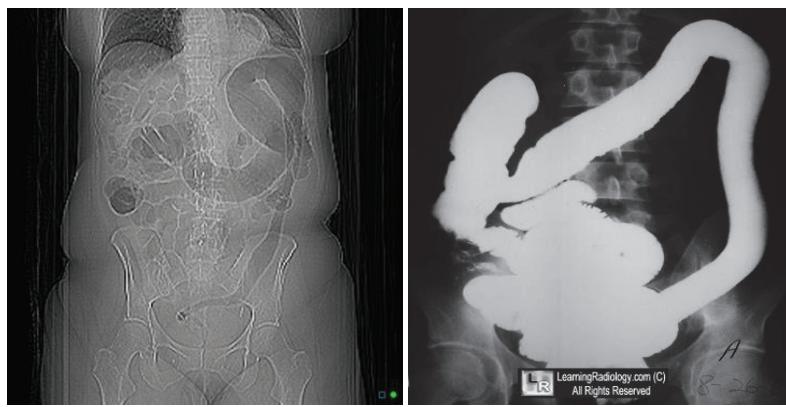


Ulcerative colitis:

Toxic megacolon if transverse colon diameter > 5cm, Collar button ulcers, pseudopolyps, contiguous mucosal involvement, back wash ileitis, ahaustral(pipe stem) colon, increased presacral space > 1cm, risk of malignancy higher than crohns

Earliest sign: blurring of mucosal stripe and granular appearance

If active disease is suspected- instant barium enema can be done as the actively inflamed colon will be devoid of feces



Ileocecal Kochs: String sign, Fleishner/inverted umbrella sign, sterlein sign, purse string sign, goose neck appearance.

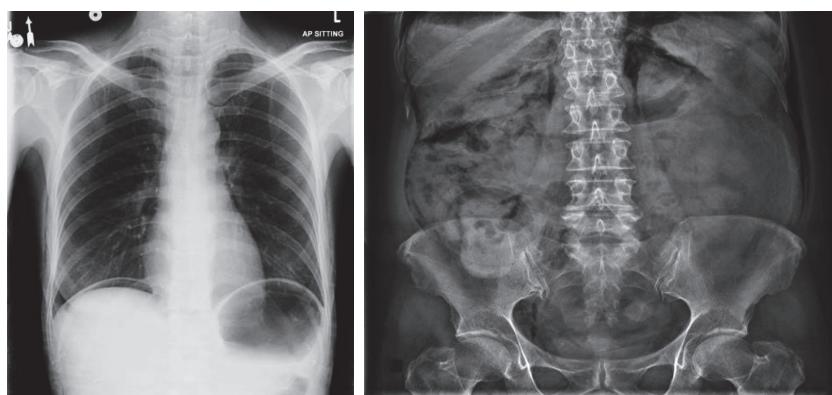


Perforation:

Best projection to demonstrate pneumoperitoneum - CXR

If erect X Ray not feasible - Lt lateral decubitus position- position for 10 min for air to rise and do X Ray

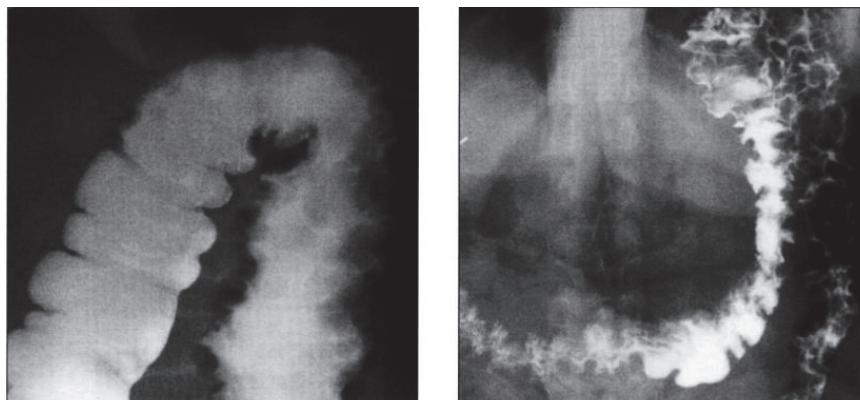
Pneumoretroperitoneum: Free air lateral to Rt Kidney and even on erect/decubitus position- air does not change position



Normal GAS pattern:

- Stomach- Always
- Small bowel-Small amount of air- usually 2-3 loops
- Large bowel-Almost always air in rectum and sigmoid. Varying amounts in rest of the colon

Pneumatosis coli: Secondary to ischemia, infection, trauma, connective tissue disorders, COPD, obstruction → dilated small bowel loops with air in the wall of the bowel → portal pyemia → high mortality



Sigmoid volvulus:

- MC GI Volvulus; MC in constipated elderly patients;
- Inverted U of sigmoid colon, coffee bean sign, birds beak/bird of prey sign on barium enema
- Sigmoid volvulus- bowel loop points towards RUQ
- Cecal volvulus- bowel loop points towards LUQ
- Most dilated colons are noted with volvulus



ENDOSCOPY

Band & EMR

BAND LIGATION

Indications

- Bleeding Esophageal Varices
- Treatment of Non-bleeding Varices
- Treatment of Recurrent Bleeding Varices
- Dieuleufoys lesion
- Hemorrhoidal Banding

Endoscopic variceal ligation-EVL

- Standard treatment for acute esophageal variceal bleed
- Stiegmann et al (1986) - First rubber band ligation device
- Before procedure-careful examination of the esophagus and stomach-identify the location & appearance of the varices

Contraindications

- Uncooperative patient
- Massive hemorrhage that obstructs field of view
- Acute ECG changes/ respiratory instability
- Unstable vital signs
- No informed consent
- Esophageal Stricture/ Diverticula/ Perforation
- Obliterated Varices

Pre-Procedure Assessment

- Informed consent specific to Banding.
- H/o present & past bleeding episodes/treatments
- Blood investigations- LFT, Coagulopathy, CBC, Viral markers
- Lavage Nasogastric tube before removing in active bleeding
- Blood type and cross matched
- Acutely bleed is noted -? intubation for airway protection while performing the procedure

EQUIPMENT/Banding Kit

- Standard endoscope (2.8 mm working channel) or Double channel endoscope.
- Ligation unit including barrel with preloaded bands
- Trigger cord / Handle / Loading Catheter / Irrigation adaptor

Cylindrical Cap

- A short transparent cylindrical cap that carries 1, 4, 5, 6, 7, or 10 stretched bands (depending on the specific ligator)
- Soft sheath portion that fits onto the leading end of the scope
- Bands are stretched at the hard plastic portion

Other Components

- A tripwire that runs from the cap through the accessory channel to the control handle
- A control handle with a retracting spool that is fixed to the biopsy port for attachment and firing of the trip wire.
- An irrigation adapter or catheter that allows irrigation of the accessory channel.

During Procedure

- Assemble Band Ligation Kit
- Monitor the patient with vitals
- Irrigate as requested to help maintain visualization and verify Hemostasis.
- Document the count of bands successfully applied
- Suction the oral cavity thoroughly as the scope is being withdrawn and remove the mouthpiece

Applying Bands

- Endoscope with ligating device- reinserted to the site for placement
- Best to treat the most distal varices & then ascend proximally as deployed bands can occlude the esophageal lumen
- Continue in a helical fashion for 5-8 cm proximally with suction and draw the mucosa into the chamber
- Watch for Red-out-caused by close approximation of the mucosa overlying the varix within the ligating chamber to the lens on the tip of the endoscope - adequate amount of tissue has been captured by the device
- Maximum wall suction is sufficient to achieve adequate aspiration of the esophageal mucosa- never portable suction devices
- Trying to place a band on a small amount of tissue will usually result in the band sliding off à mucosal damage with bleed & non- visualization
- Action: Tight compression that leads to vascular compromise (or hemostasis) and subsequent thrombosis, necrosis, and sloughing
- One band per varix and avoid passing over already applied band ? dislodgement

Esophageal variceal banding



Number of Bands

- Goal: Eradicate varices in the lower 5 cm of the esophagus
- Theoretically no limit to the number of bands
- 6-10 bands – initial session
- Subsequent sessions → Lesser number of esophageal variceal bands
- Randomized, prospective study- placement of > 6 bands per session did not improve patient outcomes but prolonged procedure time and increased the number of misfired bands

NG Tube and Rebleed

NG Tube

- Avoid placing a NG tube after EVL to avoid dislodging the bands
- But if there is a need to keep the stomach decompressed/ provide medications/nutrition enterally place as gently as possible.

High Rebleed risk factors

- CTP C status
- Portal vein thrombosis
- High TC- > 10,000/cmm
- Ascites
- Elevated -PT-INR
- Grade of varices

Acutely Bleeding Varices

- Diminished visibility created by blood accumulating in the tip of the device & tunnel vision produced by the ligating device on the tip of the endoscope can make EVL challenging
- Accumulation of blood can often be overcome by injecting water through a blunt needle passed along the trip wire as it exits from the valve on the endoscope handle.
- Worse case: semi-blindly place bands at the GE junction which reduces bleeding

AASLD- Follow up Endoscopy protocol

- In patients who bled from varices and were treated with EVL or those who underwent EVL for primary prophylaxis, EVL should be repeated every one to two weeks until obliteration with the first surveillance EGD performed one to three months after obliteration and then every 6 to 12 months to check for variceal recurrence

Post-Procedure Care

- Elevate the head of the bed to reduce aspiration risk
- Provide outpatients with written discharge instructions to include:
 - ▶ Diet instructions: full liquid or soft diet for 24-48 hours.
 - ▶ Return appointment for follow-up exam.
 - ▶ Instructions for calling physician with signs of any further bleeding orally or rectally, inability to swallow, shortness of breath, increasing chest pain or fever.

Classification of Varices

Size of varix	Two-size classification	Three-size classification
Small	<5 mm	Minimally elevated veins above the esophageal mucosal surface
Medium	--	Tortuous veins occupying less than one-third of the esophageal lumen
Large	>5 mm	Occupying more than one-third of the esophageal lumen

Variceal hemorrhage is diagnosed on the basis of one of the following findings on endoscopy:

- Active bleeding from a varix
- "White nipple" overlying a varix
- Clots overlying a varix
- Varices with no other potential source of bleeding

Variceal band ligators

Manufacturer	ConMed (Utica, NY)	Scandimed International and ConMe	Boston Scientific	Cook Endoscopy
Name	Stiegmann Goff and S-G ClearVue endoscopic ligators	Auto-Band Ligator multiple-band ligator	Speedband, Superview Super 7 multiple band ligators	4, 6, 10 Shooter Saeed multiband ligators
No. bands per ap	1	5, 7, 10	7	4, 6, 10
Endoscope tip diameter (mm)	9-11	86-115	86-115	8.5-9.2, 8.6-11.3, 9.5-11.5, 9.5-13, 11-14
Band color	Blue	Black	Blue	Black
Band material	Rubber	Latex-free rubber	Neoprene	Natural rubber latex

Complications

- Fever/Mediastinitis
- Esophageal stricture- 1%
- Post Procedure pain- uncommon - ? Esophageal Spasm - If Dysphagia/odynophagia- better with lignocaine-antacid
- Bacteremia- Antibiotic Prophylaxis- 3.3%
- Ulcers caused by EVL are usually approximately 1 cm in diameter
- They typically develop within 3 to 10 days after EVL, when the necrotic tissue within the band sloughs off
- No empiric therapy with acid-suppressing drugs or has been shown to reliably minimize the effects or presence of these ulcers.
- Previous variceal bleeding, esophagitis, high platelet ratio index (APRI) score, and low prothrombin index are independent risk factors for bleeding from post EVL ulcers

Endoscopy

Baveno 5

- Ligation (EVL) is the recommended form of endoscopic therapy for acute esophageal variceal bleeding, although sclerotherapy may be used in the acute setting if ligation is technically difficult.
- Endoscopic therapy with tissue adhesive (e.g. N-butyl-cyanoacrylate) is recommended for acute bleeding from IGV and GOV2 that extend beyond the cardia.
- EVL or tissue adhesive can be used in bleeding from GOV1.

Baveno 6

- In the absence of contraindications (QT prolongation) pre-endoscopy infusion of erythromycin (250 mg IV, 30–120 min before endoscopy) should be considered.
- In patients with altered consciousness, endoscopy should be performed with protection of the airway .
- Ligation is the recommended form of endoscopic therapy for acute esophageal variceal bleeding .

Principles of colonoscopic banding

- The principle involves suction of the internal haemorrhoids into the ligating drum, which is attached to the colonoscope.
- The ring is deployed to the neck of the internal haemorrhoids through a trigger passed through the biopsy channel.
- A single band is released per internal haemorrhoids
- Maximum of 4 bands – applied in a session

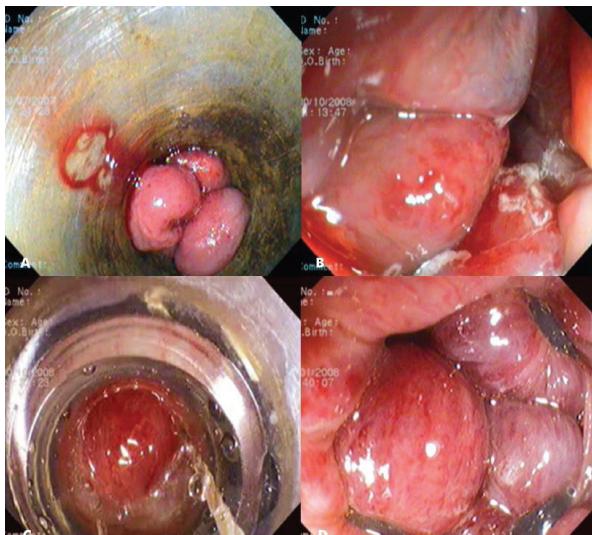


Fig. Colonoscopic haemorrhoidal banding

	BOSTON 7 	COOK 6 
Bands	7	6
Band material	Polyisoprene Latex free- good for allergic patients	Latex/Neoprene
Shape of bands	Square- molded- retains shape	Round
Visualisation	Unobstructed by bands	Partly obstructed by bands
Deployment/trip wire	Single strand/stronger suction	Double strand
Slippage	Less likely	Larger resting diameter with lower retraction force? Early slippage

BAND EMR/ Ligation-Assisted EMR

- Born from the extrapolation of tissue acquisition during variceal band ligation to EMR
- Technique involves the application of bands around aspirated tissue and subsequent snare-cautery resection
- Band will incorporate the mucosal and submucosal layers while leaving the muscularis propria in situ as a consequence of insufficient contractile force.
- In the simplest form of the procedure, a standard variceal band ligator device is used to aspirate the target lesion and apply a band around it.
- After removal of the banding device, a separate snare is used to resect the lesion
- A submucosal injection may also be made before tissue aspiration, though this step is not universally applied. Methylene blue/Indigocarmine can be mixed with saline as it helps when transmural cut happens target sign with yellow over blue background suggests perforation
- If no band is used- Crescent shaped EMR (Snare master- Olympus) can be used - with thin pliant wire design. Injection of submucosal plane, prelooping with suction with hard and wide oblique rim EMR cap at the distal end of the scope. Snare placed at the bottom of suctioned area and resected. Snare wire is 0.3mm with a loop of 2.5cm. the cap ensures appropriate distance between the scope tip and the target lesion

Indications

- Dissection of mucosal and submucosal lesions. Device is for single use only
- Superficial (mucosal +/- minimal submucosal) lesions which are dysplastic or cancerous
- Size depending on location in GI tract, EMR usually for smaller lesions
- Lesion lifts with submucosal injection (esp for EMR) e.g. Early gastric cancer, Barrett's esophagus with high grade dysplasia, laterally spreading tumour in colon
- First Assess the lesion: Superficial cancer or dysplastic lesion (NBI, Chromoendoscopy), Lesion depth – if in doubt EUS may be helpful, Delineation of margin - important for complete resection, NBI or chromoendoscopy may be useful

Contraindications

- Specific to the primary endoscopic procedure that must be performed to gain access to the desired site for mucosal resection.
- Contraindications specific to esophageal banding include, but are not limited to: cricopharyngeal or esophageal narrowing or stricture, tortuous esophagus, esophageal varices, diverticula,
- known or suspected esophageal perforation, asymptomatic rings or webs,
- Coagulopathy, and patients with bleeding disorders,

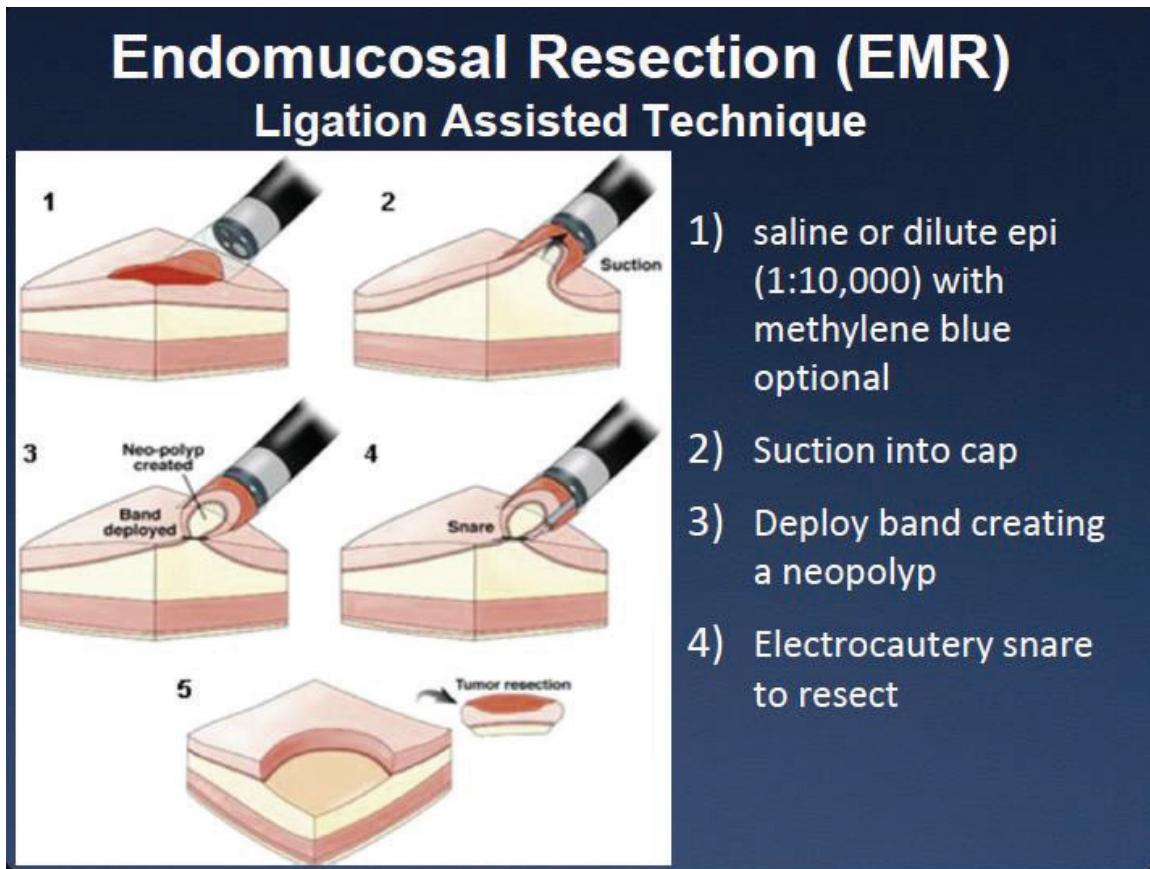
Adverse Events:

- Pain, tissue damage, infection
- Perforation 5% for ESD and lesser for EMR, stricture formation, acute bleeding, delayed bleeding,
- Transmural burn

Disadvantages: Tumors with a diameter above 2 cm and sessile tumors require a "piecemeal technique" (overlapping resection). As a result, R0 resection is not ensured



Captivator™ EMR Device



EMR/ESD:

- Significant Advances in Therapeutic Endoscopy in past two decades
- Expansion of gastroenterology and surgical subspecialties
- Availability of better flexible video endoscopes – enhanced imaging (NBI, confocal laser endomicroscopy), therapeutic channels, waterjets, better maneuverability
- Availability of Endoscopic Ultrasound (Visualize the GI wall layer and beyond the lumen)
- Availability of accessories for resection, dissection, hemostasis, clipping, etc.
- Media and communication – rapid dissemination of knowledge
- EMR and ESD are used for management of superficial lesions of the gastrointestinal tract
- A minimally invasive technique for removal of superficial malignancies or dysplastic lesions
- Histology of resected specimen provides information on depth and stage of tumor

Pre requisites:

- Assess the suitability of lesion for EMR/ESD
- Assess the fitness of patient
- Ensure all the equipments and accessories are available
- Keep the surgery colleagues on board

Accessories at hand:

- Chromoendoscopy – electronic (NBI), dye spray
- Spray Catheter, Injection needle
- Electrosurgical Snare
- Dissection devices
- Distal attachment
- Electrosurgical unit
- CO₂ Insufflator
- Flushing Pump

Principle of EMR/ESD:

- Marking around the lesion (to ensure en-bloc resection)
- Submucosal injection to lift the lesion (protect the deeper layers)
- Resection with snare (EMR) or dissection with knife (ESD)

Different techniques of EMR/ESD:

- Injection assisted EMR
- Cap assisted EMR
- Ligation assisted EMR
- Underwater EMR
- Hybrid procedure (EMR and ESD)

Classification

Forrest Classification

Grade	Endoscopic Picture	Risk of rebleeding
I	Active haemorrhage	
IA	Spurting	85-100%
IB	Oozing	10-27%
II	Signs of recent haemorrhage	
IIA	Visible vessel	50%
IIB	Adherent clot	30-35%
IIC	Haematin covered flat spot	<8%
III	No signs of haemorrhage - clean bed of ulcer	
		<3%

Forrest JA, Finlayson ND, Shearman DJ. Endoscopy in gastrointestinal bleeding. Lancet 1974; 2:394.

