5/12/25

Chronic Diarrhea

Prof N E. Daryani
Tums

1404/02/23

Why is This Important?

1. Chronic diarrhea is common
   - You will see it!!!
   - Affects 1-5% of adult population
2. The differential can be broad
   - Distinguishing alarm features is critical

Step-Wise Approach to Diarrhea

1. Does the patient truly have diarrhea?
2. Is the diarrhea really chronic?
3. Can you categorize the diarrhea?
4. Are there historical clues to a diagnosis?
5. Is it diet or medication-induced?
6. Is there a factitious component?

Schiller LR, et al. CGH 2017;15:182-93

- Fecal incontinence?
- Overflow from fecal impaction?
- Perception vs reality of volume/frequency?

Arasardnam RP, et al, Gut 2018;67:1380-99

- Faecal impaction with overflow diarrhoea should be considered especially in the elderly. We recommend clinical judgement rather than marker studies to confirm this (Grade of evidence level 4, Strength of recommendation strong).
- For patients with persistent faecal incontinence we recommend anorectal manometry and endoanal ultrasonography once conservative measures have been exhausted (Grade of evidence level 3, Strength of recommendation strong).
- If a fistula is suspected, cross-sectional imaging with contrast is recommended (Grade of evidence level 3, Strength of recommendation strong).

Define: chronic diarrhea

- ↑ stool frequency (typically > 3x/day)
- ↓ stool consistency (Bristol score 6-7)
- Lasting ≥ 3 - 4 weeks

- On average Western diet, can be defined by stool weight of >200 g/day

M Donowitz, et al. N Engl J Med 1995; 332:725-729.

Step-Wise Approach to Diarrhea

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Schiller L.R. et al. CGH 2017;15:182-93

- **Small bowel:**
- Large volume, vitamin and mineral deficiencies

- **Colon:**
- Smaller volume (not always), frequency, tenesmus with rectal involvement

Step 3: Can you categorize the diarrhea?

- Large or small bowel
  - Often differs in volume and frequency
- Watery
  - Secretory versus osmotic
- Inflammatory
  - Bloody stools, abdominal pain, fever, tenesmus
- Fatty
  - Greasy, oily, difficult to flush, floating stools
    - NOT specific!!!

Chronic diarrhes:

A:Functional (related to IBS)

B:organic (related to an identifiable bowel pathology)

Gastroenterology 2016;150:1393-407.

- Which of the following has been shown to be a risk factor for the development post infectious IBS?
  - Young age
  - History of anxiety/depression
  - Fever
  - female gender
  - Long duration of diarrhea


ted to IBS)
to an identifiable

In the bush of IBS…

CD

IBS

IBS, irritable bowel syndrome.
Image provided by Prof. Danese, Istituto Clinico Humanitas Milan

Fecal calprotectin

IBD
vs
IBS

monitoring

Fecal Calprotectin for Separating IBD From IBS

Patients with IBD and IBS share many clinical symptoms, including:

-Abdominal pain

-diarrhea

Calprotectin had a sensitivity of

Table 3: False-positive results reported for fecal calprotectin assays [44, 45, 48].

False-positive results of fecal calprotectin
Gastric cancer
Colo-rectal carcinoma
Celiac disease (untreated)
Infectious gastroenteritis
Diverticular disease
Microscopic colitis
Cystic fibrosis
Autoimmune enteropathy
Nutritional allergy (untreated)
Liver cirrhosis
Aspirin or non steroidal anti-inflammatory drugs
Proton pumps inhibitors

Tests Based on Characteristics

- **Inflammatory:**
  - CRP, fecal calprotectin or lactoferrin
  - If positive, it is non-specific
  - Could be:
    - Infection, inflammation, ischemia, radiation
  - If found, and no infection structural evaluation
    - Colonoscopy w/bxs, enterography

