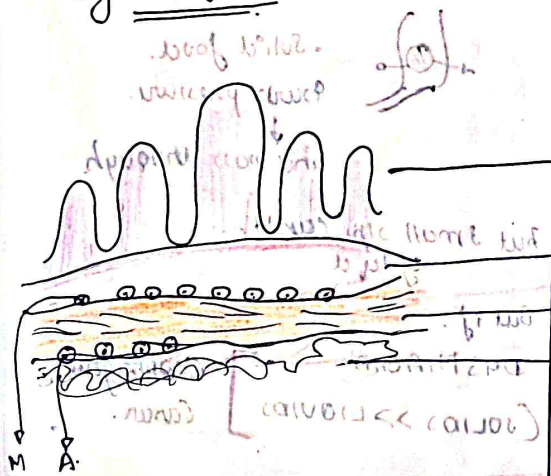
prachi sharma

Lecture Note

parts of GIT.

- oral cavity → squamous epithelia.
- Esophagus → squamous epithelia
- Stomach & intestine → columnar epithelium.
- Anal canal → squamous epithelia

Layers of GIT.



- gall bladder - doesn't have submucosa.

∴ SCC of / carcinoma of mucosa quickly spreads to muscularis propria

that's the reason why gall bladder cancer has poor prognosis.

more common cancers

- squamous cell carcinoma → SCC
- adenocarcinoma

NOTE:

- mutations in RET (receptor tyrosine kinase) is responsible in myo of familial cases & 10% sporadic

Common site → rectum. can be seen proximally from rectum too

- mucosa
- ⊖ Gall bladder
- submucosa
- muscularis propria
- Serosa
- ⊖ Esophagus.

NERVE PLEXUS

① MEISSNER PLEXUS

submucosal plexus

② AUERBACH'S PLEXUS

MUSCULAR PLEXUS.

meissner has 2 S

S - submucosa. controls. Secretions

Aurbach → motor activity.

- In plexus... we can see cells with dot in center.

ganglion cells.

present in all Nerve Plexus

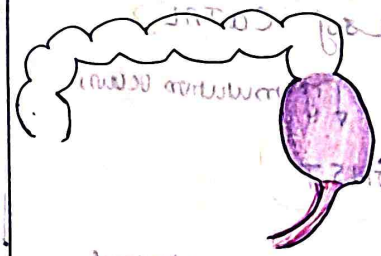
Aganglionosis

Hirschsprung's disease

⊖ Ganglion cells missing

due to

Failure of migration of Neural crest cells.

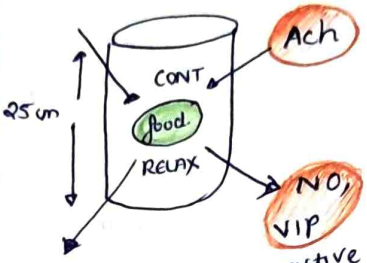


also called megacolon

- We can see dilated & constricted portion.
- don't get it wrong's
- ganglion are absent in constricted part ✓ not dilated

there is a Constricted Aganglionic Segment

ESOPHAGUS.



above food → contraction ✓
below food → relax

Cont → Ach
relax → NO, VIP.

NO → arginine derived.

ACHALASIA CARDIA

Definition

- It is the loss of Inhibitory Neurons that releases NO & VIP.

⇓

No relaxation.

- contraction ✓
  relaxation ✗.
- Constriction mainly at Lower esophageal sphincter.

CAUSES?

PRIMARY : Idiopathic.

2° : Infections →
- T. cruzi ; CHAGAS DISEASE
- HERPES.

DIABETS → affects Neurons

CLINICAL FEATURE

DYSPHAGIA.
(Liquids >> solids) — Achalasia Cardia

- Solid food.
  Exerts pressure.
  ↓
  and pass through
  but small slips can't.
  of liquid

But if.
DYSPHAGIA
(SOLIDS >> LIQUIDS) — Esophageal Cancer.