Zargar classification

Endoscopic classification of caustic injuries	
Grade	Normal
Grade 1	Superficial mucosal edema and erythema
Grade 2	Mucosal and submucosal ulcerations
Grade 2A	Superficial ulcerations, erosions, exudates
Grade 2B	Deep discrete or circumferential ulcerations
Grade 3	Transmural ulcerations with necrosis
Grade 3A	Foal necrosis
Grade 3B	Extensive necrosis
Grade 4	Perforations

Zargar SA, Kochhar R, Metha S, Metha SK. The role of fiberoptic endoscopy in the management of corrosive ingestion and modified endoscopic classification of burns. Gastrointest Endosc. 1991;37:165-9.

Modified Paquet classification

Grade I

- Varices extending just above the mucosal level

Grade II

- Varices projecting by one-third of the luminal diameter that cannot be compressed with air insufflation

Grade III

- Varices projecting up to 50% of the luminal diameter and in contact with each other

Paquet, KJ. Prophylactic endoscopic sclerosing treatment of the esophageal wall in varices – A Prospective Controlled Randomized Trial. Endoscopy 1982; 14: 4–5

Japanese Research Society for Portal Hypertension classification

Color

- White
- Blue
- Red color sign
- No/slight red wale markings/cherry red spots (A)
- Moderate/severe red wale markings/cherry red spots (B)

Shape

- Straight (F1)
- Enlarged, tortuous (F2)
- Very large varices (F3)
- Lower third
- Middle third
- Upper third

Beppu K, Inokuchi K, Koyanagi N, Nakayama S, Sakata H, Kitano, S, Kobayashi M. Prediction of variceal hemorrhage by esophageal endoscopy. Gastrointest Endosc. 1981 Nov;27(4):213-8.

Location

Grade 1

- Linear varices < 2 mm, reddish/blue, not raised on moderate insufflation, can be revealed by applying pressure with the endoscope

Grade 2

- Blue, 2–3 mm, slightly tortuous, raised above the surface of the esophagus on moderate insufflation, sometimes also visible in the form of an “anterior sentinel vein”

Grade 3

- Prominently elevated bluish veins, 3–4 mm, straight or tortuous, isolated distribution in the esophageal wall, “good mucosal coverage”

Grade 4

- > 4 mm, circular extension around the esophageal wall; varices almost meet in the middle of the lumen; with or without “good mucosal coverage”

Grade 5

- Racemose varices occluding the lumen, particularly marked with cherry red spots or varices on varices (“cherry red varices”)

Dagradi AE, Stempien SJ, Owens LK. Bleeding esophagogastric varices. An endoscopic study of 50 cases. Arch Surg. 1966 Jun;92(6):944-7.

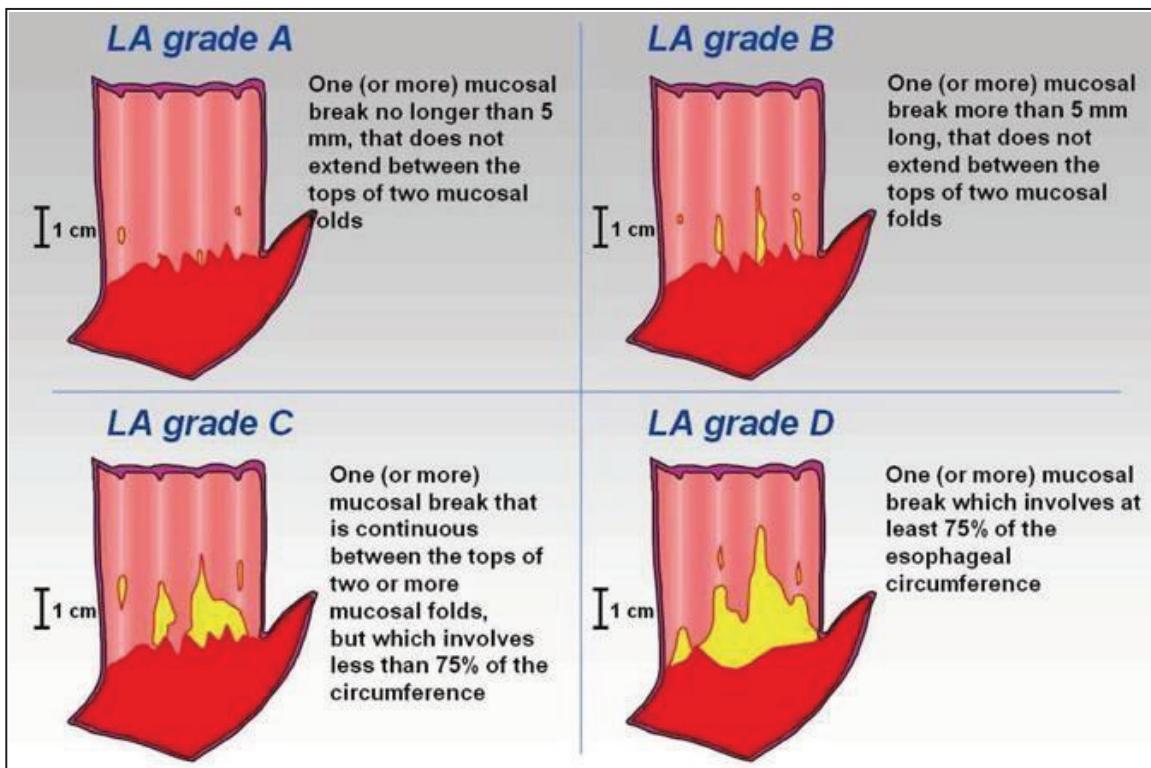
Sarin Classification

- Gastroesophageal varices, type 1 (on the endoscopic appearance, a continuation of esophageal varices into the lesser curvature of the stomach beyond the level of the cardia, usually with an elongated course)
- Gastroesophageal varices, type 2 (endoscopically, pass from the cardia towards the greater curvature into the fundus of the stomach, often with a sinuous, cluster-like course)
- Isolated gastric varices, type 1 (this is the term for varices that course in the gastric fundus or cardia, but do not pass into the esophagus and do not reach the cardia)
- Isolated gastric varices, type 2 (this is the term for “ectopic” varices in all other sections of the stomach)

Sarin SK, Kumar A. Gastric varices: profile, classification, and management. Am J Gastroenterol. 1989;84(1244-9).

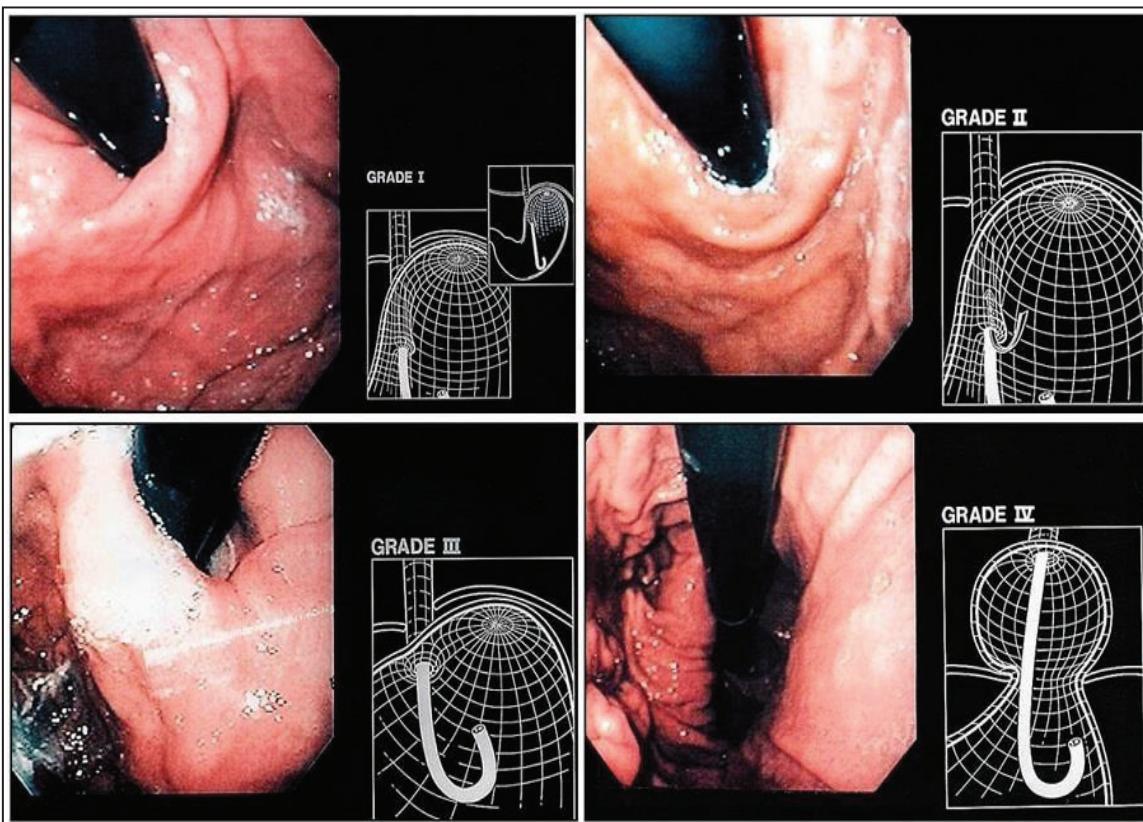
Gastric varix: Location, size, Red color sign, Bleeding sign, Mucosal change			
Location	GOV1	Continuation of esophageal varices and extent for 2 to 5 cm below the GE junction along the LC side of the stomach	
	GOV2	Continuation of esophageal varices and extend into the fundus	
	IGV	Isolated gastric varices located in the fundus	
	IGV2	Isolated ectopic varices anywhere in the stomach	
Size	Small	Less than 10mm	
	Medium	10-20mm	
	Large	Greater than 20mm	
Example	GOV1, medium size, RCS0 IGV1, large size, RCS2, white plug		

Reflux esophagitis

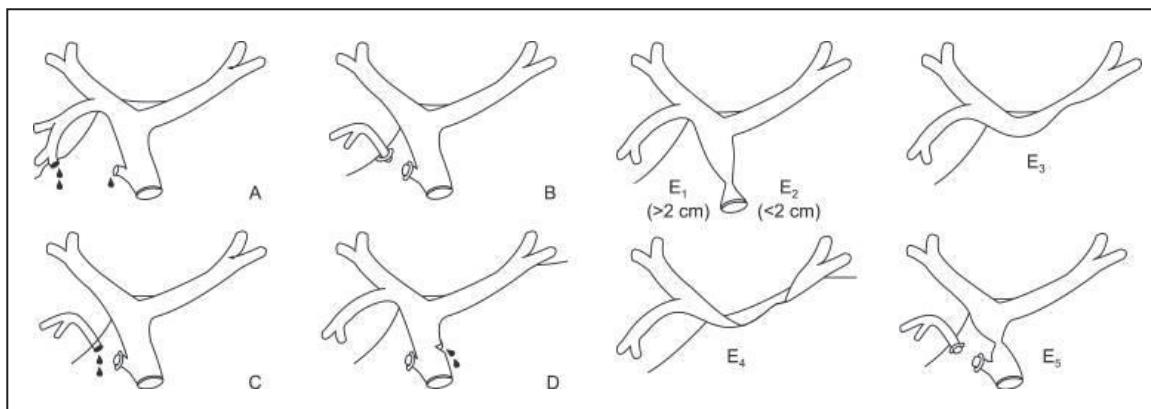


Armstrong D. Endoscopic evaluation of gastro-esophageal reflux disease. Yale J Biol Med 1999; 72(2-3): 93-100.

Hill grade

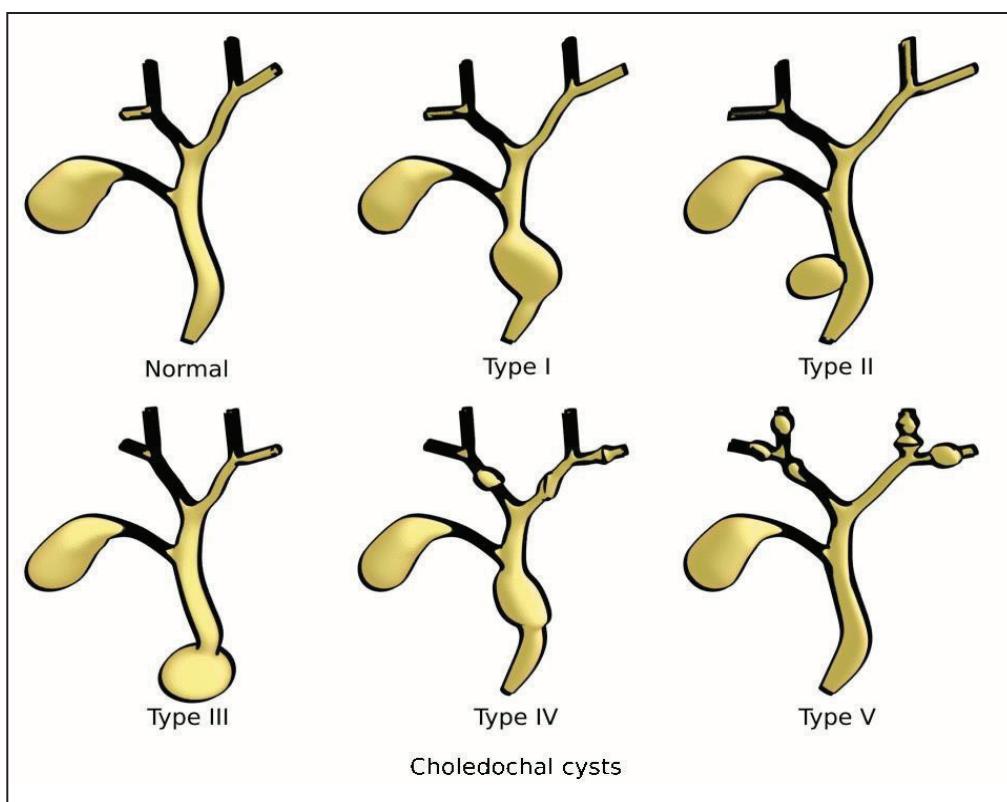


Strasberg classification



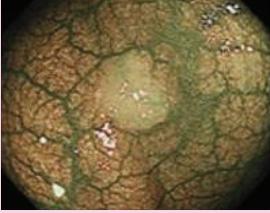
Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg 1995; 180:101-125.

Todani classification



Todani T, Watanabe Y, Narusue M, et al. Congenital bile duct cysts, classification, operative procedures, and review of thirty-seven cases including cancer arising from choledochal cyst. Am J Surg. 1977;134:263e269.

Nice Classification NBI

	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels may be present coursing across the lesion	Brown vessels surrounding white structures**	Has area(s) of disrupted or missing vessels
Surface pattern	Dark or white spots of uniform size, or homogeneous absence of pattern	Oval, tubular or branched white structures** surrounded by brown vessels	Amorphous or absent surface pattern
Most likely pathology	Hyperplastic & sessile serrated polyp (SSP)***	Adenoma****	Deep submucosal invasive cancer
Endoscopic image			

* Can be applied using colonoscopies with/without optical (zoom) magnification.

** These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.

*** In the WHO classification, sessile serrated polyp and sessile serrated adenoma are synonymous.

**** Type 2 consists of Vienna a classification type 3, 4 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma. The presence of high grade dysplasia or superficial carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (e.g., depressed area)

Clip



Resolution Clip:

Indications: Haemostasis, Endoscopic marking, Closure, Anchoring jejunal feeding tubes

Advantage: Engineered to enable opening and closing up to five times prior to deployment

Working length: 155-235cm

Clip opening: 11mm

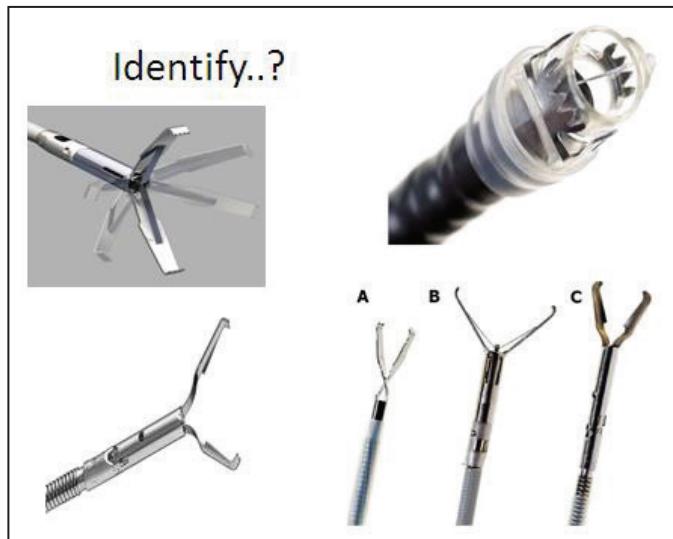
Minimum working channel: 2.8mm

Clip at the base:

The approach of the clip is from a low, tangential angle with the clip near the tip of the scope and suctioning the lumen into the jaws of the clip so that good amount of tissue can be grasped.

How to close a perforation?

Always start at the edge of the perforation and like a zipper close with multiple clips.



TTS Vs OTD

Clips	Indications
<ul style="list-style-type: none"> ● Resolution (11mm) and instinct (16mm) can be reopened 5 times after placement for repositioning ● Quickclip (9, 11mm) - multiple use applicator ● Oversco clip-Arterial bleed >2mm - similar to band applicator 	<ul style="list-style-type: none"> ● Hemostasis in GI tract ● Base of pedunculated polyp ● Endoscopic marking for RT/embolisation ● Closure of GI luminal perforations/fistulas ● Anchoring jejunal feeding tubes

Dilators

Dilators are used for dilatation of lumen within the gastrointestinal tract. There are different types of dilators and they can be classified as:

Equipment: Dilators: 3 types

1. **Semirigid/Bougie/Polyvinyl:** fixed diameter, push type, length: 70-100cm, radiopaque marker at the site of maximal diameter, dilators to be kept kink free.

2 types

Wire guided - OTW- over the wire (Savary Guillard/American dilators)

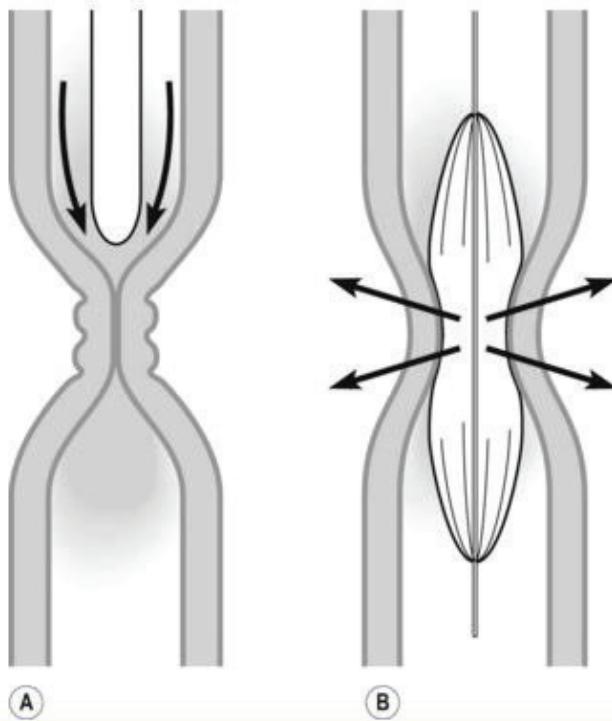
Non wire guided - Maloney/Hurst dilators (liquid metal filled- mercury/tungsten). Non wire guided are flexible, curl easily and higher complication rate. Dilation is by tactile feel. A longitudinal force is converted to radial expandable force.

Probs: Perforation is noted prox. to stricture.

2. **Through the scope (TTS) Balloon dilators:** Wire guided and non wire guided, single use, allows real time visualisation of the stricture.
3. **Pneumatic dilators:** Achalasia cardia- directly without the scope- Rigiflex balloon dilator

Principle of dilation:

All dilators use radial/shear expandable force to dilate the stricture



Structure:

Simple: Symmetric, straight, short and allow passage of endoscope

Complex: Length >2cm, tortuous, presence of trachea-esophageal fistula, non traversed stricture, angulation, presence of diverticula, proximal strictures - wire guided/use of fluoroscopy might help.

Plan: Choose the dilator size slightly smaller than the estimated size of the stricture.