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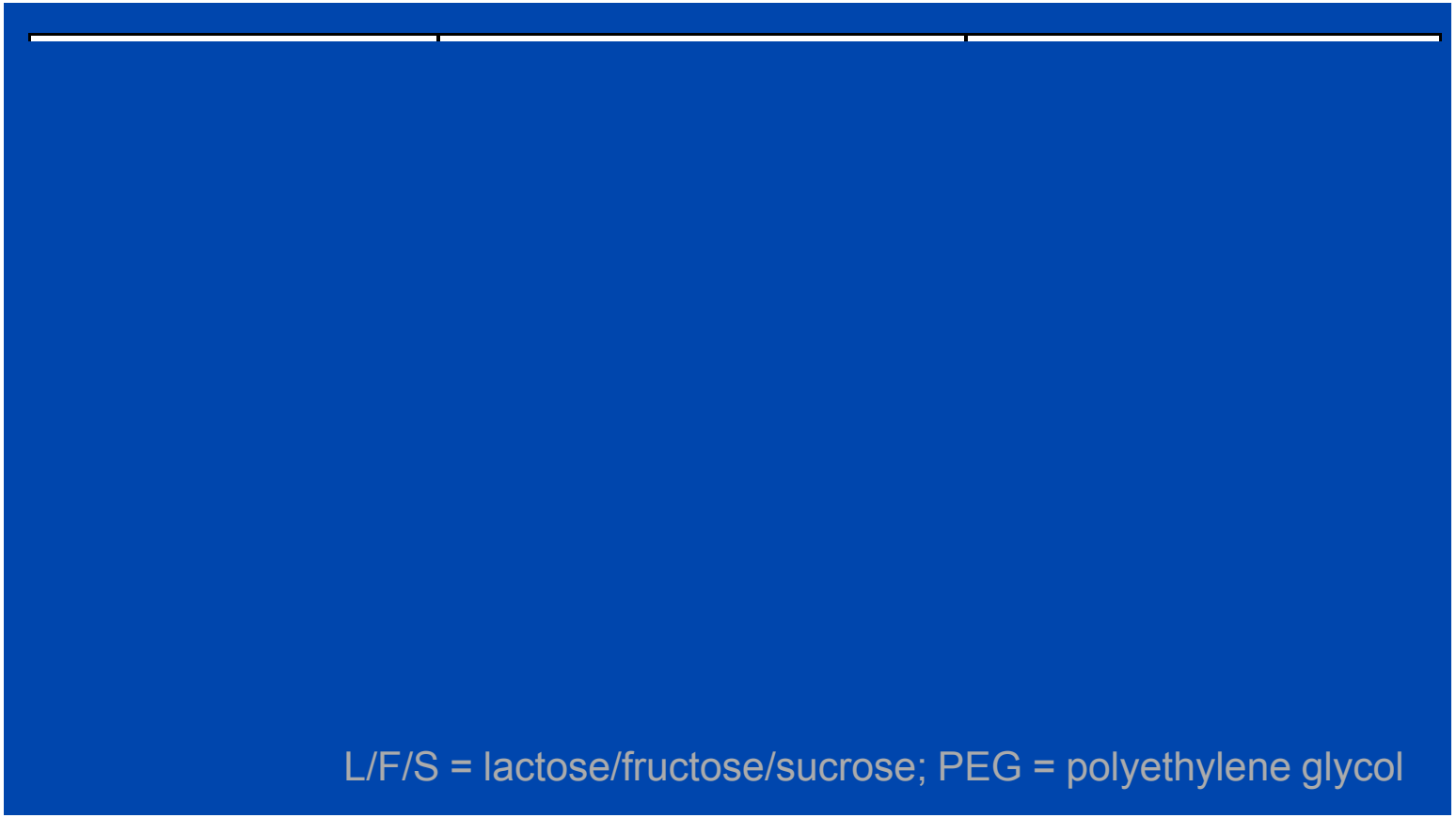
    - NOT specific!!!

Tests Based on Characteristics

- Watery: Secretory vs. Osmotic
  - Osmotic gap = 290 mOsm/kg–2(stool Na+K)



L/F/S = lactose/fructose/sucrose; PEG = polyethylene glycol

medication-induced diarrhea?

- Caffeine
- Soda, fruit/juice (fructose)
- Sweeteners (sucrose)
- Sugar-free gum/candy (xylitol)
- Dairy (lactose)
- Wheat (celiac, allergy, sensitivity)
- Syrups, elixirs (sorbitol)

	Osmotic	Secretory
Volume daily	<1L	>1L
Effect of fast	Stops	Continues
Stool osmolality	290	290
Osmotic gap	>125	<50
CommonCauses	•L/F/S malabsorption •PEG,lactulose •Mg+antacids •Sorbitol/xylitol -Sweeteners/Elixirs	•Infection/toxins •Bile acids •Neuroendocrine •Diabetic diarrhea •Microscopic colitis