DIAGNOSTIC MODALITIES

1) BARIUM STUDY
↓
BIRD BEAK APPEARANCE / rat tail

2) Esophageal manometry
→ detect pressure changes in Esophagus.

PACEMAKER CELLS OF GIT
↓
Cells of CAJAL
↓ if mutation occurs
GIST

Gastrointestinal stromal tumours
↓
occurs due to mutation in cells of Cajal.

---

treatment →
Surgically remove constricted area & join the rest

TREATMENT

MEDICINE: INJECTION OF BOTULINUM TOXIN.
↓
↓Ach → make flaccidity ✓
↓
opens / relaxes.

SURGERY: HELLER'S MYOTOMY.

ALLGROVE SYNDROME

A - Achalasia
A - Alacrimia
A - ACTH resistant adrenal insufficiency.

- GROW - all symptoms grow with time.
- AAAS gene.

ESOPHAGITIS

Cause:

① CHEMICALS - bisphosphonates.
② REFLUX - spicy food, chronic smoking, Binge drinking, too much tea/coffee.
(most common)

- If reflux is chronic.
↓
GERD.
↓
Barrett's esophagus.

③ INFECTIVE -
- Candida.
- CMV
- HERPES

④ EOSINOPHILIC.

NOTE:

bisphosphonates -
→ they are drugs given for osteoporosis
→ you are not supposed to swallow and lie down after it within 30 minutes
→ cause it can stick to esophagus
→ and cause esophagitis

- we all get acid reflux sometimes due to, spicy food, coffee etc.
- But when it's chronic
↓
GERD
↓ finally leads to
Barrett's esophagus.

INFECTIONS

① CANDIDA → pseudomembrane + pseudohyphae.
Curdy white appearance - lesion.

② CMV
Esophagitis - shallow ulcers
CMV → owl eye appearance.
→ blue inclusion nucleoli.

CMV has both
- Intranuclear inclusion
- Intracytoplasmic inclusion.

HERPES ESOPHAGITIS
Esophagus → punched out ulcers.

Herpes virus (3 Ms)
M - multinucleation
M - Moulding. {fitting into each other}
M - Margination. {margin of nucleus are darker}

CANDIDA - pseudo → mem hyphae
CMV - shallow ulcer.
HERPES - punched out ulcer.

Most of the time
↓
Immunocompromised HIV +

- One infection that can occur in Immuno-Competent patients also
↓
Herpes.

Eosinophilic Esophagus

① WHY? : ALLERGY

② IL-5 $\{\overset{ABCD}{E-5}\}$ } E - eosinophil }

③ EOSINOPHILS

≥ 15 cells / High power field.

↓ GROSS.

Striped appearance of esophagus

↓

FELINE ESOPHAGUS

Rx - removal of allergen.

REFLUX
Alcohol Induced Laceration

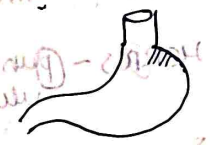
MALLORY WEISS SYNDROME.

M - mucosal tear only → Superficial tear only → never full length tear

AL - alcohol - cause

LO - longitudinal tear → BeLOw gastroesophageal junction.

RY -



BOERHAAVE Syndrome
{opposite to Mallory}.

★ FULL THICKNESS TEAR.

• ABOVE G-E JUNCTION
(~2.5 cm above)

Clinical presentation

Both Cases

↓

there'll be bleeding

↓

hematemesis

Mackler's Triad.

• Chest pain.] PAINFUL HEMETEMESIS
• Vomiting]

• Sub cutaneous emphysema. {air through tear in mediastinum.

↓

Hammans crunch heard on auscultation

{air in subcutaneous tissue}

sq
• when does painless hematemesis occur.

↓

Rupture of esophageal varices

{due to portal hypertension}

BARRET'S ESOPHAGUS.

Type of METAPLASIA

↓

Esophagus. - Squamous epithelium

↓ GERD.

↓

damage to Sq. Epithelium

↓

changes to Intestinal COLOUMNAR EPITHELIUM.