Complications

- Bleeding (tachycardia, hypotension) - 0.2%
- Perforation (chest pain, respiratory distress, abdominal distension, neck crepitus) - 0.1%
- Aspiration (cough, expectoration)
- Bacteremia (max. bacteremia of all procedures, better to do under antibiotic prophylaxis)

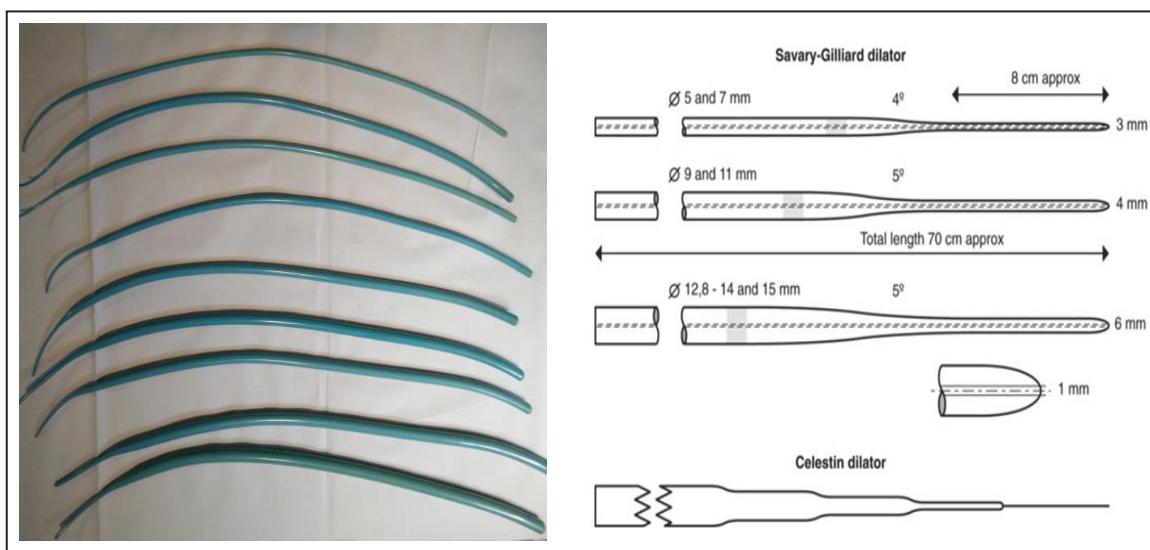
Contra-indications

- Coagulopathy, Uncooperative patient, Recent myocardial infarction
- Active ulcer/Esophageal varices, Recent biopsy, Perforation, Severe cervical arthritis

BOUGIE DILATATION

Dilators eg:- Savory Guillard (Cook Medical), American dilators

Sizes: 5mm to 20mm - and 13mm size is not available as it is considered an unlucky number.



Technique:

- Left lateral position with neck of the patient slightly hyperextended (sword swallowing position)
- Position the tip of the guidewire distal to the stricture under fluoro guidance
- Maintain straight path without coiling
- Over the wire, SG/Bougie dilators are passed with lubrication while the assistant provides continuous traction
- Gradual increase the size of the dilators. **Rule of 3:** After moderate resistance is noted on a dilator, size of the dilators should not be increased by additional 2 consecutive dilators. **Caution:** Total loss of resistance=perforation
- Repeat sessions are usually advised at 3 weeks

Other techniques:

- Inability to pass the guidewire, ERCP cannula is used and contrast given. Confirm the stricture anatomy and pass the guidewire. Aspiration to be prevented.
- Narrow diameter scope can be used to negotiate strictures
- Through mature PEG site, retrograde dilation can be tried (GE Jn noted, pass guidewire retrogradely with balloon catheter over the wire. Can double exchange for antegrade dilation)

Foot Notes:

SG dilators produce both shear and radial stress. In a comparative study between Maloney bougie, SG dilator and esophageal balloon, the shear stress was highest for Maloney followed by SG dilator. Esophageal balloon produces only radial force. McLean and LeVeen, "Shear Stress in the Performance of Esophageal Dilation." SG dilators are relatively safe and effective. Success of symptom relief with SG dilator use is case and operator dependent. Success rate for corrosive esophageal stricture is ~75% (Singhal and Kar) 100% esophageal web (Sreenivas et al)

Singhal and Kar, "Management of Acid- and Alkali-Induced Esophageal Strictures in 79 Adults by Endoscopic Dilation." and 100% for esophageal web

Sreenivas et al., "Results of Savary-Gilliard Dilatation in the Management of Cervical Web of Esophagus."

MALONEY AND HURST DILATOR: For self dilatation of stricture

Characteristics

- Weighted with tungsten for assistance from gravity
- Depth markings
- Radioopaque
- Silicone material becomes slippery when wet
- Available as alternate sizes between 16 – 60 Fr
- Maloney has a tapered tip, Hurst has blunt rounded tip
- No guidewire required

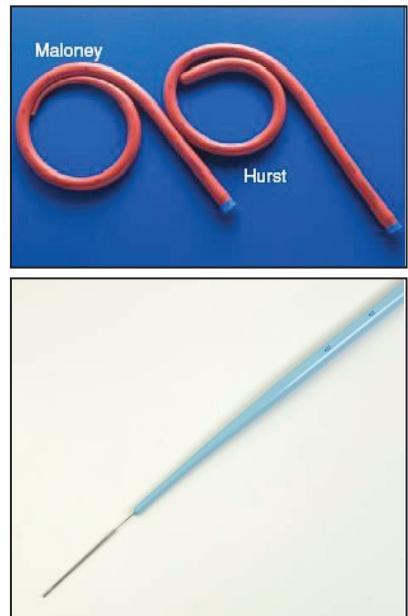
Use:

- Self dilatation of esophageal stricture

American Dilatation System (ConMed, Utica, NY)

Characteristics:

- Shorter tapered tip – minimizes trauma to esophageal wall
- Hollow core
- Total radio opacity throughout the length
- Available as a set of 15 dilators (15 – 60Fr)
- Measurement system from tip to aid in proper placement of the dilator
- The system includes a spring tip wire for guidance



Controlled Radial Expansion Balloon: CRE™ (BOSTON SCIENTIFIC)

Characteristics

- 180 cms length- 6Fr
- Balloon length 8 cm

Advantages:

- High compliance balloon - **PEBAX material**
- Three distinct pressure controlled diameters can be achieved
- Provides high radial vector force
- Has anatraumatic tip – reduces potential risk of tip impactions
- Can also be used for endoscopic biliary dilatation of major papilla

Available sizes:

Inflated balloon outer diameter (mm)	Inflation pressure (ATM) using ALLIANZ II inflator
6mm - 7 mm - 8mm	3 – 6 – 10
8mm - 9mm - 10mm	3 – 5.5 – 9
10mm - 11mm - 12 mm	3 – 5 – 8
12mm - 13.5mm - 15mm	3 – 4.5 – 8
15mm - 16.5mm - 18mm	3 – 4. 5 – 7
18mm - 19mm - 20mm	3 – 4. 5 – 6

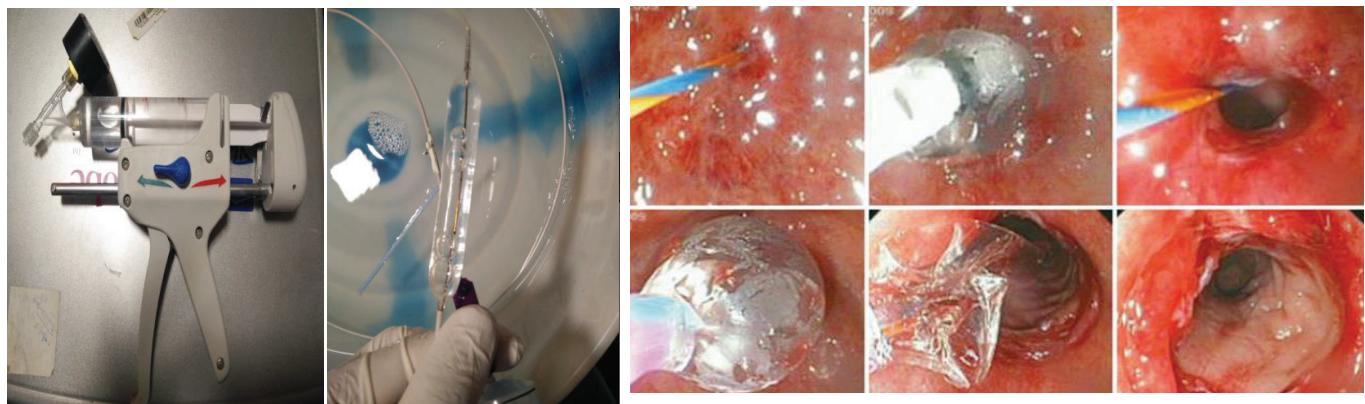
Use:

- Short tight esophageal strictures
- Helpful in tortuous anatomy
- Sphincteroplasty

Balloon Dilation Procedure:

- Scopy in left lateral position and sedation
- Assess distance of the stricture from major anatomical landmark (ex. UES in UGI)
- Pass lubricated TTS/OTW appropriate sized balloon under fluoro/endoscopic guidance without resistance
- Place the balloon with stenosis at the center of the balloon
- Gradual inflation of the balloon is done using alliance gun with water/diluted contrast. Prevent proximal or distal migration of the balloon
- Assess the stricture through the shoulder of the balloon. Once dilated maintain dilation for 30 sec-2 minutes.
- Rule of 3 **doesnot** apply for balloon dilation. If mucosal tear is noted/2-3 diameters of balloons used - do stop.

- Scope and balloon advanced with a gentle push beyond the stricture.
- Scope removed, balloon deflated completely and withdrawn.
- Check scope done to assess the stricture, length and the distance from landmarks.



Sphincteroplasty:

Staritz et al. Lancet 1982- papillary balloon dilation with reduced complication rate (as compared to sphincterotomy) and preservation of sphincter of Oddi function.

Primary indication: large stone that cannot be removed by conventional basket or balloon sweep despite adequate sphincterotomy

DASE: Dilation assisted stone extraction: Post procedural pancreatitis noted in 1.5%

Principle:

- Size of the balloon is determined by stone size and diameter of the distal bile duct
- Slow inflation by dilute contrast to facilitate fluoroscopic monitoring
- Balloon is maintained in position (mid point of balloon is better) by traction or counter-traction during inflation. Much of the balloon can be inside the bile duct by some authors-Donatelli et.al., Video J Encycl GIE 2013
- Inflation maintained for 30-60seconds- ideal time unknown
- Waist obliteration is to be noted. If not achieved- can use a larger balloon size- wise not to go above 15mm
- Too short < 1 min dilation interval results in inadequate stretching of the sphincter muscle and edema increasing risk of pancreatitis
- Adverse event of perforation occurs if stone gets impacted between the balloon and the duct. Stones should be pushed above the dilation balloon prior to inflation of the balloon.
- Stone clearance success rate-88% with only 7% requiring lithotripsy-Ersoz et.al., GIE 2003

Important and common questions related to oesophageal dilatation:

1. Can biopsy and dilatation be done simultaneously?

Ans: Traditionally biopsy is done after dilatation as there is a risk of the biopsy site acting as lead point for perforation. Barkin et al in an observational study did not note any complication in 48 patients who underwent dilatation immediately following biopsy.

Barkin JS, Taub S, Rogers AI The safety of combined endoscopy, biopsy and dilation in esophageal strictures. Am J Gastroenterol. 1981;76(1):23.

2. What is the end point of esophageal dilatation?

Ans: No definite guidelines. However, dilatation to 18 mm usually allows intake of regular diet.

3. What is a French?

Ans: French is a measure of circumference i.e $\pi \times$ diameter (mm). 3Fr is 1mm.

4. What is a refractory stricture?

Ans: Kochman criteria:

Refractory stricture is anatomic restriction because of cicatricial luminal compromise or fibrosis that results in the clinical symptom of dysphagia in the absence of endoscopic evidence of inflammation.

Refractory: Inability to successfully remediate the anatomic problem to a diameter of 14 mm over 5 sessions at 2-week intervals (refractory)

Recurrent: Inability to maintain a satisfactory luminal diameter for 4 weeks once the target diameter of 14 mm has been achieved (recurrent).

This definition is not meant to include those patients with an inflammatory stricture (which will not resolve successfully until the inflammation subsides) or those with a satisfactory diameter who have dysphagia on the basis of neuromuscular dysfunction (e.g., those with postoperative and postradiation therapy dysphagia).

Q: Comparision of SG and CRE dilators?

Ans: saeed et al., GI endoscopy 1995-Both are equally effective in achieving a dilation of 12mm and relieving dysphagia. Scolapio et al., GIE 1999- Both SG and balloon dilators are similar in efficacy. Severe the stricture- the repeat dilation chances are higher in < 1 year

Q: In CRE whether pressure and dilation are correlated?

Ans: Vargo et al., TTS balloon dilators-poster-Boston CRE has under inflation and correlates up to 96.5% of the time

Q: Does Endoscopic biliary sphincter dilation assist in biliary stone extraction?

Ans: Attansaranya et al., GIE2008-90% of stones can be removed with biliary sphincterotomy alone. 95% of stones can be removed if combined sphincterotomy and sphincteroplasty were done. Itoi et al., AmJ2009- combined sphincteroplasty and sphincterotomy reduce the procedure time and chance of lithotripsy in large CBD stones. Amit Maydeo., Endoscopy 2007-Accepting 8% chance of minor bleeding, if bile duct stone is larger than the sphincterotomy size sphincteroplasty after sphincterotomy can be safe and effective

Q: How to convert ATM to kPa?-

Ans: 1ATM = 101.3kPa; 1.5ATM= 151.kPa- every 0.5 increase in ATM app. 51kPa should be added to the earlier value

PNEUMATIC DILATATION

Indication

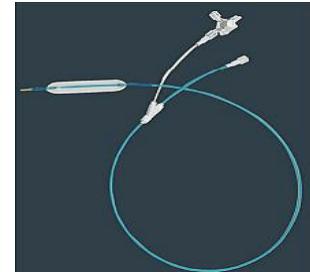
- Achalasia cardia

Instruments:

Rigiflex II- Boston Scientific	Achalasia Dilator- Shaili
Sizes: 30mm/35mm/40mm	Sizes: 25mm/30mm/35mm
Balloon length: 10cm	Balloon Length: 10cm
5 radioopaque markers- for accurate placement of balloon-1 proximal; 2 in center and 2 at shoulders	2 markers
Working length: 90cm	Working length: 110cm
Pneumatic hand pump and monitor	
Atraumatic soft tip	

Contraindications

- Coagulopathy/ Esophageal varices- Relative
- Ephiphrenic diverticula
- Lack of manometric confirmation of problem
- Uncooperative patient- Patient unfit for surgery



Technique:

- Thorough endoscopic examination performed to rule out pseudoachalasia
- Distance of gastroesophageal junction (GEJ) is then noted
- Position of GEJ may be marked by externally applied radioopaque marker or 1 ml of contrast injection into the submucosa at the level of GE junction
- Through the working channel a SG guidewire is passed into the stomach
- The endoscope is then withdrawn
- Over the guidewire the lubricated balloon is passed into the esophagus
- Balloon is positioned such that the middle of the balloon corresponds to the GEJ
- Balloon is inflated and waist formation noted under fluoroscopy
- Balloon inflated with air till waist completely obliterated and maintained for 1 minute
- Average inflation pressure required is 7 – 15 psi
- Two such sessions are done
- Post dilatation gastrograffin contrast may be administered to assess for any esophageal perforation

Post procedure care

- Notify immediately if chest pain, respiratory distress nausea, and vomiting, circulatory collapse.

Goals of treatment:

- A decrease in post dilatation lower esophageal sphincter (LES) pressure to < 10 mmHg

Csendes et al., "Late Results of a Prospective Randomised Study Comparing Forceful Dilatation and Oesophagomyotomy in Patients with Achalasia." Eckardt, Gockel, and Bernhard, "Pneumatic Dilation for Achalasia."

Response to pneumatic dilation:

- Initial response rate 71% – 90%
- Over 5 years ~ 50% have relapse of symptoms

Predictors of outcome:

- Outcome is favourable if reduction in LES pressure is < 10 mm Hg
- Younger age (<40 years) has a less favourable response
- Patients with type II achalasia respond very well to pneumatic dilatation

Complications:

- Esophageal perforation (3%- 5%)
- Bleeding
- Hematoma
- Mucosal tears
- Gastroesophageal reflux disease (< 2%)

Common questions related to Achalasia cardia:

■ PD versus Laparoscopic Heller's myotomy (LHM):

A metaanalysis of three randomized controlled trials comparing LHM with PD, suggested that at one year follow up LHM may provide a better response rate compared to PD Yaghoobi et al., "Laparoscopic Heller's Myotomy versus Pneumatic Dilatation in the Treatment of Idiopathic Achalasia.". The meta-analyses did include one large trial of 201 patients where all patients underwent two consecutive dilatation sessions with 30mm and 35 mm balloon Boeckxstaens et al., European Achalasia Trial Investigators, "Pneumatic Dilatation versus Laparoscopic Heller's Myotomy for Idiopathic Achalasia.". In this trial LHM was not found to be superior to PD.

■ Newer treatment options:

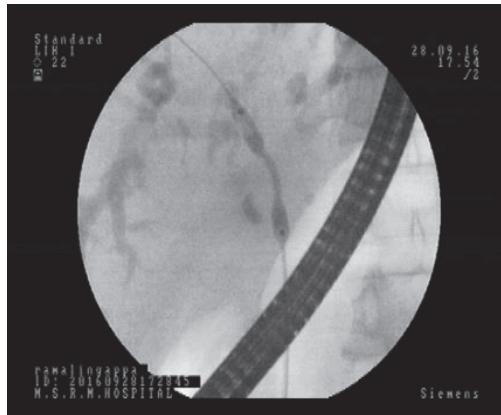
- ▶ Per oral endoscopic myotomy (POEM)
- ▶ Chinese study showed successful use of FCSEMS (30 mm) placed across GE junction for management of Achalasia Cardia



Biliary/Pancreatic balloon Dilators

- 4Fr. Tip for less traumatic passage across the stricture
- Lengths 2 and 4 cm; 4,6,8,10mm diameter sizes; 2 RO positioning markers for accurate positioning
- Aim: To obliterate the stricture waist slowly
- Uses: Dilatation of biliary/pancreatic strictures
- Pneumatic noncompliant polyethylene balloons
- Stricture at mid point of the balloon
- Balloon inflated with dilute- 10-20% contrast and pressure adjusted to obliteration of waist
- For pancreatic strictures - first guide wire is placed across - dilated either using graded Teflon catheters of 5,7,10Fr or balloon - but balloon kept inflated for longer time of 2-3 min - persistence of waist - tight stricture+. The choice of the balloon depends on the normal part of the duct downstream from the obstruction

Hurricane Rx single use biliary balloon dilator (Boston Scientific Corporation)	Quantum TTC biliary balloon dilators (Wilson Cook Medical Inc.)
Sizes: 4mm, 6mm, 8mm and 10 mm	Sizes: 4mm, 6mm, 8mm and 10 mm
Length: 2 cm and 4 cm	Length: 3 cm
Length: 180 cm	Length: 180 cm
Catheter size: 5.8F	



SOHENDRA BILIARY DILATATION CATHETER: (Cook Medical Systems)

Uses: For dilatation of papillary orifice/ biliary strictures/pancreatic strictures

Sizes: 6 Fr – 11.5 Fr

Characteristics:

Tapered tip length is 3 cms

- Marker corresponds to the maximum diameter of the dilator
- The diameter at the tip
 - 6Fr and 7Fr – 4Fr
 - 8.5Fr – 5
 - 9Fr and 10Fr – 6Fr
 - 11.5 Fr – 7Fr
- Minimum accessory channel – 2.8 mm
- Guide wire: 0.035 inch

Contraindications:

- General contraindications to endoscopy
- Stricture related to portal biliopathy

Technique:

- A guidewire is placed across the stricture
- The biliary dilator is then advanced over the wire and passed across the stricture
Position of dilator confirmed by visualization of radio opaque marker

Common questions related to biliary dilatation:

1. Causes of biliary strictures:

- a. Infective:
 - i. Tuberculosis
 - ii. Recurrent pyogenic cholangitis
- b. Inflammatory:
 - i. Chronic pancreatitis
 - ii. IgG4 cholangiopathy
 - iii. Primary sclerosing cholangitis
 - iv. Eosinophilic cholangitis
 - v. Portal hypertensive biliopathy
 - vi. Mast cell cholangiopathy
- c. Iatrogenic:
 - i. Post-operative
 - ii. Post liver transplantation – Anastomotic strictures and Non anastomotic strictures
 - iii. Post radiation
 - iv. Post PAIR for hydatid cyst

d. Neoplastic:

- i. Cholangiocarcinoma
- ii. Ca Gall bladder
- iii. Pancreatic head cancer
- iv. Ampullary cancer
- v. Lymphoma
- vi. Ca Stomach with liver metases
- vii. Histiocytosis X

2. How to differentiate benign from malignant bile duct strictures:

- a. Brush cytology – Sensitivity 45%
- b. Brush with biopsy - Sensitivity 60%
- c. Brush cytology with fluorescence in situ hybridization – Sensitivity 75%
- d. EUS: Sensitivity 80%
- e. Spyglass with spybite – Sensitivity 90%

3. Management of benign bile duct stricture:

- a. Multiple plastic stents
- b. Fully covered SEMS

Surgery

Q: Three common areas of strictures in GIT?

Ans: Esophagus/Pylorus/Colon

Q: Four benign strictures of Esophagus?

Ans: Anastomotic stricture/post RT/Web/Schatzkis ring

Q: Prior dilation, three rules?

Ans: Diameter of stricture and diameter of dilator and rule of 3

Q: Why fluid is used for dilation instead of air?

Ans: Fluid is compressed state and risk of perforation is lesser. Fluids used are- water/contrast/saline

Q: What does CRE stand for?

Controlled radial expansion- Indicates single balloon can inflate to 3 distinct sizes

Q: Why Alliance gun should not be filled upto 35ml?

Ans: Negative pressure allows vacuum to be created and deflation of balloon happens

Q: What are CRE balloon characters?

Ans: PEBAX material allows 3 distinct sizes for 3 distinct pressures without waisting. Rounded shoulders are for endoscopic visualisation. Endoscopic exit marker is for marking complete exit of the balloon from the scope.

Q: What is different with wire guided CRE as compared to fixed wire CRE?

Ans: Balloon is smaller to facilitate complex and tortuous strictures and the wire fixes the balloon during dilation. There is a double lumen catheter which facilitates injection of contrast through the guidewire port.

Q: Precautions to take while using rigiflex balloon?

Ans: remove as much air as possible before introduction, do not attach inflation device till the balloon is in position and adequate lubrication is needed for safe passage across the esophagus

Q: Why air is used for Rigiflex dilation?