L/F/S = lactose/fructose/sucrose; PEG = polyethylene glycol

Infections? Stool Exam Low-Yield

Parasites

- Ameba
- Giardia
- Cryptosporidia
- Cyclospora

Bacteria

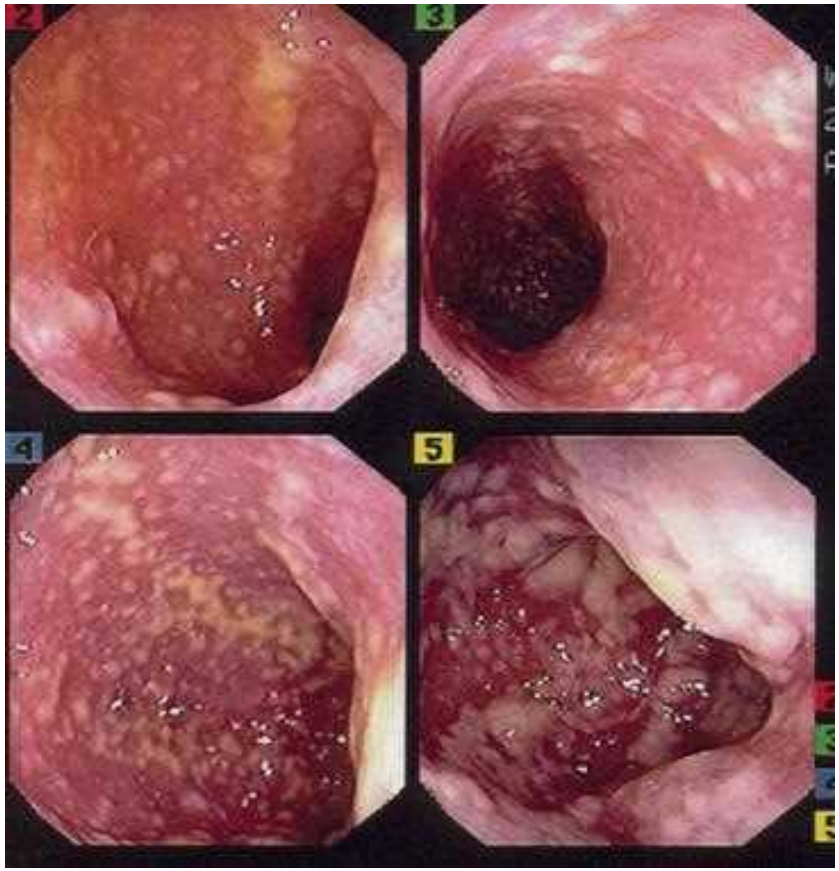
- Salmonella
- Aeromonas
- Plesiomonas
- C. difficile (recurrent)

Yeast?

Blastocystis hominis

Candida

C. difficil Colitis


2
3
4
5

Symptoms of CDI

- Asymptomatic colonization
- Diarrhea
  - mild → moderate → severe
- Abdominal pain and distension
- Fever
- Pseudomembranous colitis
- Toxic megacolon
- Perforated colon → sepsis → death

New Risk Factors

- Community acquired
- Pregnant women
- IBD patients
- Cirrhosis
- PPIs

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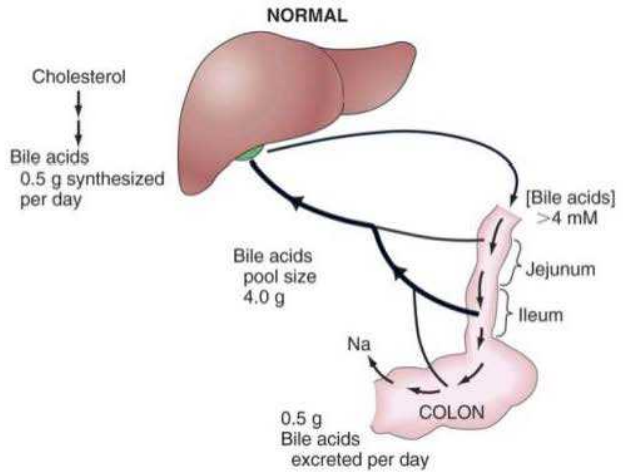
~~Secondary~~ bile acid malabsorption