↓

Hallmark ★

i) GOBLET CELLS

↓

which contains

↓

ACIDIC MUCIN ★ ★

↓

stained by

↓

ALCIAN BLUE.

Clinically

Heart burn. and regurg.

chest pain

↓

"Intestinal metaplasia" term

ENDOSCOPY

Pale pink (normal Eso)

Red / salmon → Barret.
velvety

< 3 cm.
Short segment BE.

> 3 cm
Long segment BE.

How to identify it by Histology.

- Goblet cells
- Glands formation.
  ↓
  ie, glandular metaplasia.
- Acidic mucin
  ↓
  ALCIAN BLUE.
  ↓
  light Blue colour.

why is it so Impt

BARRET'S ESOPHAGUS (metaplasia) Glandular metaplasia.
↓
Dysplasia.
↓
Adenocarcinoma.

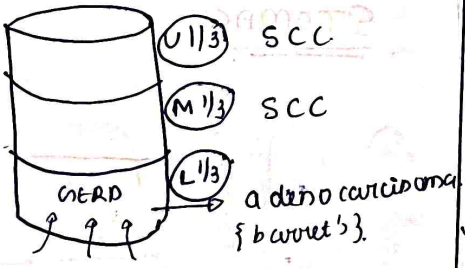
*BARRET'S IS A PRE CANCEROUS LESION.

REIDEL & VIENNA CLASSIFICATION

↓
dysplasia classification (grades)
↓
Just know the term, ik?

ESOPHAGEAL TUMORS

- Benign → Leiomyoma (smooth muscle) — Most common
- malignant



*m.c overall → SCC.

CARCINOMA.

SCC
Adenocarcinoma

RISK FACTORS FOR SCC

- Alcohol A
- Smoking.
- Hot Beverages B
- Celiac disease C
- drugs/solutions D
- Epidermolysis Bullosa E
- Fanconi anemia. F
  (MURSIK).
- HPV P
- Tylosis palmaris et plantaris P
- plummer vinson P.
  syndrome.

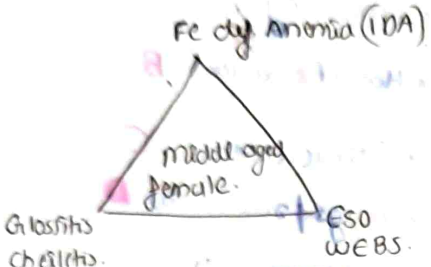
*SOX 2 mutation.

HPV → attack all kind of sq. cell anywhere.

HPV ♡ ♡ Squamous cells

TPP : tylosis ⇒ thickening
due to Hyperkeratosis.
↓
on palms & soles.

PLUMMER VINSON SYN
PATTERSON BROWN KELL SYN
SIDEROPENIC DYSPHAGIA



Sidero → Iron
penic → reduced } IDA.

dysphagia → due to Esophageal webs
↓
risk : forms SCC later.

GOLD STANDARD FOR DIAGNOSIS OF ESOPHAGEAL CARCINOMA
↓
BIOPSY.

SCC → Keratin pearls are seen.

adenocarcinoma → glands are seen.

Treatment
Surgery, chemotherapy.

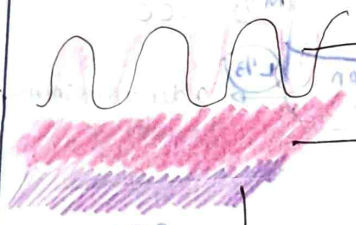
STRESS ULCERS

BURNS → hypovolumia, ischemia
↓
Curling ulcer.
↓
duodenum
↓
Superficial ulcer.

CUSHING ULCER
↓
ICT →
↑ parasympathetic
↓
(+) vagus
↓
↑ acid secretion
↓
site : Stomach Cardia
↓
deep ulcer

1. CURLING BURNING (rhymes)
2. Cushing tension
3. cushing → pushing → deep ulcer
4. CUS - cardia stomach

STOMACH



pale pink → FOVEOLAR CELLS (mucin).

PINK → PARIETAL
- HCl (acid)
- IF (castle).