Ans: For rapid inflation which will cause tearing of muscle fibers and prevent sphincter spasm during peristalsis

Q: What is the difference between Hercules CRE and Boston Scientific CRE?

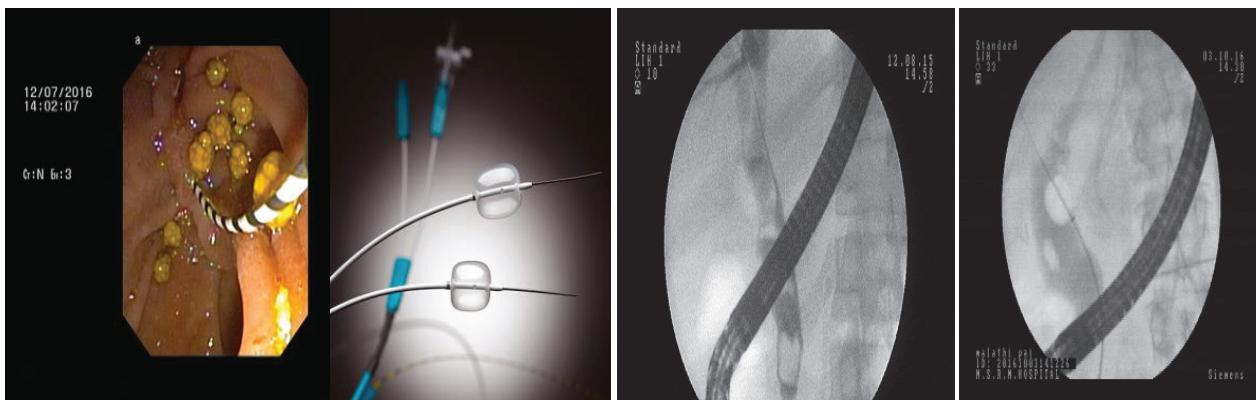
Ans: Hercules is 2cm longer with square shoulders as compared to smaller balloon with Boston and rounded shoulders. Rapid deflation is feasible with Hercules (COOK medical) with PETFLEX material as compared to PEBAK in Boston.

Q: What is the difference between wire guided and nonwire guided dilators?

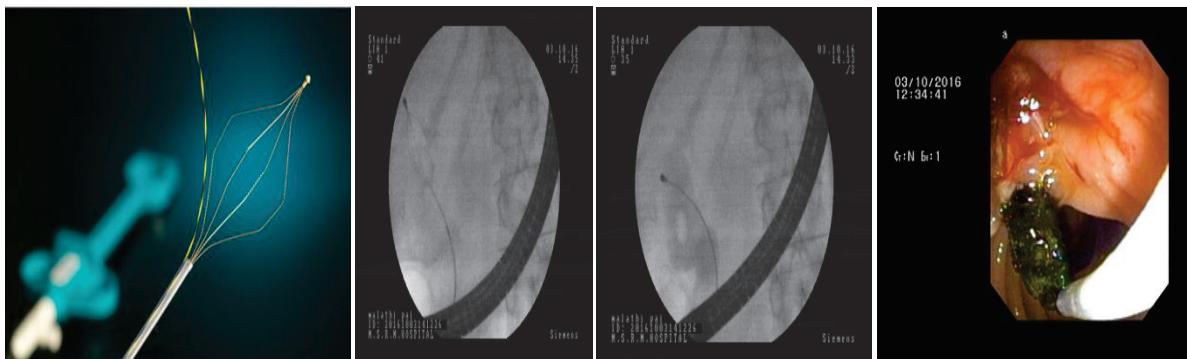
Ans: Non-wire are used for self dilation and for simple <2cm strictures- Mercury/bougie; Rounded tip- Hurst dilators and tapered end- Maloney. Wire guided have RO markers and require a wire placement under fluoroscopic guidance and follow rule of 3. There is no 13mm dilator.

STONE EXTRACTION BALLOON:

- Each of the three balloon sizes can be inflated to two distinct diameters: 9–12mm; 12–15mm; 15–18mm to better accommodate anatomical variations
- Squared shoulder balloon facilitates stone removal by maintaining contact with the duct wall on all sides during the sweep thereby preventing slippage of small stones, stone fragments/ sludge
- Triple-lumen Retrieval Balloon- Catheter is designed to be easily back loaded over a guidewire, injection-above or injection-below options for contrast and another for inflation of balloon by a higher flow rate for 50/50 contrast/water mix.
- The current recommendation is to remove all the stones at the time of sphincterotomy and to place a temporary stent if that cannot be achieved
- The stiff tip of the balloon catheter may make cannulation difficult and is best done over an established guidewire. Inject contrast from IHBR down – avoid filling GB- concern of chemical cholecystitis
- When there are several stones- best removed one at a time starting with those nearest the papilla
- With adequate sphincterotomy, stone can be expelled from the CBD by downward deflection of scope and right rotation. Avoid pulling the balloon too hard against the stone as it can rupture the balloon or slip past the stone



Stone Extraction Basket:



- Braided stainless steel or nitinol wires
- Open basket diameter of 1.5-3cm
- Recommended guidewire- 0.035"- recommended working channel of 3.2mm
- Silver tip in trapezoid basket disengages in case stone does not break and avoid basket impaction
- Alliance II inflation device can be used for crushing the stones
- Injection can be done with wire and basket in place
- Basket is inserted and opened above the stone and withdrawn in a fully opened position
- Basket is moved gently up and down or jiggled around the stone to trap it
- Basket can be withdrawn till papilla in fully open position and scope suction can be used for sludge removal
- Important to remove lowest stone and avoid trapping too many stones at a time
- Never close the basket tightly around the stone unless one is committed to remove the stone. Excess tension on the basket wires can cause the wires to cut through the stone and make it difficult to release the basket in case stone could not be retrieved- basket impaction (0.8-5.9%)
- Caution: Avoid pushing the stone into the IHBR as a tip of release of stone impacted in a closed basket is to release in proximal CBD
- Pancreatic calculi are harder and difficult to retrieve. ESWL and pancreatic stents have to be used multiple times till complete clearance is achieved.

Lithotripsy:

- Large stones > 15mm(stones bigger than the scope on fluoroscopy), Multiple large stones > 10 stacked in non dilated duct, Impacted stones, unusual shape of duct or stone, stones proximal to stricture, stones at unusual locations- IHBR,cystic duct, bile duct diverticulum, anatomical alterations of bile duct are difficult to remove
- Soehendra Lithotripter (COOK Endoscopy): 14Fr- metal sheath- rail roaded over the plastic sheath basket which held the stone- metal sheath advanced all the way to the level of stone under fluoroscopic control and tightened slowly by using a handle
- Standard baskets are not designed for lithotripsy- if traction applied- basket might break but not the stone.
- Stones greater than 20mm- require fragmentation before removal-Riemann JF et.al., Endoscopy 1982
- Electrohydraulic lithotripsy can be used with constant irrigation of saline under cholangioscopic control with 85-98% success and complication of 2-9%- pancreatitis/cholangitis/hemobilia. Binmoeller. Endoscopy 1993; Itoi T et al., Dig Endoscopy 2013
- ESWL is rare for CBD stones

Q: What is the most important predictor of success at ERC and stone extraction?

Ans: Cipoletta et.al., Br J Surg 1997- Stone size. Garg et.al., GIE 2004- Stone and duct size - both are important. Impacted stone or failure of the basket to capture the stone are most important.

Q: What are the concerns of intrahepatic choledocholithiasis?

Ans: Hepatolithiasis- stones in IHBR.MC in biliary strictures secondary to PSC/oriental cholangiohepatitis/parasitic infections/post operative/recurrent cholangitis. Main treatment is surgical resection of the afflicted segment as there is potential risk of cholangiocarcinoma. Mainstay of Mirizzi syndrome is surgery.

Endoscope and Endoscopy

Diagnostic Indications:

- Upper gastrointestinal symptoms – pain/ nausea that persist despite an adequate trial of therapy; Alarm features: weight loss, or who are over the age of 50 years, dysphagia, odynophagia, persistent vomiting of an unknown cause, or diarrhea
- Upper gastrointestinal bleeding – Active or recent upper GI bleeding/ chronic blood loss and iron deficiency
- Abnormal imaging – suspected neoplasms, ulcers, strictures or obstructions

Caustic ingestions — to assess the degree of injury

Screening/surveillance — Barrett's esophagus

Screen patients for gastric cancer- older patients with atrophic gastritis or pernicious anemia or with partial gastrectomy/gastrojejunostomy, sporadic gastric adenoma, immigrant ethnic populations from countries with high rates of gastric cancer, and patients with familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer (particularly if gastric cancer has occurred in the kindred).

Screen patients with portal hypertension for the presence of esophageal varices and to screen patients with a history of a caustic ingestion for esophageal squamous cell carcinoma.

Therapeutic intervention

- Treatment of bleeding lesions (ulcers, angiodysplasias, varices)
- Prophylactic banding of esophageal varices
- Removal of foreign bodies
- Placement of feeding or drainage tubes
- Removal of selected polypoid lesions
- Dilation of stenotic lesions
- Management of achalasia
- Palliation of stenosing neoplasms
- Endoscopic therapy of intestinal metaplasia
- Management of operative complications (eg, anastomotic strictures)

Contraindications:

- Risk > Benefit
- Uncooperative patient
- Perforated Viscus
- Recent Myocardial Infarction- only in case of GI bleeding
- Special Considerations: Small mouth or a limited range of motion in the jaw (factors that may make it difficult to insert the protective mouth piece) Zenker's diverticulum

Patient preparation:

- Diet — Nil by mouth for 4-8 hours or longer in gastroparesis; Liquids 2 hours prior
- Medications — small sips of water; Modify anti diabetic medicines due to decreased oral intake
- Management of anticoagulants — Aspirin and NSAIDs – no problem; Other anti coagulants – monitor PT/INR
- Antibiotic prophylaxis — Variceal bleed/ percutaneous endoscopic gastrostomy
- Preprocedure testing — NO routine preprocedure test. But selective testing depending on risk factors
- Pregnancy testing with uncertain pregnancy history; (particularly if fluoroscopy is going to be used; Coagulation studies for patients with active bleeding/ bleeding disorder/anticoagulant use.
- Chest radiograph for patients with new respiratory symptoms or decompensated heart failure.
- Hemoglobin, platelet count, PT/INR, PTT for patients with preexisting significant anemia or active bleeding, or if there is a high risk of significant blood loss during the procedure.
- Serum chemistry testing for patients with significant endocrine, renal, or hepatic dysfunction.

Sedation:

- Prior difficulties with sedation, narcotic or benzodiazepine use, diminished mental capacity, and agitation or severe anxiety
- Increased risk for aspiration (ascites, non-empty stomach, active bleeding)
- Difficult airway management (eg, obesity, non-visibility of the uvula, prior history of difficult intubation)
- Increased cardiopulmonary complications of endoscopy (eg, comorbidities, obesity, older age)

Consenting: 5- Nature of the procedure/Benefits/Risks/Alternatives/Limitations of procedure

Written documentation of the discussion of consent is mandatory

Technique: High-definition white light endoscope- Steps:

- Oral intubation with the endoscope
- Oropharyngeal examination
- Esophageal examination
- Examination of the esophagogastric junction (EGJ, also referred to as the gastroesophageal junction)
- Gastric examination, including retroflexion
- Traversing the pylorus
- Duodenal examination
- Tissue sampling
- Therapeutic maneuvers

Intubation with the endoscope: Topical pharyngeal anesthesia with Lignocaine spray (risk of methemoglobinemia) and Lignocaine gel for topical pharyngeal anesthesia.

Upper GI endoscopy: Left lateral side positioning with their neck flexed forward, knees flexed. Proper orientation from mouth to upper esophageal sphincter (UES) under direct visualization- view epiglottis, the vocal cords, both piriform sinuses, and the arytenoid cartilages.

UES is traversed with air insufflations and mild pressure on scope at 15-18cm from incisors.

Esophageal intubation should be done slowly and gently (Caution: Zenkers/proximal esophageal strictures)

Esophagus and esophagogastric junction: Tubular esophagus- app. 25cm in length. Slow examination and complete visualization with air insufflations. Elements to note include the color of the mucosa and evidence of erythema, erosions, ulcers, strictures, rings, webs, varices, or diverticula.

The top of the gastric folds is the landmark to represent the esophagogastric junction (GE Jn). The squamocolumnar junction is the area where the squamous epithelial lining of the esophagus meets the columnar lining of the stomach. The columnar mucosa of the stomach is salmon-colored, whereas the squamous mucosa is pale pink.

Stomach — Post GE Jn- Initial visualization is usually of the relatively large folds of the greater curvature → along greater curve scope passed towards pylorus.

First- Avoid full insufflation of the stomach initially, as it may induce retching or belching.

Second, suctioning the pool of fluid that is often seen in the fundus upon entering the stomach improves visualization of the area, minimizes the risk of reflux and possible aspiration. A plastic trap can be placed in line with the suction tubing to collect this fluid for pH analysis if needed. Avoid suction artifacts.

Adequate visualization of the proximal stomach and esophagogastric junction is achieved through retroflexion. Retroflexion allows the endoscopist to see areas that are not well visualized during the initial direct examination.

Retroflexion: Distending the stomach with air → advancing the endoscope to the region of the angularis in the lesser curvature in the antrum → turning the endoscope up-down dial to the maximal up position to achieve a 140 to 160 degree bend at the tip of the endoscope → Withdrawing the endoscope in order to pull the tip of the endoscope toward the esophagogastric junction and rotating the endoscope to obtain a 360 degree view of the upper stomach.

Pyloric intubation: Pylorus traversed under direct visualization- opening of the pylorus requires air insufflations-looping/ pressure on gastric wall/removal of air from stomach- can help pyloric intubation.

Duodenum: After passing through the pylorus, the endoscope enters the duodenal bulb → then advanced through the duodenal sweep and into D2.

D1: Raised bumps and polypoid areas → prominent Brunner's glands or heterotopic foci of gastric mucosa

D2: Distinctive circular rings called valvulae conniventes

Ampulla: ? standard forward-viewing endoscope- more detailed examination with use of a side-viewing duodenoscope

Tissue sampling: Biopsies/Brushings/polypectomies

Biopsy: Biopsy forceps is placed through the accessory channel of the endoscope- advanced to the target area, and the forceps is opened and closed to obtain a **pinch biopsy**. Spike on forceps allows for acquisition of more than one sample at a time.

Turn in technique: Tubular esophagus may be difficult to biopsy because the forceps comes out of the accessory channel parallel to the wall of the esophagus. Tip of the endoscope is turned to be more perpendicular to the wall of the esophagus, allowing for a more direct angle in which to obtain a biopsy. Suctioning of the mucosa prior the biopsy forceps allows a larger sample to be obtained with each "bite" of the biopsy forceps.

Typically, biopsy forceps can only sample mucosal lesions. If a submucosal lesion → Tunnel biopsies- the same location is biopsied multiple times with the hope of obtaining deeper samples

When urgent diagnosis of suspected cancer is needed in a hospital setting- squash biopsy/frozen specimen for immediate cytology preparation

Polypectomy: Polypectomy is carried out in a manner similar to that used during colonoscopy. Small polyps may be removed using a biopsy forceps. Larger polyps can be removed using snares that are passed down the accessory channel of the endoscope. Lesions larger than approximately 2 cm may require removal using specialized techniques

Photodocumentation and reporting: All endoscopic procedures should include a complete report detailing the extent of the tissue examined and all normal and abnormal findings encountered.

Trouble shooting: Complete mucosal examination

Excessive motility in the stomach or small bowel: Patience is necessary to allow the bowel to "quiet" for complete visualization. Medications- Glucagon/Buscopan (important for APC)

Bubbles and excessive mucus: Adequate washing using an irrigating syringe - agents that lower surface tension of bubble- simethicone or mucolytic agents-N-acetyl cysteine

Residual material in the stomach: Prokinetics - Erythromycin or metoclopramide

Abnormal anatomy (eg, a J-shaped stomach in the chest) or surgically altered anatomy (eg, bariatric surgery) - changing the patient's position or the application of external abdominal pressure to "splint" the stomach, may facilitate instrument passage in some situation.

Complications: Overall complication rate was 0.13 percent, and the mortality rate was 0.0002 percent.

Methemoglobinemia: Fe²⁺ irons of heme are oxidized → Fe³⁺ → unable to bind oxygen (Cause- Lignocaine) suspect when normal Pa O₂ on ABG with cyanosis and chocolate brown blood

Bleeding: Thrombocytopenia or coagulopathies. Diagnostic upper endoscopy is generally thought to be safe in patients with platelet counts as low as 20,000/cmm

Perforation:

Diagnostic endoscopy with a flexible endoscope: 0.03 percent

Stricture dilation: 0.09 to 2.2 percent

Sclerotherapy: 1 to 5 percent

Pneumatic dilation for achalasia: 2 to 6 percent

Infection: The risk of infection related to gastrointestinal endoscopy is low: breach in protocols of disinfection

ERCP

Sphincterotome: Types

- Standard or non wire guided
- Wire guided
- Pre cut sphincterotome
- Billroth II sphincterotome
- Needle knife sphincterotome

Cutting wire- Nose

- Long: Dis adv: Leakage of current and diff. to bow as the cutting wire might be within the channel
- Short: Adv: Higher current per unit area
- Long nose: maintains orientation during cutting but needs deep cannulation
- Short nose: cannot maintain orientation but doesnot require deep cannulation

Ultratome XL

- Triple Lumen- cutting wire, guidewire & injection
- 20mm cut wire
- 5.5Fr Tip size
- Radio opaque distal tip
- Monofilament cut wire
- Calibration in distal part sphincterotome- length of CBD

Indications for sphincterotomy:

- Choledocholithiasis
- Bile leaks
- Bile duct stent placement
- SOD dysfunction

Contraindication:

- Coagulopathy
- Stop clopidogrel for 7 days; Aspirin and NSAIDS no risk- Onal IK.et.al.,Clin Res Hepatol Gastroenterol 2013

Technique:

- First guidewire is used to cannulate the required duct. GW provides the necessary anchor while sphincterotomy is done. Advance the tip of the sphincterotome into the ampullary orifice and gentle advancement of GW into the desired duct.
- When bowed- the cutting wire of the sphincterotome is in line with the duct then proceed with the cut. When more deviation is noted- more towards right- increased risk of perforation/bleeding/pancreatitis. Excess bowing will result in Zipper cut.
- Sphincterotome is adjusted until only 1/3rds of the cutting wire is inside the papilla.

- Blended (cut + coagulation) current in short bursts to de-roof the papilla in step wise manner is the principle. Whitening of the tissue upon passage of current is the beginning of the cut. If tissue does not blanch after passage of current- pull back the sphincterotome, increase the wire contact with the tissue and increase the current density. Too little contact generates smoke and no cut. Pure cut increases chance of bleed with no difference of pancreatitis as compared to blended current - Verma D et.al., GIE2007
- Axis of the cut should be along 11'0 clock. Do not manipulate the scope position. If axis of cut is 12'0clock there can be chance of perforation/bleed
- Adequacy of cut depends on the distal bile duct and the shape of the papilla. The cut should not go beyond the impression of the bile duct on the duodenal wall.

Needle Knife papillotomy:

- 5mm needle knife- no nose
- Used when standard cannulation techniques fail
- Can also be used for transgastric pseudocyst drainage
- Pre cut sphincterotomy

Technique of pre cut papillotomy: Cut prior to obtaining deep access by GW. Goal- not to do complete sphincterotomy but only to access desired duct

- If standard sphincterotomy fails - pre cut sphincterotomy can be done. If PD cannulation succeeds - prophylactic PD stent can be placed
- If ampullary edema is noted - second attempt can be planned after 24-48 hours as identifying ductal planes can be difficult
- Double wire technique can be used- with a wire in PD and the tip of cannula/sphincterotome directed towards 11'0 clock. PD wire /stent stabilises PD and orients CBD orifice for selective access
- Negotiating PD wire across into body and tail must be gentle as GW can repeatedly enter side branches and risk of PD perforation/pancreatitis
- Cut is below upwards and layer by layer fashion by gentle motion of big wheel and left torque tracking intraduodenal portion of CBD
- Needle should be only 2-4mm exposed and cuts should be precise and of 1-2mm increments
- Depth of the cut should be assessed periodically by saline/CO₂
- Proximal extent of the cut must stop short of the upper margin of the ampullary mound
- Intramural CBD is noted as yellow white longitudinal muscle and biliary orifice as a nipple/most prominent portion once de roofed
- Gentle suction- might get a speck of bile and can be used for guidance. Once GW cannulation is done- sphincterotomy as standard procedure follows
- Pre cut fistulotomy: Cut from above down is done in impacted ampullary stone/large bulging infundibulum. It has less chances of pancreatitis and perforation as the upper end of the cut is predetermined - Mavrogiannis et.al. GIE 1999. Upper end is at junction of upper third and lower 2/3rds and lower end stops short of papilla.
- Do not do both the cuts. Always note the papillary orifice. Do not destroy land marks
- Transpancreatic Sphincterotomy: If sphincterotome is in PD cut along 11'0 clock through the septum- advantage is that no exchange for needle sphincterotome is required

Sphincterotomy - Ikeda Cramer technique- check

Q: What is ampulla and what is papilla?

Ans: Mirilas P.Am Surg 2005- Ampulla-dilated part of a duct topographically to describe the dilatation at the confluence of the bile and MPD. First description was by Santorini rather than Vater. Papilla of Vater is an eponym and should be replaced by hepatopancreatic ampulla/ biliaropancreatic ampulla/ major or greater papilla.

Q: When is the sphincterotomy adequate?

Ans: A gush of bile flowing from the bile duct, fully tightened/bowed sphincterotome can be passed into the bile duct without any resistance

Q: What are the rules of pancreatic sphincterotomy?