Bluish → chief cells
↓
gastrin

RISK FACTORS FOR ADENOCARCINOMA

- Barett's Esophagus.
- P16 RB gene mutations.

H. pylori - protective action against Adenocarcinoma Esophagus.

Stomach - villain.
Esophagus - Hero

GASTRITIS

acute
- alcohol
- smoking
- Tea, coffee.
- spicy food.
- DRUGS (ASPIRIN/NSAIDS)
- STRESS ULCERS

chronic
- Type A → autoimmune
- Type B. Bacteria.

Chronic Gastritis:

Type A : Autoimmune.
- Ab against PARIETAL CELL.
- ↓ HCl
- ↓ IF → ↓ vit B12
- PERNICIOUS ANEMIA / MEGALOBLASTIC.
- parietal cells – more in fundus & body of stomach.
- Common site: FUNDUS AND BODY.

Type B (Bacteria).
- H. pylori.
- ↑ HCL.
- Common site → ANTRUM.

HELICOBACTER PYLORI
- PUD ★★
  - CagA – proliferation
  - VacA – proliferation.
  - Bab A. – Blood group O.
  - flagella – movement.
  - Urease.
- Cancers.
  1. GASTRITIS
  2. peptic ulcer.
  3. ADENOCARCINOMA – CagA, VacA gene mutation.
  4. maltoma.

H. pylori causes 2 cancers
- adeno
- maltoma.

- PUD → Blood group O.
- Adenocarcinoma (Stomach) → A.

IDENTIFICATION – H. PYLORY.
- WARTHIN STARRY SILVER STAIN. (WSSS) → Black
- MODIFIED GIEMSA STAIN – faster.
- Urease test positive.

Features of H&E stain. We'll see:
- Epithelium → Neutrophils
- Subepithelium. → plasma cells

We'll suspect H. pylori and confirm then go for WSSS, mod. giemsa, Urease test etc..

if Gastritis is treated.
↓
then all good...

• if not → peptic Ulcer

Protective factors	damaging factors
• mucus	• HCl
• HCO_3^-	• pepsin.
• COX 1	• H pylori.

↓
Gastroprotective

→ NSAIDS/ Asp — COX inhibitors.
↓
peptic ulcer
Causes.

Gastric ulcer.	Duodenal ulcer.
less common	more common
lesser curvature	• first part of duodenum.
	• NOCTURNAL PAIN / ↓ RELIEVED ON taking food.

why?
food goes to Intestine & Alkaline secretions in duodenum
↓
relief.

COMPLICATIONS

① BLEEDING - all ulcers bleed.
↓
gastric ulcer → left gastric artery
duodenal ulcer → gastro-duodenal artery.

② PERFORATION.
↓
DEATH CAUSING COMPLICATION.

Gastric - risk of cancer {gandhi}.
duodenal - NO RISK.

• PUD - especially duodenal ulcers can have a complication known as.
↓
GASTRIC OUTLET OBSTRUCTION.

G.O.O - causes
- Children → Infantile hypertrophic pyloric stenosis.
- ADULTS → stomach >> PUD.

since there is obstruction
↓
vomiting out of everything you eat including HCL.

• HCl - lost
⇒ metabolic alkalosis.
{so to compensate, we should excrete more alkali ie, alkaline urine}

But,
Here, there is ACIDURIA
paradoxical ACIDURIA
{due to RAAS}

INFANTILE HYPERTROPHIC PYLORIC STENOSIS

{earlier called congenital}

• T18, T21 trisomy - congenital.

• 1-2 week of life:
↓
if exposed to ERYTHROMYCIN / AZITHROMYCIN

Cl-
① vomiting.
② Non bilious
③ demand repeated feed
④ OLIVE LUMP

↓
Tt-Py Ladomyotomy.

Menetrier's Disease.

Impt in medical! Just bw 5 points

① Gender: m/c — MEN.

② Cause → increase in TGF-α.

③ Clinical → protein losing Enteropathy.
{protein: serum ↓}.
↓
Edema.

④ GROSS.
Giant Cerebriform rugae.
{looks like brain}

⑤ microscopy →
FOVEOLAR CELL HYPERPLASIA

TNF α → no-apetite → fever, cancer.
TGF α → GA → gastric disease : menetrier's.
TGF β → Big time fibrosis.
↓
fibrogenic mediator.

ZOLLINGER ELLISON SYNDROME

KEYWORD: GASTRINOMA

→ they are not in stomach X
→ they are not benign X {oma}

- They are gastrin releasing tumor in pancreas or small intestine
↓
↑ Gastrin level.
↓
↑ acid secretion. ⇒ ↑ parietal cells in stomach
↓
duodenal ulcer.

Microscopy

diagnosis: serum gastrin Lvl >1000.

Rx: surgical removal, chemo.

- Gastrinoma → also cause diarrhea
- they'll ask you, if it single / multiple tumors.

→ if Sporadic → usually single tumor.
→ if Familial → multiple tumors. associated with MEN-1 / wermer syndrome.

MEN 1 / wermer → Autosomal dominant disorder
→ multiple Endocrine tumors will develop in different glands at the same time.
- In such cases, it won't be solitary tumor like in sporadic.

GASTRIC TUMORS

most Common malignant gastric tumor → Gastric Adenocarcinoma. 90% (epithelium)

most Common malignant mesenchymal gastric tumor

→ Gastro Intestinal stromal tumor → GIST.

GASTRIC ADENOCARCINOMA.

Risk factors

food:
- Smoking
- alcohol
- hot beverage
- salt & smoked food.

3 Ab:
- Pernicious anemia → Pernicious anemia → Ab against parietal cell. → can lead to adenocarcinoma.
- Adenomatous polyps.
- Blood group A

virus & bacteria:
- EBV → most common Cancer caused by EBV is Gastric Adenocarcinoma → actual cause in EBV caused cancer → Lymphoepithelial carcinoma → affect B cells.
- H. pylori.

most Common site of G.A.C.: Antrum

most common site of cancer in pernicious anemia patient: fundus { cause parietal cell are in fundus }.

GROSS TYPES

- proliferative
- flat
- Ulcerated.
- Linitus plastica. (within walls)

Linitus plastica
- only within walls.
- leather bottle appearance of stomach wall.

MICROSCOPIC TYPE

LAURENS CLASSIFICATION.

Intestinal Type.
- AD
- arrange in glands
- cells are stuck to each other.
- E-cadherin ✓ {glue}

↓ E - cadherin (condition)

Diffuse gastric cancer.

Invavis Lobular Carcinoma breast

ILC

GLUE -

GD → Diffuse gastric cancer.

LV. → ILC.

CDH1 mutation
E-cadherin

Earliest clinical feature of GAC.

↓

EARLY SATIETY.

Diffuse gastric Type.

- E-cadherin ↓
- Shows Signis plastica. (gross)
- Signet Ring. cells. (microscopy)

- here, nucleus is pushed to one corner cause of mucin

SPREAD.

- pouch of Douglas = BLUMMER SHELF.
- OVARY = Krukenberg's Tumor.
- Periumbilical nodule = Sister Mary Joseph nodule.
- Axillary Lymphnode (common: Left) = Irish node.
- Lft Supra-clavicular = VIRCHOW'S NODE

Pouch of douglas
It is the shelf in our body cavity.

where else can you give IMATINIB.

↓

TK Inhibitor

GIST CML.

where else does see CKIT / CD117 mutation.

GASTROINTESTINAL STROMAL TUMOR

- Cells of origin
  - CELL OF CAJAL.
- mutations
  - most common - CKIT / CD117
  - others : PDGFR β
  - SDH → succinate dehydrogenase. → {S - small baby → pediatric GIST

- mechanism.

CKIT mutation = ↑ Tyrosin kinase.

↓

GIST.

Treatment : surgery

IMATINIB - Tyrosine Kinase Inhibitor.

GI = GIST.