Ans: Once sphincterotome is engaged- there should be a low threshold to inject contrast for delineating the path. Proper orientation is a must. For removal of PD stones/placement of stents/transpapillary drainage of pseudocysts/ less likely for SOD dysfunction. Only small amount of cutting wire to be used to maximise the current density and minimise tissue trauma. Pancreatic axis is 1-2'0clock and the duct is smaller- GW must be 0.021" or 0.018" placed in body of pancreas and cut till septum between CBD and PD is noted- slightly bowed sphincterotome is pushed through the orifice without resistance. ? pure cut can be used instead of blended current to prevent possible late stenosis. Always place PD stent after pancreatic sphincterotomy to prevent pancreatitis due to edema. The typical cut length will be 5-10mm. Complications- Bleeding/perforation/pancreatitis and late > 3 months- PD stricture. Pancreatic sphincterotomy with placement of PD stent have 64% relief of pain at 7 year follow up-gabbrielli A et.al.,GIE 2002.

Q: What is the technique of Minor sphincterotomy?

Ans: Needle knife can be used. GW cannulation followed by placement of 3/5Fr pD stent into proximal PD through minor papilla. Once stent in position, GW removed, cut the mound above the stent. Cut is directed in 11'0 clock. First done by Cotton- Endosc Digest 1978. Significant pain relief at 2 years-Vitale GC Surg Endosc 2007

Q: Is cannula better or sphincterotome better for cannulation?

Ans: Costamagna et.al., Endoscopy 2003- Higher cannulation rates with sphincterotomes Vs biliary cannulas. No single type of sphincterotome is superior to other. Halittunen et.al., Endoscopy 2013- 0.025" Vs 0.035" GW- individual preference- no difference in success or complication

Q: When do you consider doing pre cut sphincterotomy?

Ans: 5-12minutes of standard cannulation failure

Q: What is the problem of ERCP in Billroth II anatomy?

Ans: Billroth II has antrectomy and GJ with end to side anastomosis of afferent limb - leading to papillas and efferent limb leading to distal small bowel. The presence of bile is not a reliable indicator. Afferent loop should generally be towards lesser curve. Use either duodenoscope/colonoscope/enteroscope as afferent limb is too long. A GW/clip/tattoo can be placed to identify the afferent loop prior to duodenoscopy. The endoscopic image is inverted. Bile duct orifice is at 5'0 clock. Billroth II papillotome (Cook medical)/rotatable sphincterotome can be used with the cutting wire in the opposite direction. Straight biliary cannulas can be used for cannulation.

Q: What is the incidence of choledocholithiasis in patients who undergo cholecystectomy?

Ans: 10% Ko CW et.al. GIE 2002. ERC and standard sphincterotomy can be successful in removal of 85-90% of them-Yasuda I-Dig Endoscopy2013.

Q: What is the role of EUS in failed cannulation?

Ans: Dhir et.al. GIE 2012- EUS rendezvous or antegrade approaches can be used by puncturing CBD/IHBR by 19G FNA needle under EUS guidance and passing GW through the FNA needle and exchanging for duodenoscope-helpful in surgically altered anatomy.

Q: When is biliary sphincterotomy done along with pancreatic sphincterotomy in chronic pancreatitis?

Ans: Kim MH Endoscopy 1998- Presence of cholangitis/CBD > 12mm/Alkaline Phosphatase > 2X ULN/difficult to access MPD/Need for biliary intervention. Double wire technique can be used. Prior BS can help in PS as it exposes pancreaticobiliary septum.

Q: What are pancreaticogram findings in P Divisum?

Ans: Cannulation of minor papilla results in pacification of dorsal PD to tail. Cannulation with pull type sphincterotome and PD stent must be placed.

Q: What percentage of pancreatic stones respond to endotherapy?

Ans: Guda et.al. Rev Gastroenterol Disord. 2005 - 65% of chronic pancreatitis with strictures and stones respond to endotherapy

Q: What are the strictures amenable for endotherapy?

Ans: Adler et.al., GIE 2006- MPD strictures are termed high grade if MPD dilation > 6mm beyond the stricture and failure of contrast to flow through the stricture. Endotherapy is ideal for head strictures and not good for tail strictures or multiple strictures giving a chain of lakes appearance. Large bore stents 7-10Fr can be used for treating as they have longer patency. Dominant PD strictures should be treated with single 10Fr stent with stent exchanges once a year

Q: What is the treatment for pancreatic duct leak?

Ans: Adler DG GIE 2005-PD leak - extravasation of contrast on pancreaticogram. Corner stone in treatment is PD stent and better if it bridges the leak. Disconnected pancreatic duct leak: DPDS - complete discontinuity of PD so that viable portion of PD does not drain down stream- symptoms are dependent on the site of disruption- head- more severe.

Q: What approach is better for pseudocysts?

Ans: Pseudocysts are nonepithelial lined fluid collections from transient or persistent PD disruption. Treatment is indicated in symptomatic pseudocysts or development of complications- infection, bleeding, biliary or gastric outlet obstruction - size alone does not dictate the need for intervention. There is low rate of spontaneous resolution with pseudocysts in chronic pancreatitis. The placement of multiple side by side plastic stents in biliary stricture allows biliary drainage both through the stents and between the stents.

Contraindication for endoscopic cystogastrostomy: Cyst to stomach wall distance > 1cm, Vascular structures in projected needle path which cannot be avoided by EUS and pseudoaneurysm.

Caution: Presence of debris in a cyst increases risk of infection. Transpapillary drainage when PD is communicating with MPD, small symptomatic pseudocysts < 6cm and takes care of the ductal pathology as well. Transduodenal is better than transgastric drainage.

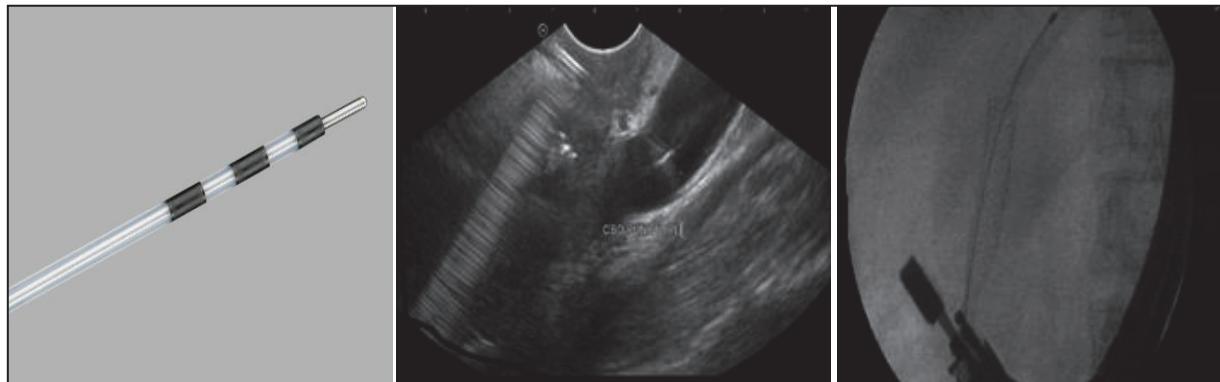
Conventional transmural drainage: Duodenoscope into stomach - extrinsic compression- needle sphincterotome using blended current - puncture- cyst fluid aspirated - dish water appearance- guidewire looped in the cyst cavity - puncture site dilated and 2-4 pig tail stents are placed.

EUS transmural drainage: EUS can visualise safe site of puncture

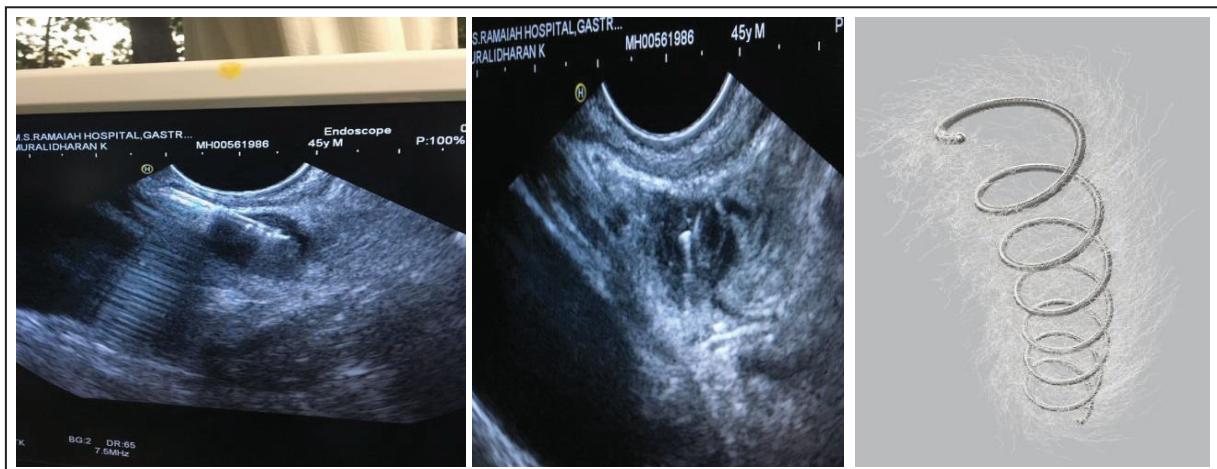
Cystotome: Cook Medical

- To electrosurgically puncture a hole in the transgastric or transduodenal wall and into a pancreatic pseudocyst, when there is a visible bulge or under EUS guidance.
- Supplied sterile and is disposable — intended for single use only.

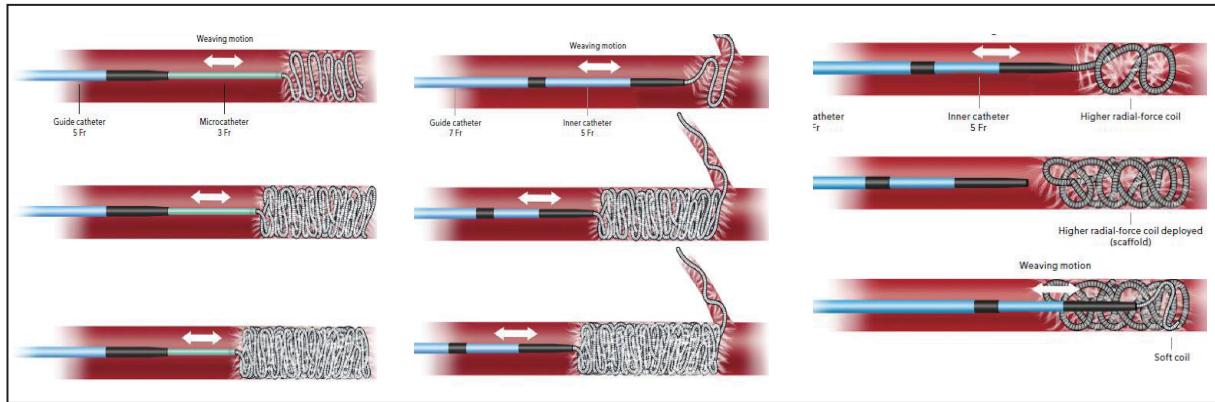
- Make initial incision with .038" needle knife in a 5 Fr catheter with pure cut and d the puncture site enlarged with the 10Fr outer sheath using blend diathermy
- Accepts .035" wire guide to maintain position after first incision and facilitate placement of a stent
- Combining a needle knife and diathermic ring eliminates need for instrument change, reducing procedure time



Embolisation Coils: Nester- Cook Medical



- Soft platinum Nester coils are available in .018 and .035 inch sizes.
- The coils lengths are 3 to 20 cm and diameters are 2 to 20 mm when coiled.
- Nester conforms inside the vessel to create a tight occluding mass and synthetic fibers help promote clot formation.
- They are easily visible under fluoroscopy



Techniques: useful in preventing embolization of coil

1. Coaxial Technique: Weaving motion of the needle as well as the stylet with which the push of the coil is done
2. Anchor Technique: get the end of the coil at a branch and deploy
3. Scaffold technique: make a loop and coil is released

On Linear EUS scope, transesophageal puncture is made using 19G FNA needle and aspirated blood to conform intravariceal needle placement. Target is either intragastric fundal varix or perigastric collateral. Once inside the blood vessel- Nester coil is placed inside the 19G needle and introducer is removed. The stylet is used as a pusher tube and with small movements of needle and stylet the coil is placed intravariceally. EUS and fluoroscopic visualisation of coil placement is good.

RISKS FOR BLEEDING

LOW RISK FOR BLEEDING	HIGH RISK FOR BLEEDING
All investigations procedure ± MUCOSAL biopsy Argon plasma coagulation Barrett's ablation ERCP – balloon or stent dilation without sphincterotomy	All therapeutic procedures EUS with FNAC

LOW RISK OF COMPLICATIONS

LOW RISK OF COMPLICATIONS	MODERATE TO HIGH RISK OF COMPLICATIONS
Solitary AF	AF with previous stroke
Single episode of DVT/PE >3 months ago	Multiple episodes of DVT/PE or < 3 months old
Coronary artery stents > 12 months ago	Recent acute coronary event (<4-6 wks), Recent (< 6 months) CVA or TIA DES < 12 months ago, Bare metal stent < 1 month
Non DES stents	Any mitral valve prosthesis, Any caged valve or tilting disc AV prosthesis H/O mechanical valve thromboembolic event
Bioprosthetic valves anywhere	Severe Hypercoagulable states
Any Valve at aortic position	CHAD score > 3

SPECIAL SITUATION CONSIDERATION

CONDITION	ASSOCIATED DIAGNOSIS	MANAGEMENT
Atrial fibrillation	None (lone AF)	Hold warfarin 3-5 days prior, Restart within 24 hrs
Atrial fibrillation	Mechanical valves, CVA history, TIA history, Systemic embolism history	Hold warfarine and start UFH when INR < 2, stop UFH 4-6 hrs before procedure, restart UFH just after procedure, start warfarine on the evening of procedure, continue both till you achieve INR (LMWH can also be considered instead of UFH)
Valvular heart disease	Mechanical bileaflet valve , aortic valve	Hold warfarine 48-72 hrs before procedure for a target INR 1.5, restart warfarine within 24 hrs

CONDITION	ASSOCIATED DIAGNOSIS	MANAGEMENT
Valvular heart disease	Mechanical mitral valve mechanical aortic valve + complications (e.g. AF) or > 1 mechanical valves	Hold warfarine and start UFH when INR < 2, Stop UFH 4-6 hrs before procedure Restart UFH just after procedure Start warfarine on the evening of procedure Continue both till you achieve INR (LMWH can also be considered instead of UFH)

For **Endoscopic Procedures** in patient taking dual antiplatelet therapy or monotherapy with clopidogrel consider continuing spirin (dual therapy patients) or starting aspirin (clopidogrel monotherapy patients) in the periendoscopic period. But for **Acutely Bleeding Patients** hold even aspirin and transfuse platelets !!

Drugs	Category	Stop prior to	Reversal
Aspirin		10 days	Platelets
Eptifibatide & tirofiban Abciximab	GPIIb/IIIa inh.	4 hrs	Platelets ± ? HD for tirofiban
Dipyridamol (di=2)		2-3 days	Hold
Ticagrilor (tica=3)	Thenopyridine	3-5 days	
Clopidogrel	Thenopyridine	5-7 days	Platelets ± desmopressin in overdose
Prasugrel (prasu=5)	Thenopyridine	5-7 days	
Ticlopidine (ticlo=10)	Thenopyridine	10-14 days	
Warfarin		5 days	FFP ± vit. K ,factor VIIa, ? Protamine sulphate
UFH (unfractionated heparin)		IV = 4-6 hrs SC = 12-24 hrs	Protamine sulphate
LMWH		12-24 hrs	Protamine sulphate
Rivaroxaban(non dialysable) Apixaban Edoxaban	Xa inhibitor All are oral	1-2 days	Charcoal Non/activated PCC
Dabigatran(dabi=2) – oral	Direct thrombin inh.	1-2 days	Direct Thrombin Inhibitor

RECOMMENDATIONS :

A. Elective endoscopic procedures

Patients receiving anticoagulant therapy

- We recommend that elective endoscopic procedures be deferred until short-term anticoagulation therapy (eg, warfarin for VTE) is completed.
- We suggest discontinuing anticoagulation (ie, warfarin [Coumadin], NOACs) for the appropriate drug-specific interval in the periendoscopic period if high-risk endoscopic procedures are planned in a patient at low risk for thromboembolic events.
- We suggest continuing warfarin and NOAC in the periendoscopic period in patients undergoing low-risk endoscopic procedures.
- We suggest bridge therapy for patients undergoing high-risk endoscopic procedures who are at high risk for thromboembolic events.
- We suggest that warfarin (Coumadin) be restarted on the same day as the procedure in all patients who do not have ongoing bleeding.
- We suggest that the reinitiation of NOACs after high-risk endoscopic procedures be delayed until adequate hemostasis is ensured, given their rapid onset of action and lack of reversal agents. If therapeutic doses of NOACs cannot be restarted within 12 to 24 hours after a high-risk endoscopic procedure, thromboprophylaxis (ie, UFH bridge) should be considered to decrease risk of thromboembolism, given the short half-life of the NOAC agent, in those with a high risk for thrombo-embolism.

Patients receiving APA therapy

- We suggest that continuation of low doses of ASA and nonsteroidal anti-inflammatory drugs may be continued safely in the periendoscopic period.
- We recommend that thienopyridines be continued for all low-risk endoscopic procedures.
- We recommend discontinuation of thienopyridines at least 5 to 7 days before high-risk endoscopic procedure or switching to ASA monotherapy and continuing until the thienopyridine can be safely resumed.
- We recommend that elective endoscopic procedures be deferred in patients with recently placed intracoronary stents and/or ACS until the patient has received antithrombotic therapy for the minimum recommended duration.
- We suggest that thienopyridines be withheld for at least 5 to 7 days (ticagrelor 3-5 days) before high-risk endoscopic procedures and that ASA be continued for patients requiring dual APA.

B. Urgent and emergent endoscopic procedures

Patients receiving anticoagulant therapy

- We recommend patients with acute GI bleeding on anticoagulation therapy have anticoagulant agents held to facilitate achievement of hemostasis.
- We recommend either (1) 4-factor PCC and vitamin K or (2) fresh frozen plasma be given for life-threatening GI bleeding in patients on warfarin anticoagulant therapy.
- We suggest endoscopic therapy not be delayed in patients with serious GI bleeding and an INR < 2.5
- We suggest patients who require anticoagulation receive UFH because of its relatively short half-life after successful endoscopic hemostasis for high-risk stigmata.

Patients receiving APA therapy

- We recommend consultation with the prescribing specialist (or their colleague) before stopping APAs in situations of significant GI bleeding in patients (1) with recently (< 1 year) placed drug eluting intracoronary stents, (2) within 30 days after insertion of a bare metal intracoronary stent, or (3) within 90 days of ACS. The risk of an adverse cardiac event associated with cessation of the APA therapy likely exceeds the benefit of decreasing postendoscopic.
- We recommend patients on APAs with life-threatening or serious GI bleeding should have these agents held after discussion with their cardiologist.

My understanding is that if patient is on dual antiplatelet treatment coming with UGI bleed, stop both drugs , go for endoscopic procedure and restart aspirin with PPI as soon as bleeding is controlled.

How to tackle a patient with both MI and UGI bleed:

If bleed is life threatening, perform endoscopic therapy before PTCA. however if bleeding is occult then go for PTCA before going for endoscopic hemostasis

PEG

Per Cutaneous Gastrostomy - PEG - Endoscopic PEG placement:

Push (Sachs-Vine) / Pull (Ponsky) / Introducer (Russell) / Versa (T-fastener) techniques.