- A
- M
- E
- S

down, up, down, up

AM = AML
MA = mastocytosis
ME = melanoma
SE = Seminoma.

we are playing a running game - up, down. Cmd for that game, we need a KIT

GIST

most common site?

m/c → stomach

then, Intestine.

(G, comes first in GIST).

Markers

CKIT / CD117

⇓

most sensitive.

DOG1 = most specific

CD34 = miscellaneous marker.

DOG1 > CKIT/CD117 > CD34

Syndromes in which GIST can be seen?

- NF 1
- ~~CARNEY~~
- Carney's Triad. (GPC)
  - GIST
  - paraganglioma.
  - pulmonary chondroma.
- Carney Stratakis syndrome. (GP)
- GIST
- paraganglioma.

don't Confuse with Carnoy. Fixative.

↓

Karyotyping fixative.

Prognosis

① tumor size < 5cm :)
> 10cm :(

② most common site → Gastric → less aggressive.

GASTRIC LYMPHOMAS

- most common GI is

NHL – diffuse large B cell lymphoma.

- MALT oma.

Mucosa Associated Lymphoid Tissue. → max malt is in peyers patches → small intestine, ileum.

MALToma can occur anywhere

most common site of maltoma → Stomach.

m/c

MALT → Ileum ✓

maltoma → Stomach ✓

m/c lymphoma in stomach is DLBCL.

MALTOMA – MZL

Marginal Zone Lymphoma

- associated with → H. pylori → Rx: early cases can be treated with antibiotics
- a/w translocation t(11:18) → Can't use Antibiotics for Rx ... Duh!

Microscopy

we can see LGL

lympho Epithelial lesions

⇓

we can see lymphocytes invading epithelium (glands)

⇓

here, epithelium is normal but lymphocytes are the invading ones

⇓

Lympho epithelial Lesions

⇓

lymphocells invading epithelial cells.

Question And Session

INTESTINE

- Malabsorption Syndrome
- Ulcer of Intestine
- IBD
- polyps of Intestine
- Intestinal Carcinoma

MALABSORPTION SYNDROME

- Malabsorption means — there is a problem in absorption of protein, carb fat etc...

But what is the Hallmark?

Hallmark of Malabsorption:

STEATORRHEA.

fat in stool.

when patients come to see you, they won't gonna say, I have fat in stool. He'll say.

↓

BULKY.

(F)ROTHY.

(F)OUL SMELLING.

(F)LUSHING DIFFICULT.

Lie, struggle to toilet pan.

WHIPPLE'S DISEASE.

Organism: G+ve organism

↓

TROPHERYMA WHIPPLEI.

↓

Enters body

↓

Intestine. + Lymphatic transport defect

↓

LAMINA PROPRIA.

↓

Macrophages eats up T. whipplei

↓

FOAM CELLS.

↓

Macrophage with engulfed organism.

normally → macrophage — pinkish

but foam cells → white/hollow

↓

looks white due to engulfment of organism.

→ Macrophages will eat a lot of organism, but they'll be cleared normally.

But, in whipple's disease there is also Lymphatic transport defect

↓

Foam cells can't be cleared so, it stays there and also goes to many parts of body by lymphatics.

Organs?

GIT, CNS, JOINTS, CVS

Diagnosis.

foam cell?

But macrophage eats a lot of organism...

But I should know which specific organism is engulfed.

↓

So,

STAINING.

PAS(+) staining macrophage in Lamina propria

↓

we do BIOPSY.

usually, we do biopsy for cancer...

But here, we're doing it for an infectious disease.

Here, we'll see PAS(+) pink macrophage in lamina propria.

Confusions?

When I see foam cells, in our country we first think of TB.

But TB → ZN(+)

Whipples → ZN(−)

So, cleared!!

Rx → Cotrimoxazole

Whipple's Disease

- pas(+)
- foam cells

PAS the FOAMY WHIPPED Cream in a CAN

- whipples
- can be TB
- can involve CVS, joints, Neural

CELIAC DISEASE/ CELIAC SPRUE/ GLUTEN SENSITIVE ENTEROPATHY

Gluten food?

B R O W → diarrhea

- B → Barley
- R → Rye
- O → oats
- W → Wheat

HLA DQ2, DQ8 polymorphism (DQ2, DQ8)

pathogenesis

GLUTEN → BROW

↓

α - Gliadin — the whole gluten isn't the problem, it's α-gliadin the problem.

↓

Tissue trans glutaminase

↓

Deamidated gliadin

↓

in people with HLA DQ2, 8 polymorphism

↓

Interact

↓

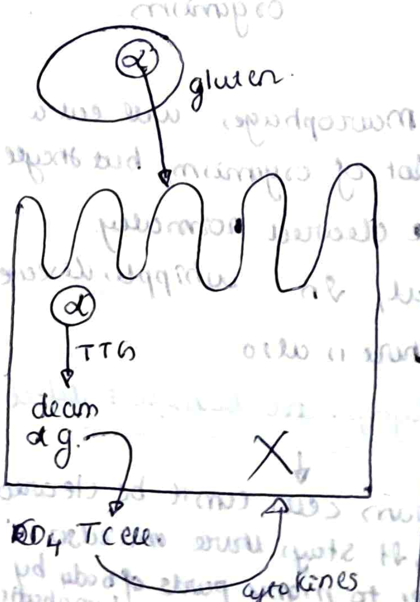
activate CD4 cells

↓

cytokines

↓

Intestinal cellular damage



Role of CD8

α - gliadin

↓

Expression of IL15 on cells

↓

activate CD8 T cells

↓

cellular damage

↓

makes way for more gliadin inside.

Since Immune sys (+)

Ab formed —

- Anti TTG Ab → most sensitive
- Anti Gliadin Ab
- Anti endomysial Ab → most specific

They are IgA type.

D's.

- D - Diarrhea.
- D - max impact - Duodenum. → ↓ iron absorption → iron def. anemia
- D - Dermatitis Herpetiformis → dermatitis due to IgA Ab
- D - Dapson (Rx).

Pathologist will look into.

Duodenal Biopsy.

MARSH CRITERIA.

- when a person has celiac disease.

① villous atrophy - villous shortens. → due to Ab attack

② Crypt hyperplasia / glands → glands grow into parts where villi were present... villi shortens right?

But,

③ overall thickness is same → Cause one ↓ & other ↑.

④ Intraepithelial lymphocytes (CD8)★. → why, Cause IL5 Expression on surface of cells → CD8 → comes to cells. {CD4 just release cytokines}

Rx →

- don't take BROW
- Steroids.

Risk of cancer?

Yes.

E Enteropathy - Intestine.
A associated
T T cell
L lymphoma.

Intestine associated.
T cell ↑ → T cell is repeatedly getting activated.

① TROPICAL SPRUE / ② ENVIRONMENTAL ENTEROPATHY

Cause. - E coli

Intestine affected. - Total intestine is affected.

Fe, B12, Folic acid. → megalo blastic anemia.

Anemia - megalo blastic Anemia.

Rx - antibiotics.

- Risk of cancer: NO

ABETA LIPOPROTEINEMIA

Cause ?

mutation in MTTP → microsomal, TG, Transfer, protein.

Effects on

Intestine — RBC

Microscopy

① Intestinal cells
↓
pale.
↓
due to fats

② RBC → spikes
↓
spur cell / Acanthocytes

'Abeta lipoproteinemia'
↓ acanthocytes
problem with TG

---

recent update – 10th edition

MICROVILLOUS INCLUSION DISEASE / DAVIDSON DISEASE

electron microscopy — MICRO villous inclusions

Intractable diarrhea

M V I D

M → MYO5B

D → davidson disease

- CD10 + → IHC.

INFECTIONS. causing Malabsorption

① Coccidian parasites

② Giardia.

Vimpt (see figures from 1Note)

① Cryptosporidium
↓
along brush border cell surface!
not inside cell

② Giardia Lamblia
↓
Sickle shaped organism in lumen
↓
luminal organism

{ pear – front view
side – sickle. }