Indications:

- Intact and functional gastrointestinal tract is a must
 - ▶ Neurologic conditions associated with impaired swallowing
 - ▶ Neoplasms of the oropharynx, larynx and esophagus/ facial trauma
 - ▶ Gastric decompression

Contraindications:

Inability to appose anterior gastric wall to the anterior abdominal wall

- Intestinal obstruction
- Obesity - Transillumination is not feasible. But, 9cm spinal needle as the introducer needle with a 0.025" guidewire and larger skin incision can be used in markedly obese ($BMI >40 \text{ kg/m}^2$) patients.
- Proximal small bowel fistula
- Neoplastic and infiltrative diseases of the gastric wall
- Obstructing esophageal lesions - require dilation followed by placement of PEG
- Gastric varices- might increase the bleeding risk
- Ascites - leak of ascites from PEG site and peritonitis
- Past surgery - Note for adhesion/interposed bowel

Pre procedure:

- Ensure standard cardio-resuscitation equipment is available.
- **KIT:** Regular or therapeutic gastroscope, PEG kit, injectable xylocaine, chlorhexadine swabs, sterile gloves, and snare/grasper forceps
- Ensure the patient is NPO.
- Check that the **Hb, Plt count, PT/INR, APTT** is within therapeutic range to do procedure.
- Check that **prophylactic antibiotics** and Betadine oral gargle was given
- Confirm any **abdominal or gastrointestinal surgeries** with the patient or from the chart.
- Ensure baseline vital signs, allergies and nursing history is completed.
- Ensure patent intravenous line for sedation, Glycopyrrolate for reducing secretions
- Drugs - Antiplatelets/anticoagulation should be noted

Pull Technique

- Gastroscopy is performed for ruling out esophageal/gastric/duodenal obstruction, ulcer /cancer at the site of PEG placement
- Stomach insufflated with air - transilluminated to the anterior gastric wall

■ **Site for placement:**

1. **Transillumination** on anterior abdominal wall in dark room
 2. **Indentation** noted on gastric wall when finger/needle cap is pressed on abdominal wall
 3. **Guiding needle track** - for infiltrating xylocaine- needle is passed perpendicularly through abdominal wall. The needle must be seen in endoscopic vision. Xylocaine is injected by constant withdrawal of needle and piston. If air/blood/stool noted in the needle on suction- site is changed.
- Abdominal wall should be prepared with iodine, 5-8mm skin incision is made followed by intravenous catheter introduction through abdominal and gastric walls and needle removed
 - Once the needle is within the stomach, a snare is placed around the needle. A long blue soft looped wire is then passed through the needle and grabbed with the snare. The endoscope with snare and wire is removed out of the mouth. Sterile gloves are used and the wire is attached to a loop at the tapered end of the PEG tube as figure of 8. Once attached, the second operator gently pulls on the wire to slowly advance the tube through the mouth and esophagus and into the stomach.
 - Once the gastric wall is reached (at which point there will be a significant increase in resistance to passage of the tube), the introducer needle is removed, and moderate traction is placed on the blue wire by the second operator to pull the tube through the abdominal wall. The tapered end of the tube acts as a dilator. Once the entire tube has been pulled through the abdominal wall, the internal bolster will rest along the gastric wall.
 - **Care** must be taken to not pull the internal bolster out through the abdominal wall. Endoscope is reintroduced for position of internal bolster. Once the tube is in place, an external bolster is placed on the tubing, allowing for 1 to 2 cm of in and out movement. The **measurement on the external tube should be recorded** in the endoscopy report for future reference
 - If the tissue between the internal and external bolsters is compressed, it may lead to pressure necrosis, buried bumper syndrome, or breakdown of the gastrostomy tract.
 - **PEG-J:** J-tube extension (gastrojejunostomy tubes) and have a Y configuration with two ports (a gastric port and a jejunal port).
 - Gastrostomy tract can mature in upto 4 weeks
 - **Balloon replacement tube:** Have a balloon at the distal tip are placed for replacement after maturation of PEG site.
 - A Foley catheter can be used as a temporary replacement gastrostomy tube in emergency.
 - For confirmation of position, a water soluble contrast through the gastrostomy tube can be used before initiation of feeds

INITIATION OF TUBE FEEDS:

- Water and medications- 4 hours after PEG placement
- PEG feeds- after 24 hours

GASTROSTOMY TUBE CARE

- Position of external bolster
 - Avoid compression between the two bolsters
- 20mL water flush the tube to prevent clogging - If obstructed- flush with 60 mL warm water/colas. Panlipase crushed with a 650 mg bicarbonate tablet - mix with warm water - retain in the tube for 5 min and then flush - If fails, endoscopic cytology brush/ gastrostomy tube brush can be used to clear the tube.

Bulking agents: Psyllium and resins- cholestyramine should never be placed through the PEG tube.

PEG site granulation tissue: Silver nitrate/ hypertonic saline/steroid cream can be used

After PEG removal: The PEG site is covered by clean dressing. The PEG site closes within 24 to 72 hours. Occasionally, a fistula persists following tube removal- might require clip.

Sclerotherapy Needle

Uses

- Eso. Varix injection- 23G needle
- Gastric Vx- 21G needle
- Injection of bleeding peptic ulcer
- Bleeding sites - post polypectomy/post sphincterotomy
- Hemorrhoidal injection
- EMR/ESD/polypectomy
- Steroid injection for Esophageal Stricture
- Tatooing

Variceal Injection

- Intravariceal - Thrombosis and inflammation, more efficacious, less force, less time, less recurrent bleed
- Paravariceal - Fibrosis and tamponade. Less recurrence after injection

Complications

- Ulceration: increases with volume of sclerosant; no difference in intravariceal or paravariceal injection
- Rebleed/ Perforation: 2-5%
- Hematoma
- Stricture: Frequency & volume of sclerosant

For injections

Sclerosant

- Sclerosants → vascular thrombosis due to epithelial damage: ethanolamine (5%), Sodium morrhuate, absolute alcohol, 0.5-2% polidocanol, 1-3% sodium tetradecyl sulfate

Detergents - Disrupt vein cellular membrane (protein theft denaturation)

- Sodium tetradecyl sulfate- Only FDA-approved sclerosant; Anaphylaxis in 1:700
- Sodium morrhuate
- Ethanolamine Oleate
- Polidocanol- better: Hemostasis → acute edema; Later → inflammation & fibrosis; painless upon injection, does not produce tissue necrosis if extravasated, and has a very low incidence of allergic reactions,

Osmotic agents - Damage the cell by shifting the water balance through cellular gradient (osmotic) dehydration and cell membrane denaturation

- Hypertonic sodium chloride solution- naturally occurring body fluid; PAIN and significant tissue necrosis are drawbacks
- Sodium chloride solution with dextrose

Chemical irritants - Damage the cell wall by direct caustic destruction of endothelium

- Chromated glycerin
- Polyiodinated iodine

Volume:

- Depends on sclerosant, number and size of varices
- The average volume injected per puncture is 1 to 3mL

The total volume of solution injected during the first procedure varies from 10 to 20mL, depending on the size and number of varices

Thrombin:

- Most physiologic agent for injection.
- Fibrin sealant - Fibrinogen and thrombin: Better with double channel endoscope as the viscosity of the fluid is high and needle clogging can happen.

Plug technique: Preinject with epinephrine- followed by 4 quadrant injection with 0.5mL of fibrin sealant.

Drawbacks: Cost/derived from human plasma.

Injection for MW tear/DU Injection for ulcer bleed

- **Epinephrine:** MC for ulcer; vasospasm/plt. aggregation; Dose: 10-30mL, 1: 10000 dilution- Epinephrine provides temporary hemostasis and must be followed by hemoclipping or thermal coagulation to coapt the underlying artery for definitive hemostasis. Inject in 4 quadrant around the ulcer in aliquots of 0.5-2ml with needle protruding 5mm beyond the needle sheath. In chronic ulcers & side viewing scopes - **metallic needle** instead of disposable needle can be used. Mucosal edema and blanching with cessation of bleeding will be the end point.
- **Forrest classification:** Type 1a: spurt; 1b: ooze- Type 2a: non bleeding visible vessel; 2b: adherent clot; 2c: pigmented base- Type 3: clean base

Does larger volume of epinephrine cause less bleed?

Larger volume of diluted epinephrine (1:10000-1:100000) resulted in less recurrent bleeding in high risk ulcers in comparison with smaller volumes- 5 to 10mL.

Epinephrine does not damage tissue → but transient tachycardia might happen. Caution: in patients with marginal hepatic reserve and severe ischemic heart disease

How do you recognize NBVV?

As a discrete small (< 5mm usually), raised, smooth protuberance in an ulcer crater. Distinct from a spot which is flat & from a clot that is amorphous & larger (> 6mm)

Gastric ulcer needs check scope after PPI treatment for 6-8 weeks for complete healing of the ulcer- else might biopsy for r/o cancer.

How do you remove an adherent clot with out severe bleeding?

Use Pre-injection with epinephrine and with snare- guillotine the clot in sections. Plan is to shave the clot and not pull the clot. If any bleeding occurs- repeat injection with adrenaline is done. Once base of the ulcer is noted for vessel- either thermal or clipping is performed to reduce the chance of rebleed to less than 5% (Jensen adherent clot Gastro article 2002 volume 123:407).

Technique:

- Pass the injection needle through the biopsy channel of the endoscope and advance it to the target area
- Carefully monitor the bleeding patient during the procedure.
- Check the needle out and retract the needle in before insertion into the biopsy port
- Load the syringe with sclerosant, attach the syringe with sclerosing agent to the sclerotherapy catheter and flush with 1 to 2 cc for dead space correction
- Make sure that the needle is inside the catheter before insertion into the biopsy port.
- Suction oral airway as needed throughout the procedure
- Communicate when the needle is outside and inside the catheter (ie., needle out and needle in).
- When asked to inject, verbalize the amount injected ie., 1 cc or 2 cc.
- **Choose a target** for injection. Begin the injections at two or three points in each line of varices at 2- to 3-cm intervals, from just above the gastroesophageal junction up to the proximal esophagus. Successful obliteration of varices in the distal esophagus usually eliminates the proximal varices or at least decreases their size. In case of injection – inject 4 quadrant/around the target - blanching should be observed
- Observe the endoscopy image while injecting for proper position
- Alert the endoscopist if it is hard to inject.
- Repeat the sclerosing process for each varix or as specified by the endoscopist.
- If no further therapy is needed, the procedure is complete.
- Make sure that the needle is inside the catheter before the Endoscopist removes the sclerotherapy catheter.
- Hold gauze at the biopsy port as sclerotherapy needle is being removed so as not to splash its contents.
- Section oral cavity thoroughly as the mouthpiece is removed.
- Arrange for patient's recovery per procedure.
- Keep a mental note and document the number of injections and the amount of sclerosing agent that has been injected
- The goal of the **intravariceal injection** is to introduce the sclerosant directly into the lumen of the varix, resulting in acute variceal thrombosis.
- If site of active bleeding is seen, begin injection distally, continue proximally, and finally into and around the site until bleed- ing is controlled.
- Usually 6 to 9 mL of sclerosant are injected (2–3 mL for three or four injections)
- Then inject the other varices.
- Sclerosant directly into the varices and removes the needle slowly while injecting to tamponade the injection site
- Bleeding gastric varices are difficult to treat endoscopically, & results are not as good as ES of esophageal varices.
- Injection of a large volume of sclerosant or bucrylate into gastric varices has been described.
- There are two types of gastric varixs: junctional and fundics.
- **Junctional varices** are gastric varices seen as an extension of esophageal varices and without extension into the fundus. These are treated with standard intravariceal sclerotherapy from the proximal, connecting, **Fundic varices** are gastric varices confined to the fundus, with channels extending distally to the gastroesophageal junction.

Glue:

- Cyanoacrylates - fast-acting adhesives
- Methyl-2-cyanoacrylate (MCA)
- Harry Wesley Coover Jr and Fred Joyner (Kodak Labs) in 1942
- ‘Eastman 910’ by Kodak -first true ‘super glue’

Chemistry:

- Water [OH⁻] + MCA → rapid polymerization
- Exothermic reaction
- Watery liquid → Hard acrylic plastic

Glue in Gastric varix:

- Intravariceal Glue injection- 1986* (*Soehendra N, Nam VC, Grimm H, et al. Endoscopic obliteration of large esophago-gastric varices with bucrylate. Endoscopy 1986;18:25–6*)
- Acute GV bleeding (GVB) and elective therapy for obliteration of GV
- Cheaper - interventional radiologic options

Gastric Varices - Deep varices

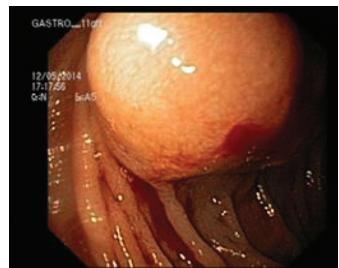
- Dilated intramural venous channels
- Muscularis propria (periesophageal/ perigastric varices)
- Extramural channels outside the muscularis propria (paraesophageal/paragastric varices)

Treatment of Gastric/Ectopic Varix:

- GOV 1: eradicated by EVL /EIS similar to EV.
- IGV 1 : splenic vein thrombosis → splenectomy
- GOV 2: Partially eradicated by Glue
- Glue extrusion - 42.8% after 2 weeks, 27.9% after 3 months, 28.9% after 6 months

Complications: Local and Systemic

- Giant ulceration/ Sinus formation
- Impaction of needle tip
- Bleed – rebleed (3.7-58%), early rebleed (0- 20.5%), Late rebleed (8%)
- Antibiotic prophylaxis – reduces rebleed
- Pyrexia and mild abdominal pain - 33% and 17%.
- Transient bacteremia – not uncommon
- Embolization - serious complication (brain/lungs/renal)
- Pulmonary Embolism - 0 – 4.3%



Technique of injection:

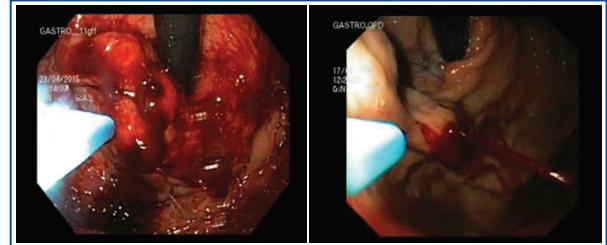
- Injection catheter: 240 cm long, 7 F catheter- transparent Teflon sheath
- Needle tip - 21G , 5–8 mm long for intravariceal injection
- Dead flush for a catheter?
- Glue with lipiodol..?: Radiographic visualization but delays solidification by 15–20s - increases cast time/ embolization
- N Butyl cyanoacrylate (NBC) is injected after first flush of **distilled water**. Chosen volume of NBC injected followed by second flush of **distilled water**
- Injection should be intravariceal and not paravariceal.
- Injection may be repeated at 1mL aliquots in case of bleeding GVs
- Transparent Teflon catheter can get the blood on puncturing the varix- Red catheter sign or Varix is soft on probing with cannula - repeat injection is done
- Endoscope is withdrawn with the needle catheter assembly in situ - the catheter tip is cut and removed from the working channel. Endoscope is rinsed with acetone immediately at the tip of the scope as well as the suction channel.
- Periodic endoscopic monitoring for complete obliteration of GV is done.
- **Large GV:** > 10 mm in diameter- larger volumes of glue & more sessions - 2–4 mL volumes of NBC or mixture per injection for large GV without any major embolic complications.

Rebleed after Glue injection:

- Incomplete obturation/early extrusion of the glue
- EUS-guided: obliteration of ‘inlet’ vessel/ complex GV / transesophageal coiling and gluing of fundal varices
- TIPSS/BRTO/BATO/PARTO/CARTO

Avoid Glue complications:

- Avoid overdilution with lipiodol
- Undiluted NBC- better
- Reducing the volume of glue used to 1 mL per injection
- Moderate speed of injection
- Avoiding excessive flushing

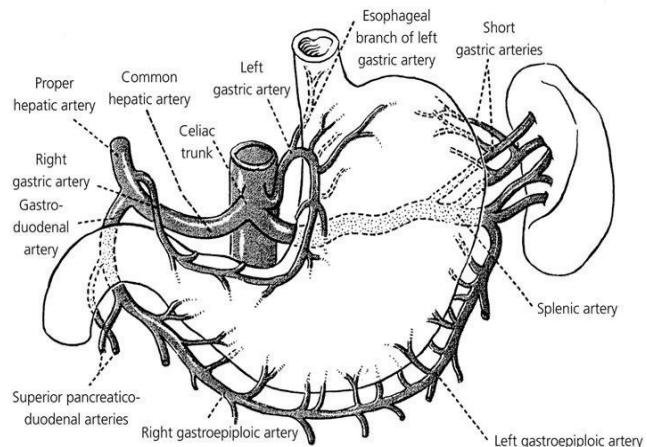
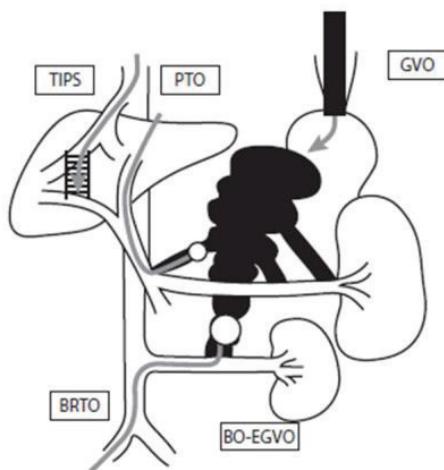


Precautions:

- Eye protection with goggles
- Protecting the endoscope - silicone oil
- Suction should be disconnected
- Injector cut before withdrawal from the endoscope tip after withdrawal of scope
- Channel and distal end cleaned with acetone

Choice of therapy:

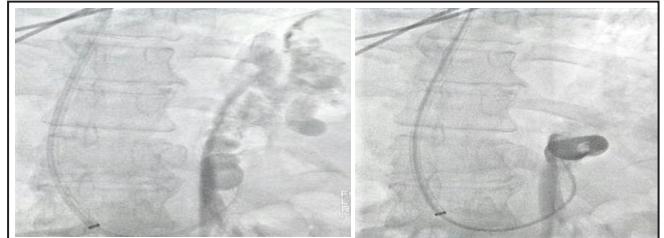
- Glue - first line with TIPS - salvage therapy – USA and Europe
- TIPS - first-line therapy in the absence of facilities for gastric glue injection.
- Japan - BRTO is the standard first-line treatment



Balloon retrograde Transluminal obliteration: BRTO

- Treatment of choice in Japan
- 100% success and safe
- Negligible rate of embolism/ complication.
- Recurrent varices :0–10%
- Trans jugular retrograde obliteration: less invasive - but high recurrence of EV than BRTO

- In patients with fundic varices, sclerotherapy only on varices that are bleeding or have stigmata of bleeding, using the retroflexed view. Inject 2mL of sclerosant into the varices.
- Cyanoacrylate has been used for the control of gastric variceal hemorrhage. Either isobutyl-2 or N-butylcyanoacrylate and injected directly into the varices, producing a virtual acrylic cast of the varices.



Foot Notes: (Saraswat VA1, Verma A2. Gluing gastric varices in 2012: lessons learnt over 25 yrs. *Journal of clinical and experimental hepatology*, March 2012; Mar;2(1):55-69).

- Technique of glueing not standardised
- Useful for active bleed with multiple in flow
- High HVPG, ascites/ hydrothorax: TIPSS
- Single inflow/outflow for GV : BRTO
- BRTO fails - BATO
- CARTO/PARTO: lower balloon rupture risk/embolization & less procedure time

Complications

- Haemorrhage
- Chest pain/Aspiration
- Ulceration and necrosis of esophagus
- Perforation of esophagus
- Fever/Mediastinitis
- Stricture/ Pleural effusion
- Portal vein thrombosis



Fig: Sclerotherapy of Forrest Ib Duodenal ulcer

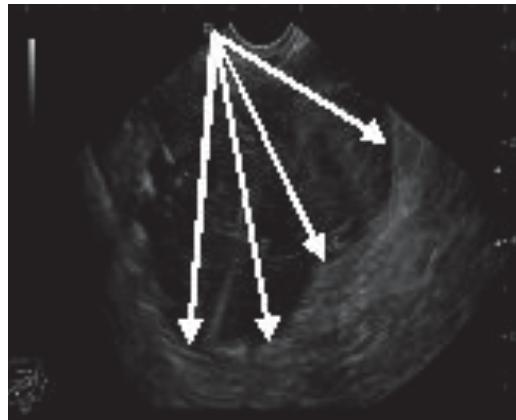
EUS-FNA Needles

- **Prototype:** Hancke-Vilmann needle
- A stiff steel needle is manipulated by a handle piston which is fixed to the biopsy port
- The handle piston can be locked and unlocked by a screw to avoid advancement of the needle in the scope channel
- The needle is supported by a stable metal spiral sheath that is firmly connected to the handle. The handle can be firmly connected to the endoscope using a Luer-lock.
- When the handle is screwed on the Luer-lock connection of the endoscope, the metal spiral extends 4-5 mm out of the distal outlet of the working channel
- Cobalt chromium needle assembly- Superior needle penetration, improved pushability, kink resistant and retain greater needle sharpness
- Echogenic pattern extends onto tip of needle designed to provide precise guidance to the target site
- FNA needles are currently available in 3 sizes-19, 22 and 25 gauge- 1.1,0.72,0.52mm respectively will need biopsy channel diameter of 2.8mm for 19G and 2.4mm for 22/25G
- All the needles have a removable stylet
- The stylet could have either a sharp/rounded tip-the latter requiring the stylet to be pulled back few millimetres before performing the FNA
- Finer needles are used to gather cytological specimens, while larger needle can be utilized when acquisition of tissue specimen for histological examination

EUS-FNA technique and protocol: EUS-FNA was done under conscious sedation with the assistance of an anesthesiologist by a single echoendoscopist. FNA was done by targeting of the lesion at the center of EUS image, closest to the transducer and avoiding intervening vessels by color doppler imaging.

Needle size and technique of FNA was chosen according to the following protocol.

- An attempt was made to fan 4x4 times as shown in the figure 1 in all the lesions to improve the yield.
- Stylet was used for expressing the aspirate onto 2 slides for cytology and remaining aspirate into formalin bottle for CB
- If excessive bloodiness as in figure2,3 was SEEN- (specimen evaluation by endosonographer/nurse) suction was switched to wicking. Visual inspection for straw-colored, pink, red, chocolate-colored and whitish-yellow tinted material was done as in figures 4,5,6 which represent tissue. Granularity was SEEN on the slide. In formalin bottle, aspirate should sink and not disperse or float as it may indicate inadequate tissue sample.
- 19G needle is used for therapeutic EUS- cystogastrostomy/hepaticogastrostomy/ choledochoduodenostomy... Comes with stiffer stylet- might need to advance the needle out of the scope when operating at an angle.



Algorithm:

Pancreas:

Suspected Cancer:

- 22G needle with aspiration of 10-60mL depending upon fibrosis- if sample poor- repeat procedure either using 22G multiple passes or with 19G standard for body and tail (through stomach window) and 19G flex needle for head and uncinate process (transduodenal)

Suspected neuroendocrine tumour:

- Highly vascularised: 25G- slow pull technique- If fibrotic can use 22G with 10mL aspiration

Suspected Autoimmune:

- 19G standard for body/tail and 19g flex for head/uncinate

Cyst:

- Diagnostic: 22G

Node:

- Sarcoid/Lymphoma/TB-19G standard- slow pull all others 22G with 10mL aspiration

For Histology Samples on Lymph Nodes

- First pass suction
- Subsequent passes – modified suction or eliminate suction altogether

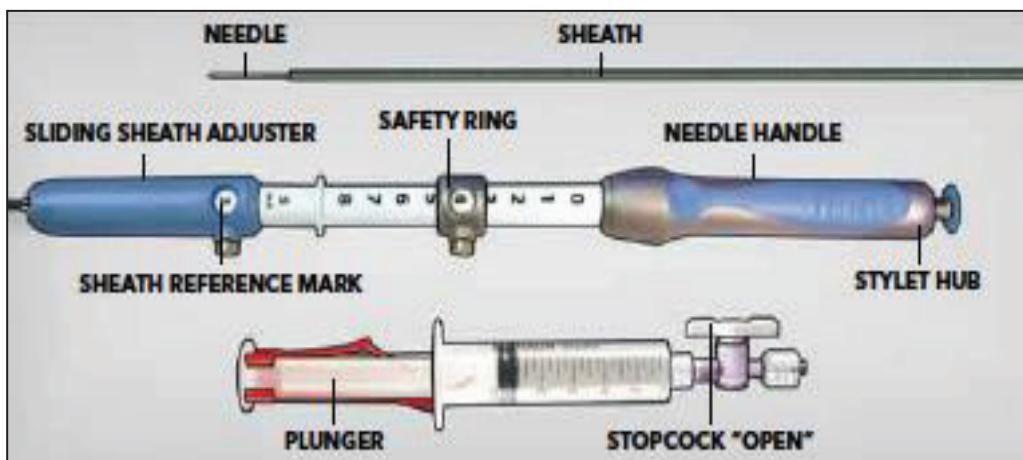
GIST/mesenchymal tumours:

- 19G - slow pull - if no tissue increase aspiration to 60mL
- Tissue is the issue
- The larger the needle – the better
- Target the center unless there are cystic changes.
- Try to stick to the solid components.
- Jab has to be quick with these lesions to keep them in place
- Use suction and always submit 2 to 3 passes for cell block
- Start out with these diseases that generally require histology for diagnosis:
- Liver lesions

Liver:

- 22G with 10mL aspiration

	BOSTON EXPECT	COOK ECHOTIP
Needle material	Chromium cobalt	Stainless steel
Sheath tip	Rounded	Bevelled
Sheath adjustment length	4cm	5cm
Max.needle extension	8cm	8cm

**19G Tricks:**

- If a physician has ever had resistance while attaching Expect™ 19ga Flex Needle to the scope:
- Rotate big wheel away, allow needle to come out, then turn big wheel back to view the lesion
- Release elevator, extend sheath another 0.5cm to 1cm, retract stylet to allow needle tip to be more flexible and use short scope position

Rapid 1st Jab

- This technique eliminates the lesion running away from the endosonographer.
- 19 G Flex Needle will feel different than using a 22G or 25G needle. Bigger the needle- harder the jab.
- Set the depth lock, if this will feel more comfortable and very slow backward pull on needle
- Make sure the stylet is pulled back before initial puncture to ensure that you are utilizing the sharp needle tip grind

Indication: Procedure of choice for diagnostic evaluation of submucosal and periluminal lesions

- Esophageal cancer staging
- Gastric cancer staging
- Rectal cancer staging and diagnosis of extraluminal recurrence

- Subepithelial lesions
- Pancreatic masses diagnosis and staging
- Pancreatic cysts diagnosis
- Bile duct tumors diagnosis and staging
- Lung cancer diagnosis and staging
- Mediastinal lesions unrelated to lung or esophageal cancer

ENDOSCOPIC TATTOOING

- The intraoperative identification of lesions previously detected by endoscopy is often difficult, particularly during laparoscopic surgery.
- Anticipate difficulty when: Small or flat neoplasms, polypectomy sites, diverticula, arteriovenous malformations, and Dieulafoy lesions.

INDICATIONS

- To localize luminal abnormality at the time of surgery or repeat endoscopic examination.
- Deep enteroscopy (eg, double balloon enteroscopy) to mark the extent of antegrade inspection for identification during subsequent retrograde enteroscopy.
- EUS-guided fine-needle tattooing using India ink or ICG for the preoperative localization of pancreatic lesions.

TECHNIQUE

- 0.5-mL aliquots of 1:100 India ink produced no gross inflammation and were seen consistently at colonoscopy, laparoscopy, and laparotomy for as long as 5 months
- The tattooing agent is delivered by an injection needle advanced through the working channel of the endoscope
- The needle should be inserted at an oblique angle to the bowel wall to avoid penetrating the serosa
- Transmural injection may result in diffuse staining of the peritoneal surface
- Once the needle's bevel is within the submucosa, the agent is injected to raise a bleb, usually in 0.5- to 1.0-mL aliquots
- Four-quadrant injection around the circumference of the bowel has been suggested to optimize operative localization.
- When using India ink, it must be sterilized and diluted before use
- FDA-approved Spot is prediluted and ready to use
- “saline test injection” techniques have been described to define the submucosal plane to prevent dye infiltration of the muscularis propria or spillage into the peritoneum.

SAFETY

- Safe with most complications related to transmural injection - abdominal pain, tenderness, and fever

Tatooing agents				
Tattooing agent	Manufacturer	FDA approved or tattooing	Price	Speial features
Indocyanine green (Cardiogreen)	Sigma-Aldrich Inc, St. Louis, MO	No	\$46.70 for 25 mg, \$80.60 for 50 mg	Available in powder form, not readily soluble in saline solution in water
India ink (Endomark)	PMT/Permark Inc, Chanhassen, Minn	No	10 mL vials, \$30 each, box of 9 for \$225	Sterile, diluted 1:50 with normal saline solution
Spot	GI Supply Inc, Camp Hill, Pa	Yes	5 mL syringe, box of 10 for \$199	Sterile, ready-to-use, prepackaged syringes



Wires & Stent

METALLIC STENTS - ESOPHAGUS:

Indications:

1. Dysphagia from Esophageal malignancy
2. Benign Eso. Strictures- peptic, radiation, drug induced, anastomotic, corrosive
3. Post operative leaks
4. Iatrogenic perforations
5. Occlusion of fistulas

BOSTON SCIENTIFIC WALL FLEX STENT	COOK EVOLUTION STENT
DEPLOYMENT: COAXIAL	PISTOL GRIP
COVERING: PERMALUME	SILICONE
SIZE OF FLARES:23 &28MM	23 & 25MM
SIZE OF BODY:18 &23MM	18 & 20MM
STENT LENGTHS:10,12,15CM	8,10,12.5,15CM
STENT CONSTRUCTION: BRAIDED NITINOL	BRAIDED NITINOL

STENT DEPLOYMENT: 1:1 control with wire braided construction for tactile feel and excellent fluoroscopic visibility with 4 RO markers. The design allows for gradual expansion of the stent in 24-72hours.

For 18X23mm stent - a minimum of 9mm and a maximum diameter of 11mm- in case of larger diameter migration chance is higher

For 20X25mm stent - a minimum of 10mm and maximum of 14mm is necessary

Knitted structure of the Nitinol in SEMS helps in peristalsis, flexibility and reduces migration risk

Crochet system is the method for both distal and proximal stent release

MRI conditional - in vitro studies - safe

Stent delivery system - 18.7Fr (6.17mm)

PROCEDURE:

Locate the stricture with endoscope and pass the 0.035"/0.038" stiff guidewire across the stricture with a coil in the stomach.

Leave the guidewire in place and insert the scope next to the guidewire. Dilate the stricture in case of tight stricture and inability to pass the guiding catheter. If fluoroscopy is used for CRE balloon dilation- 50% dilute contrast with water to be able to pass the catheter across- watch for perforation and bleeding during the dilation.

Examine the stricture endoscopically during dilation from proximal end.

4 markings important: Level of upper esophageal sphincter(UES), upper and lower extent of the growth and the gastroesophageal junction- Endoscopic and fluoroscopic placement of markers either using radiopaque externally or use anatomically as ribs/vertebra.

The length of the growth determines the length of the stent used. The SEMS length should be atleast 3cm longer than the growth with 1.5cm extending beyond at either end. The upper end of the growth should be at least 2cm beneath the UES to facilitate stent deployment and decrease chance of aspiration and foreign body sensation. For covered stent ensure that covered portion should cover the tumour and or fistula. Always remove the distal stylet before starting deployment. If stent length is questionable- choice will be for the longer stent. If more than 1 stent is required- overlap must be more than 3cm for anchoring and stent deployment should start from distal to proximal.

Stent deployment is begun by placing firmly on the inner catheter and using finger ring with the other hand-suture unravels from proximal end. If proximal release stent is used- there can be chance of 1cm distal migration during the deployment of the stent which can be corrected by counter traction. If there is resistance to stent deployment- especially if the stricture dilation is 2/3rds of the stent diameter- procedure must be aborted.

If distal release stent is used always it has to be deployed under fluoro guidance with fixation of the distal end of the stent- useful especially while placing SEMS for lower end esophageal malignancies.

SEMS can be deployed by using position ruler on the shaft ruler. The lasso is reinforced green suture at the proximal end of the SEMS for accurate positioning or removal of the SEMS.

Elongated proximal flare is designed to improve fixation and reduce the opportunity for food entrapment.

Once deployed do not move the stent. If the stent diameter does not achieve nominal diameter- CRE balloon of appropriate size can be used for dilation of the stent. DO NOT use SG dilators as axial force can dislodge the stent.

WALL FLEX FULLY COVERED	ULTRAFLEX PARTLY COVERED	POLYFLEX STENT
Make: Braided Nitinol	Knitted Nitinol	Polyester braided material encapsulated with silicone
Covered: Fully	partially	Fully
Covering material: Premalume	Polyurethane	Silicone
Stent Lengths: 10,12,15cm	7,10,12,15cm	9,12,15cm
Stent flare diameter: proximal/distal:25/23	23/28mm	23/25mm
Distal release	Proximal/distal release	Distal release

Post Procedure care:

- Head end elevation of bed as there can be chance of bleed post procedure due to dilation of the stricture
- NPO
- Chest radiograph after 24 hours with deep penetration- for position of the stent as well as the expansion
- Soft diet can be started with an advise to carbonated beverages once a week which can act like stent cleanser agent
- Antireflux measures have to be explained. If symptomatic might require use of PPI/antacid
- Pain is problematic due to SEMS expansion- can be controlled by NSAIDS- Usually resolves in 72 hours

Q: What is the role of SEMS in palliation of malignant Eso. Obstruction?

Ans: Nimish Vakil et.al.,AmJ2001membrane covered SEMS have lesser tumour ingrowth and reintervention as compared to bare stents in palliation of dysphagia secondary to malignant Eso. Obstruction. Gupta et.al., Eur Radiol 1999-SEMS is effective in relieving dysphagia in extrinsic compression- mediastinal malignancies compressing on esophagus

Q: What is the role of SEMS in anastomotic leaks?

Ans: Doneic et.al., Endoscopy 2003-Anastomotic leakage after esophagogastrectomy for cancer can be app. 60%. Use of SEMS can reduce the leaks by app. 80% with reduction of mortality

Q: Does anti reflux valve help in preventing reflux?

Ans: Marjolein Homs et.al., Gastrointestinal Endoscopy 2004-Windsock like anti reflux valve at the distal end of the SEMS in Fer X- Ella stent- provides relief of dysphagia but anti reflux valve failed in preventing reflux.

Q: SEMS in benign UGI leaks and perforations?

Ans: Jo Swinnen et.al., Gastrointest Endosc 2011- Benign causes: (1) fistula after bariatric surgery, (2) other postoperative fistulae, (3)Boerhaave syndrome, (4) iatrogenic perforations, and (5) other UGI perforations- Use of SEMSs for the treatment of benign upper GI leaks and perforations is feasible, relatively safe, and effective

Q: How to remove SEMS which has migrated/malpositioned?

Ans: Juan carlos munoz et.al.,JGH 2009- rat tooth forceps can be used to grasp the lasso for malpositioned SEMS for redeployment. Combination of foreign body hood protector and rat tooth forceps can be used to remove migrated SEMS from the stomach to prevent mucosal injury by the proximal flange

Q: Does the SEMS get impacted?

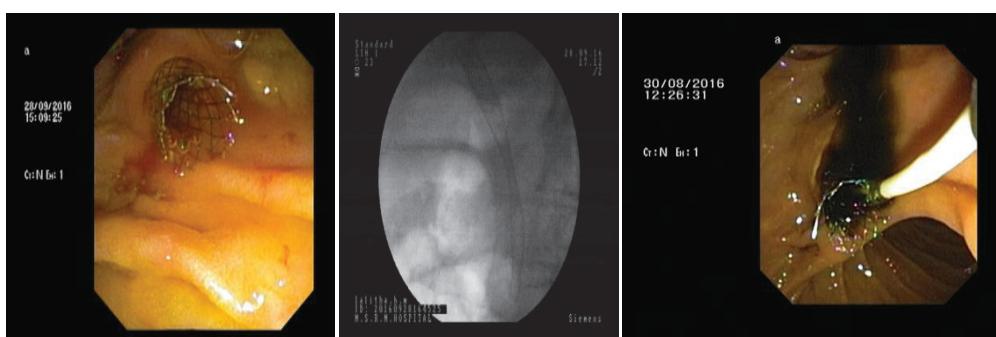
Ans: Yeon Seok Seo et.al.,GIE 2006- Segmental amputation of esophagus can happen if SEMS is removed forcibly and can lead to mediastinal and bronchial leak. Caution while removing an impacted SEMS as impaction can happen as early as 5 weeks after placement of SEMS. Polyflex can be considered if early removal is planned. Jason Wilson et.al., GIE 2009- Use of rigid esophagoscope and rat tooth forceps, through the pre-existing gastrostomy retrogradely can be used for removal. This is reported with use of Alimaxx-E (Alveolus Inc, Charlotte, NC) stent ? acid reflux related corrosion but not reported with Ultraflex. Nitinol is soft and pliable at room temperature but stiffer at body temperature. This stiffness imparts increased radial forces that may make the stent less likely to migrate but more difficult to remove

Q: Does large diameter Eso. SEMS seal traumatic Eso. Perforations?

Ans: Peter Siersema et.al., GIE 2003- use of Flamingo (proximal 30mm with distal flange 20mm) stents can be successfully used to treat perforations along with adequate drainage of thoracic cavity

Contraindications for Ultraflex stent: Benign tumours/strictures as long term effects of the stents are unknown, placement of stent proximal to 2cm from UES, following esophagojejunostomy as the peristalsis might displace the stent, bleeding ulcers.

WALL FLEX BILIARY STENT:



- Premalume covered biliary stent with 8Fr delivery system.
- Covered and uncovered for palliating obstructive biliary pathologies.
- 24Fr (8mm) and 30Fr (10mm) lumen diameters engineered for good flow.
- Premalume - synthetic polymer along with closed cell design resist tumour ingrowth.
- Excellent endoscopic and fluoroscopic visualisation with the stent can be reconstrained till the threshold of point of no return is not exceeded.
- Loop end is to minimise trauma to the tissue.
- Flared ends of the stent will resist migration.

In WALLFLEX fully covered stent proximal and distal 2mm is not covered as compared to WALLFLEX partly covered where 5mm is uncovered at both ends.

4 Fluoroscopic markers - Exterior tube marker - stays at the distal tip; Leading tip marker as the stent is being deployed this has to be observed; reconstraint marker/point of no return-not to be exceeded in case of repositioning (upto 80% is deployed) and the trailing marker- end of the stent.

Endoscopically there is an yellow marker which marks the end of the stent.

Procedure:

- Passage of guidewire across the stricture and assess the stricture diameter
- If needed, might need Hurricane dilation to allow the passage of the stent delivery system
- Advance the stent delivery system beyond the stricture under fluoroscopic guidance
- Deploy the stent under endoscopic and fluoroscopic guidance
- Might need a pull by the endoscopist as the stent is being deployed for accurate positioning
- Always constantly check the proximal and the distal ends of the stents for accurate position

Complications:

- Perforation
- Bleeding
- Stent migration
- Stent Misplacement

Q: Wallflex or plastic stents – which is better in malignant biliary obstruction?

Ans: Adrian Schmassmann et.al., AJG 1996- Wall flex stents are associated with increase in stent patency, increase in patient compliance and decrease in mortality secondary to stent occlusion as compared to plastic stents. Claes soderlundet.al., GIE2006-SEMS recommended in malignant biliary strictures with a chance median survival of more than 4.5 months and plastic stents are preferred in patients with more distant METs

Q: Covered or uncovered stents- which one is best for malignant biliary obstruction?

Ans: Atif Saleem et.al., GIE 2011-Covered SEMS have longer duration of patency, greater stent migration and tumour overgrowth as compared to uncovered SEMS in malignant distal biliary obstruction

Q: Does cholecystitis occur after placement of metallic biliary SEMS?

Ans: Hiroyuki Ishayama et.al., CGH 2006-Cholecystitis after SEMS placement is 5%. There was no difference with covered or uncovered SEMS. Only tumour involvement of the cystic duct orifice is the significant risk factor for cholecystitis.

Q: Covered SEMS for managing biliopancreatic strictures?

Ans: Hiroyuki Ishayama et.al., J hepatobiliary pancreatic surg. 2009- PTFE covered Nitinol stent by Taewoong medical, Seoul,Korea-can be used for managing distal biliary as well as pancreatic strictures secondary to chronic pancreatitis.

Q: In benign biliary strictures - FCSEMS if deployed - how safe it will be to remove?

Ans: J Garcia cano-et.al., Rev Esp.Dig.madrid 2010 - FCSEMS can be used for benign biliary strictures and can be removed after a mean period of 4 months

Q: FCSEMS- Role in post liver transplant biliary complications?

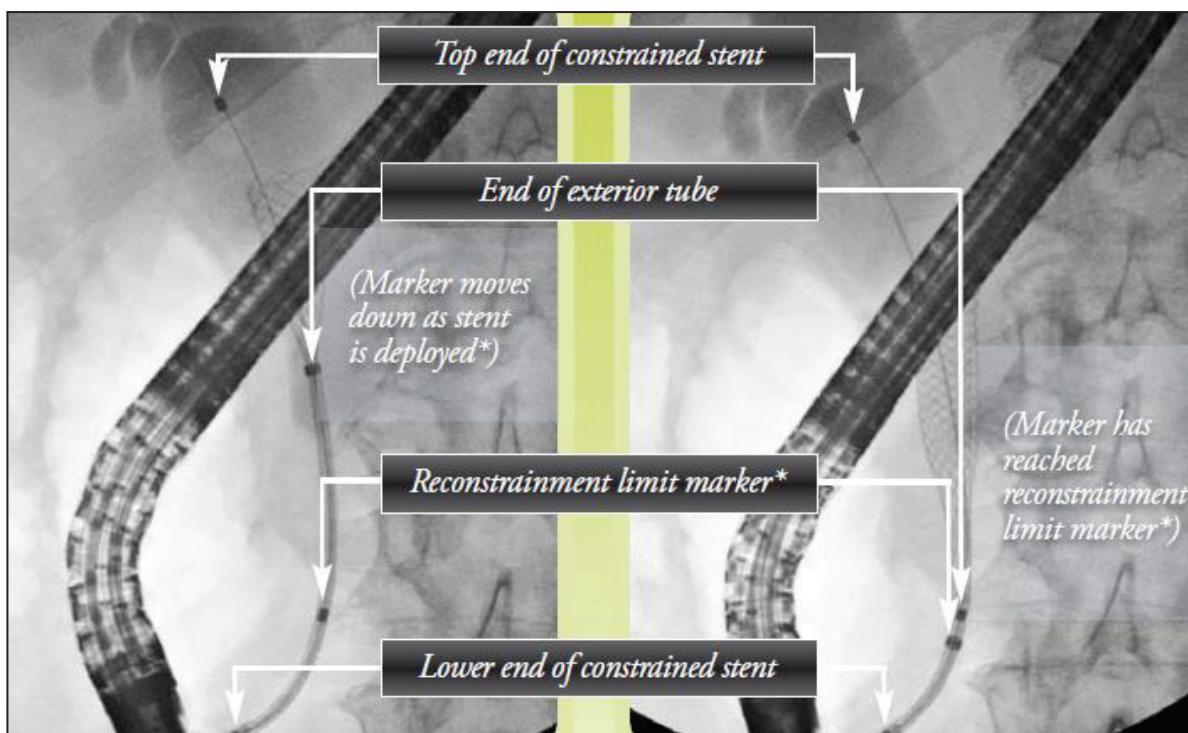
Ans: Garcia Pajares et.al., Transplantation proceedings 2010: ERCP is safe and first line in post OLTx biliary complications. FCSEMS is useful in anastomotic leaks and strictures post OLTx.

Q: What is the stent patency rate of FCSEMS after placement?

Ans: Laura Ornellas et.al., GIE 2009 - Occlusion of FCSEMS in 18% - mostly secondary to sludge and food. The stent patency rates at the end of 3,6 and 12 months were 100%, 93% and 82% respectively.

Q: What are the indications of FCSEMS in benign biliary disease?

Ans: Jorge canena et.al., Surg. Endoscopy 2012 - temporary placement of FCSEMS for 30 days or less is an effective rescue therapy in refractory biliary leaks, post sphincterotomy bleeding and perforations.



Q: What is the recommended wire for placement of SEMS in CBD?

Ans: HydraJag stiff shaft Wire- 0.035"- 260/450cm

Q: What does platinol make the difference in biliary SEMS?

Ans: Platinum core with nitinol encasement provides flexibility for tortuous CBD, enhanced radioopacity and radial force to maintain stent position.

Q: Integrated retrieval loop is it similar to lasso?

Ans: Yes. When tension is applied over the loop it makes the SEMS to narrow down the length and the diameter for removal

Q: What are the contraindications of Wall Flex stents?

Ans: Perforated bile duct, small intrahepatic bile ducts, strictures that cannot be dilated to the extent that the stent delivery system could not be passed across and in benign conditions (removable upto 12months- no data what happens if placed beyond!!).

WALL FLEX ENTERAL (COLONIC/DUODENAL) STENT:



- Nitinol with the radial force and visibility characteristics of Elgiloy- make of the stent
- Highly trackable 10Fr (3.33mm) - TTS/OTW delivery system- large stent in small reconstrainable catheter
- Flared and looped ends to reduce the risk of migration and tissue trauma
- Braided for flexibility, maintain lumen integrity and adapt to anatomy
- Large diameter flares intended to prevent obstruction and minimise migration
- Indicated for palliation of colonic obstruction and preoperative decompression to reduce the rate of stoma creation
- Can reposition the stent up to 70% after deployment

Q: What is the difference between WALLFLEX colonic and Duodenal stents?

Ans: Duodenal SEMS has body diameter is 22mm with flare diameter of 27mm with colonic being flare of 30mm and body of 25mm.

Q: What is the minimum working channel for WALL FLEX ENTERAL catheter to pass?

Ans: 3.4mm

Q: Coaxial delivery me

Ans: The outer sheath withdraws from the underlying catheter exposing the prosthesis

Q: Lengths of WALLFLEX ENTERAL STENT

Ans: 6,9,12cm

Q: Outcome of WALL FLEX ENTERAL STENT (WFES) for malignant UGI obstruction?

Ans: YimHB et.al., GIE 2001: Safe efficacious, cost effective and shorter hospitalisations than surgical alternative

Q: Acute left colonic malignant obstruction- SEMS Vs Surgery?

Ans: Laura targownik et.al., GIE 2004 - Colonic stent insertion followed by elective surgery is more effective and less costly than emergency colostomy and resurgery in acute malignant colonic obstructions. Peter carne et.al., Dis colon rectum 2004 - SEMS better with shorter hospitalisations and provide acceptable alternative for surgeries. Khot et.al., British journal of Surgery 2002: Colorectal stents – good palliation, bridge to surgery, avoid the need of stoma, lower mortality. Dilatation of malignant strictures at the time of stent deployment is dangerous and should be avoided. Hyun Jung Lee et.al., GIE 2011 - Effective and acceptable therapy for initial as well as long term palliation of malignant colorectal obstruction comparable to surgery

Q: Efficacy of Stent in stent for malignant colorectal obstruction?

Ans: Jin Young Yoon et.al., GIE 2011- Secondary stent in stent leads to good outcome especially in long duration of primary stent and stent occlusion and no peritoneal carcinomatosis

Q: Whats best for malignant colonic obstruction?

Ans: Vasileios Trompetas. Ann R Coll Surg Engl 2008 - Low risk cases- one stage primary resection and anastomosis. High risk cases-colonic stenting - failed - Hartmanns procedure. Subtotal colectomy in proximal bowel damage and synchronous tumours. Simple colostomy- no role except in patients not fit for any porocedure. 18% stent failure rate at the time of placement

Q: In GOO- SEMS Vs surgical GJ?

Ans: Shyam varadarajulu et.al., SEMS placement is less costly and shorter hospitalisation with both modalities relieving GOO in 100% cases

Q: What are the recommended foods post enteral SEMS placement?

Ans- drink during and after each meal. Drink plenty of fluids throughout the day. Cut your food into small pieces, take small mouthfuls and chew each mouthful thoroughly. Take your time, relax and eat your meals slowly. Sit upright at meal times, and for one-to-two hours afterwards. Please avoid- fresh vegetables and fruit (e.g., celery, carrots, corn, lettuce, pineapple), foods with seeds (e.g., oranges, watermelon, tomatoes), fruit or vegetable skin (e.g., potato skins), nuts (e.g., peanuts, pecans, almonds, popcorn, etc.), tough meat (e.g., steak)

WIRES

Guidewires:

Characteristics:

There are **three types** of guidewires

- **Monofilament:** They are made of stainless steel and are designed for rigidity-SG wire
- **Coiled:** They have an inner monofilament core and an outer spiral core. They are usually sheathed with Teflon coating.
- **Coated:** These have a monofilament core with an outer sheath. The outer sheath may cover the full length of the wire or may extrude from the tip of the wire. Sheath is made of Teflon or polyurethane. Coating of wire is usually done to reduce viscosity and improve radioopacity.

Commonly used GWs: Teflon coated nitinol wires

The wire tips are also configured into various shapes: Tapered/J tip/ Straight/ Angled

- ▶ Length: 150 – 650 cms
- ▶ Diameter: 0.018 – 0.039”

Use:

- **ERCP:** Used for achieving selective biliary- CBD, RHD/LHD and pancreatic cannulation/stenting, Wire guided sphincterotomy, position catheter for pseudocyst drainage. 0.035” in guidewires are traditionally used for biliary interventions and 0.025”/0.018” in guidewires are used for pancreatic interventions.
- **Upper GI endoscopy:** Guidewires provide access for dilatation, placement of metal stents and feeding tube placement.
- **EUS:** Guidewires are used for EUS guided interventions viz. eus guided biliary drainage and rendezvous procedures.

Complications:

- **Perforation:** Guidewires if used with excessive force may perforate the luminal wall
- **Wire fragmentation:** Guidewires can fragment with retention of fragments within the lumen
- **Short circuits:** Between guidewire and cutting wire may happen

HYDRA JAG WIRE:

- Diameter: 0.035” (0.89mm)
- Shaft: Either standard or stiff shaft
- Tip: Straight or Angled. 10cm hydrophilic tip is for smooth access and excellent tactile feel. Can consider switching to 5cm hydrophilic tip to meet procedural demands for firmer tip
- Length: 260 or 450cm - For short wire exchange or traditional long wire exchange system. Tungsten-filled tips aid fluoroscopic visualisation. Angled tip for deep intrahepatic positioning of the wire
- Radiopaque markers at 10cm and 15cm facilitate accurate stricture measurement
- Rx Locking device: Can be fixed to the biopsy channel for fixation of the wire during exchanges

Endoglide coating promotes smooth tracking and enhances tactile sensation. Kink-resistant, nitinol shaft is engineered for wire control and manipulation capabilities. The most important technique is torquing the wire rather than pushing the wire.

The wire is designed to make an alpha loop to facilitate duct access.

Striped wire design is to indicate wire positioning during wire advancement and device exchange and reduces the fluoroscopy use (black and yellow stripes).

Q: Does wire use prevent post ERC pancreatitis?

Ans: Fausto Lella et.al., GIE 2004- As compared to traditional contrast guided cannulation, use of soft tipped tracer guidewire for cannulation of bile duct can reduce post ERC pancreatitis (30% Vs 3%). Ito K et.al., J Gastroenterol 2010-PD stent helps in CBD cannulation but the stent characteristics- diameter/length/flaps- does not make any difference.

DREAM WIRE Vs JAG WIRE:

	Dream Wire (0.035")	Jag Wire (0.025")
Soft floppy tip	3cm	1cm
Hydrophilic coated tip area	Hydropass coat for 10cm	Glidex coat for 5cm
Taper length	Shorter Stiffer Increases push across stricture 14cm length	Longer Less push Less trauma 20cm Flimsy exchange

Q: What is the most important principle for cannulation?

Ans: AOA: Axis- luminal direction of the distal bile duct or pancreatic duct- anatomical component- unlikely to change except in diverticulum/ampullary tumours. Orientation-scope position - short or long loop. Alignment - accessory positioning. The key is the **AXIS**. The distal bile duct is represented visually by the prominence above the papilla along 11- 12'0 clock and the PD along 1-2'0 clock direction. CBD is approached from below, scope close to papilla, lift the roof of papilla with tip of the catheter/GW directed to left upper corner of papilla. PD is cannulated by dropping the catheter, withdrawal of scope, relax the angulation and elevator with approach being perpendicular aiming at 1-2'0 clock.

Q: Does looping GW help in cannulation?

Ans: Yes. Advancing GW with a loop may be easier and less traumatic. It has higher success negotiating tight and angulated strictures

Q: What is the technique of cholangiography?

Ans: Start with full strength contrast and switch to dilute contrast when stones are suspected. In cholangitis, after deep cannulation is achieved - aspirate bile before contrast injection to avoid intrabiliary pressure and subsequent septicaemia. Fill proximal CBD and CHD first and move the sphincterotome distally to fill the entire CBD. If part of CBD is not filled- change scope position. LHD fills first as it is more dependent in prone position

Q: What is the contrast used?

Ans: Iodine based water soluble contrast either hypotonic or isotonic with blood is used. 2 different concentrations - 300-350mg iodine/mL - dense- initially used - better for IHBR, occlusion cholangiogram, contrast aided cannulation as it is more viscous and has less risk of post ERC pancreatitis; 150mg/mL - less dense - less likely obscures small stones. Caution: Rare can cause allergic reactions

Q: Which patient position is better for endoscopist?

Ans: Prone position gives good endoscopic stability and AP diameter is less than lateral diameter – so less radiation scatter and more image resolution. If not supine but tricky for endoscopist

Q: On fluoroscopy which way is up?

Ans: Prone position- Right of patient is right of the image. Scout image is a must- can record - calcifications of costal cartilages/stones in PD/artifacts can be cleared

Q: Does magnification matter on fluoroscopy?

Ans: Yes - ideally- image should have GB laterally, body of pancreas medially, D3 inferiorly and Rt costophrenic sulcus superiorly.

Q: Can it happen stone on imaging and no stone on cholangiography?

Ans: Stones can spontaneously pass. If on cholangiography- no stones - better to avoid sphincterotomy. Avoid bubbles during contrast injection - better to fill the sphincterotome with water before injection.

Q: What is the conventional cholangiographic picture?

Ans: Two right anterior segments drain into anterior sectoral duct. Two right posterior segments drain into posterior sectoral ducts. Both sectoral ducts join to form RHD. LHD is formed by ducts from segments 2,3,4. Caudate lobe drains into both RHD and LHD. RHD and LHD fuse to form CHD which joins with cystic duct to form CBD. This anatomy occurs in less than 75% of normal population.

Q: What are the normal anatomical variants to note on cholangiogram?

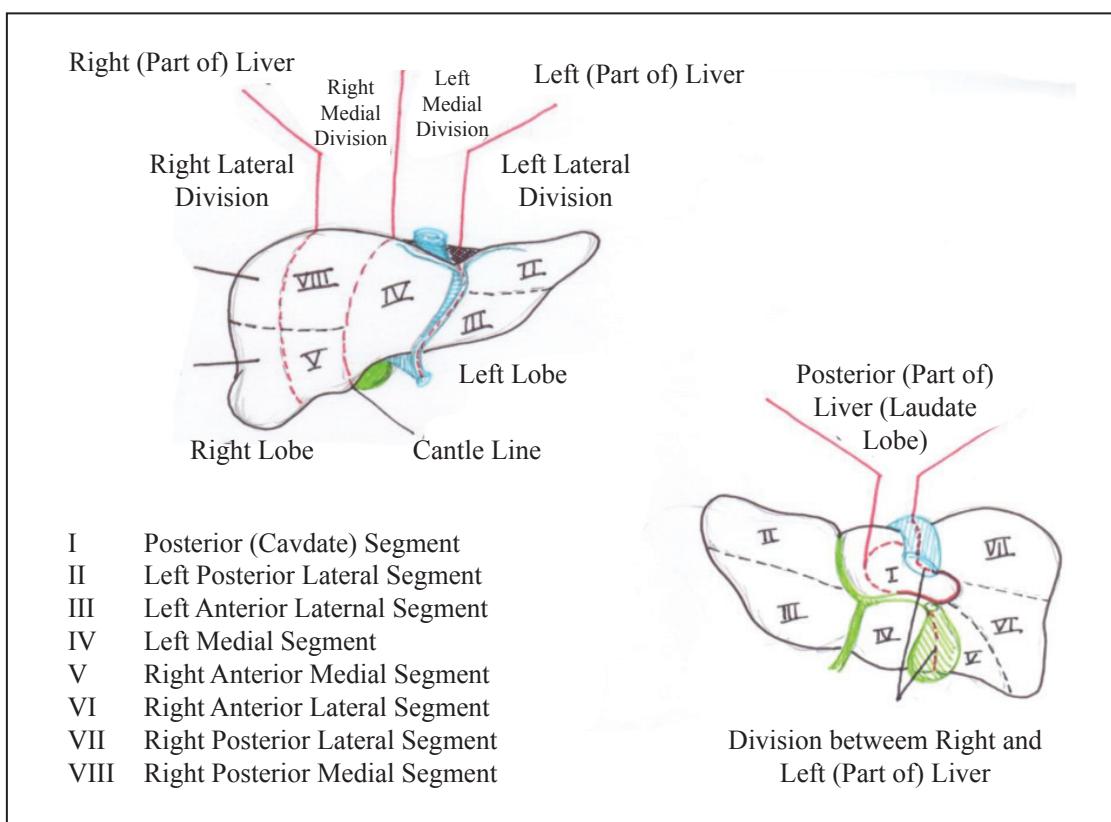
Ans: Cystic duct insertion is important when stent placement is planned to avoid cholecystitis. In 15% Rt posterior sectoral duct (RPSD) drains into LHD - important as if stent is placed in RHD in these patients - stent might drain only 2 segments. RPSD can enter into CHD below the hilum/cystic duct or cystic duct can drain into RPSD- anomalies to note for.

Q: What are the features of caudate lobe?

Ans: Derives blood from both Right and left hepatic arteries, drains directly into IVC and drains bile into both RHD and LHD

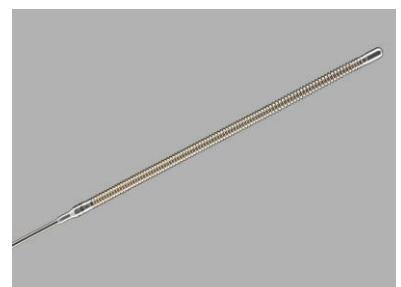
Q: What is personal protection from radiation hazard?

Ans: Lead gowns covering red marrow- spine/shoulder/pelvis, femoral bones. Turn towards the patient when fluoroscopy is on as the gowns might be open on the sides. Thyroid shields should be worn. Shortest fluoroscopy time. In pregnant women, CBD cannulation can be assessed by aspiration of bile, abdominal ultrasound can be used for noting wire in CBD, sphincterotomy and stenting can be used without fluoroscopy. The skirt of the two piece lead apron can be used as a shield for fetus.



SAVARY GUILLARD WIRE:

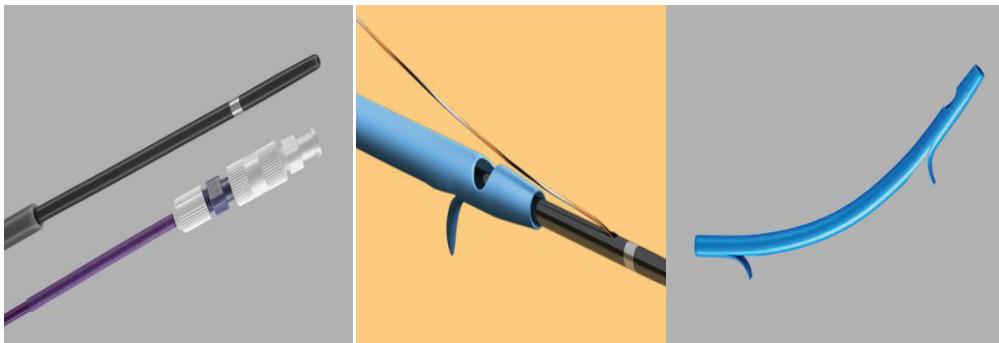
- 200-360cm in length
- Stainless steel monofilament
- Spring tip
- Reusable
- Graduated marking



PLASTIC STENTING:

Biliary:

- **Goal:** Prevent acute cholangitis and maintain luminal patency. Duodenoscope with 3.2 channel - can place 7-8.5Fr stents - smaller stents block quickly
- With larger biopsy channel of 4.2mm - 10-11.5Fr stents can be placed
- Cotton - leung (Cook endoscopy)/Amsterdam stents - **straight stents**
- Vary in length between the two anchoring flaps
- OASIS (one action stent introduction system) - Standard applicator- 0.035" 480cm guidewire with 260cm, 6Fr guiding catheter with tapered tip for cannulation. Guiding catheter has RO markings 7cm apart for positioning the stent. The outer pusher tube is teflon made.
- Suitable length of the stent is determined by separation of proximal flap of the stent should lie 1cm above the level of obstruction nad the distal flap just outside the papilla
- Single stent placement is good enough when there is communication between Rt and Lt systems. Resectable lesions always consider placing plastic rather than SEMS.
- RHD branches off 1cm beyond the hilum and LHD branches off beyond 2cm - Given a choice selective cannulation of LHD might drain 2 segments when growth involves hilum - Type I.
- **In Type II and extensive hilar blocks** - when multiple stents are planned - 2 or more guidewires are placed into RHD and LHD. Preferred to place stenting the left side first which is more difficult in anatomy and axis. **Caution:** insertion of second stent might drag the first stent in- need to monitor one endoscopy.
- **Pigtails:** Biliary have side holes in the curved tail but pancreatic have side holes in the shaft of the stent to allow drainage of pancreatic juice. Pancreatic stents are 3Fr-7Fr and rarely 10Fr are used with lengths vary from 3-12cm. With long wire exchange system, pigtail stents are placed directly with a pusher tube. Once the proximal end of the stent is at the intended site, guidewire is removed to release the stent.



Q: What is sludge?

Ans: calcium bilirubinate, calcium palmitate, cholesterol, mucoprotein and baceteria - predominantly bowel flora which ascend from duodenum.

Q: Does anti bacterial coated plastics prevent stent clogging?

Ans: No

Q: Once stent is in CBD how long does it take jaundice to resolve?

Ans: Pruritus disappears within days; S.Bilirubin declines by a mean of 2-3mg/dL/day and may return to normal after 1-2 weeks. Incomplete or slow recovery might be due to prolonged obstruction or incomplete drainage due to poor stent position. Patency can be assessed by isotope scan.

Q: When does stent in stent be considered in hilar obstruction?

Ans: Y/Stent in stent (SEMS) can be considered when distal CBD is normal in diameter and hilar obstruction mandates drainage of both the lobes. First stent is placed into RHD and second guidewire is passed through the mesh of the first stent into LHD and second stent is deployed across the growth from LIHBR to first stent.

Q: Does biliary stent migrate?

Ans: Distal and proximal. Distal migration is downward- can cause ulceration of the opposite duodenal wall and rarely can cause duodenal perforation. Can be overcome by using pig tail stents. Proximal migration is upward- if large sphincterotomy is done and the distal anchoring flaps are collapsed. Migrated stent can be removed using FB retrieval forceps- Difficult when the proximal flap is embedded in the CBD wall. If failed- sphincterotome can be used along with guidewire placed through the stent and the cutting wire can be used as an anchor. Once the tip is visible through the ampulla- snare can be used to grab the stent and removed.

Q: What is the endoscopic management of bile leaks?

Ans: Koch M et.al Surgery 2011- Bile leak is defined as : increased bilirubin in abdominal drain > 3 times the serum bilirubin, leak on or after post OP day and leak requiring radiologic intervention or relaparotomy. Goal of endoscopy is to reduce transpillary pressure gradient between the bile duct and duodenum by sphincterotomy or endoprosthesis. Large leak is leak identified before IHBR is filled and small leak is after filling of IHBR. 10Fr plastic stent patency is better than smaller stents. For hepatic/intrahepatic leaks placement of proximal stent into the affected segment should be attempted. A leak associated with duct injury might require stent across the leak for 4-6 weeks. Caution: Not to inject too much contrast as intraductal pressure can reopen the leak- occlusion cholangiography is discouraged. Post cholecystectomy bile leaks occur in 0.2-2 % of cases- common at cystic duct stump or subvesicular bile ducts. Post liver resection bile leaks- better to wait for 2 weeks after surgery. If bile rich fluid in drain- no leak on cholangiogram - bowel perforation should be considered.

Q: What is the role of endotherapy in chronic pancreatitis?

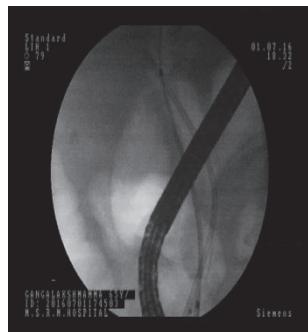
Ans: Mostly effective when stones are small, < 3 in number, not impacted, present in head/body without downstream stricture. ESWL can be considered for large PD stones.

Q: Does plastic stent exchange interval is defined by 3 months?

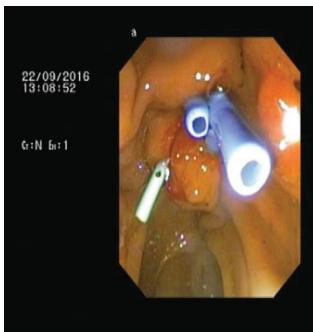
Ans: Di Giorgio et.al. Endoscopy 2013-rate of cholangitis is significantly lower in elective stent exchanges every 3 months as compared to on demand stent exchanges. Trikudanathan et.al., Nat rev Gastroenterol hepatol 2014-Mechanical grinding of stones against stents increase stone fragmentation- reduce the size of the stone and facilitate extraction of stone and in combination with ursodeoxy cholic acid.



Straight



Pig tail



<ul style="list-style-type: none">● Good flow● Easily migrated● Not used in non stricture scenario● Useful in pancreatic endotherapy● Needs OASIS for deployment● Flange at both ends like fur tree● Stent length should be 1cm beyond the stricture● 7,8.5,10,11.5Fr	<ul style="list-style-type: none">● Useful in dilated system with no stricture● More chances of clogging- side holes● Double pig tail- used in biliary and SPT-pancreatic● Needs pusher tube for deployment● 8.5,10,11.5 Fr size
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