Ex: Ileal resection

Less than 100 cm--- watery diarrhea as bile acids hit colon

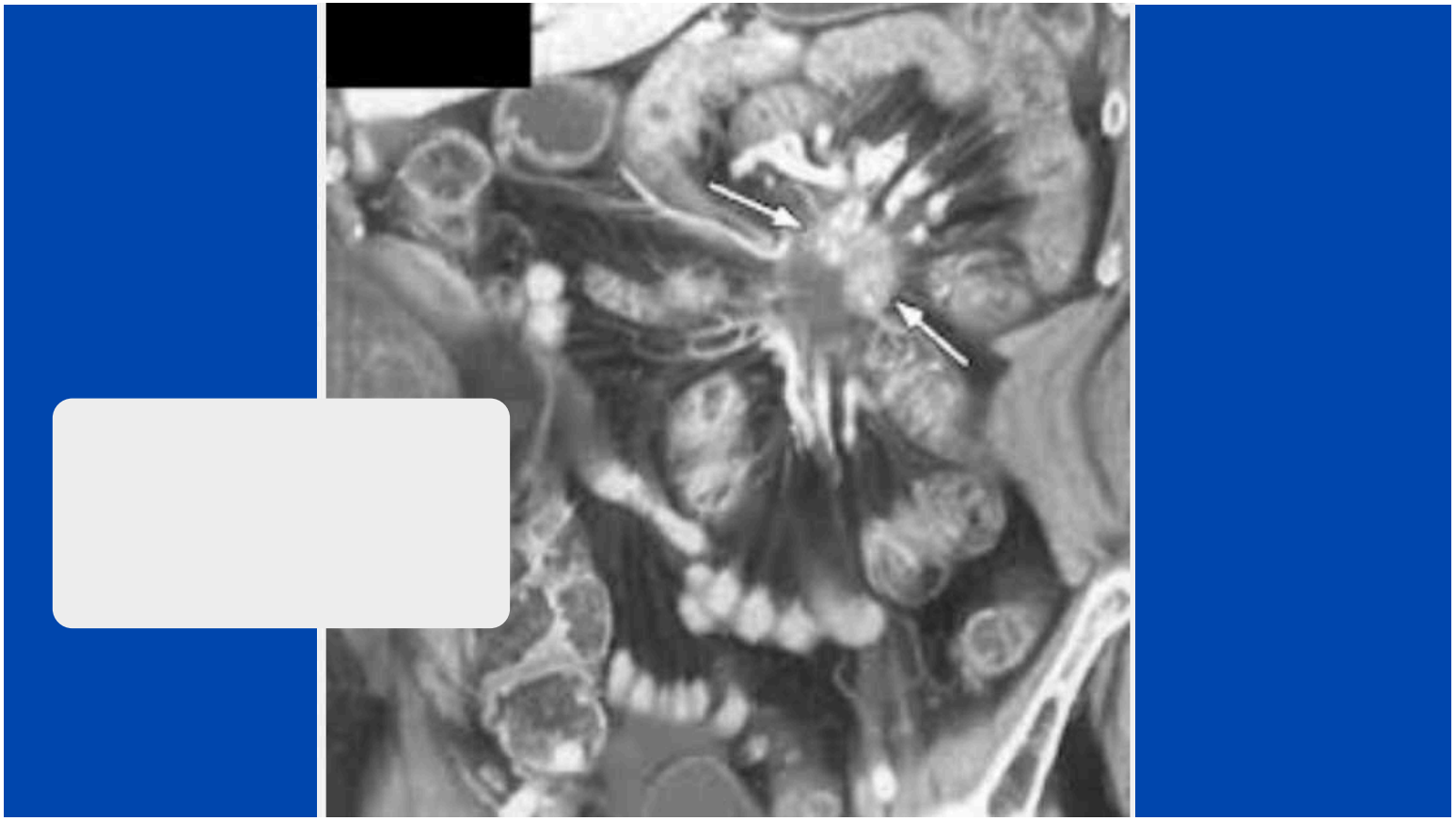
More than 100 cm- fat malabsorption as liver cannot keep up with synthesis and bile acids decreased

Enterohepatic circulation of bile acid



	Osmotic	Secretory
Testing Strategy	•Dietary review •Carb malabsorption •-Breath tests •-Avoidance •Stool magnesium	•Cultures •Structural evaluation •Colon biopsies •Cholestyramine •Hormonal levels


L/F/S = lactose/fructose/sucrose; PEG = polyethylene glycol



بیمار خانم ۴۴ ساله که از یک سال قبل به دلیل dyspepsia تحت نظر بوده ، در بررسی های انجام شده در سال گذشته برای بیمار گاستروسکوپی انجام شده بود که شواهد pancreatic rest دیده شده بود ، هلیکوباکتر منفی ، همچنین به علت وجود ۳ ضایعه در کبد که در سونوگرافی دیده شده بود ، ام ار ای دینامیک کبد برای بیمار انجام شده بود که توسط اساتید رایدولوژی گزارش زیر برای این mri داده شده بود :

3 less than 4 mm hypersignal in t2w and hyposignal in t1w nonenhancing liver lesions without diffusion restriction in DWI in segemnts 4 and 6 and 8 of liver (probably small liver cysts , f/u is recommended)

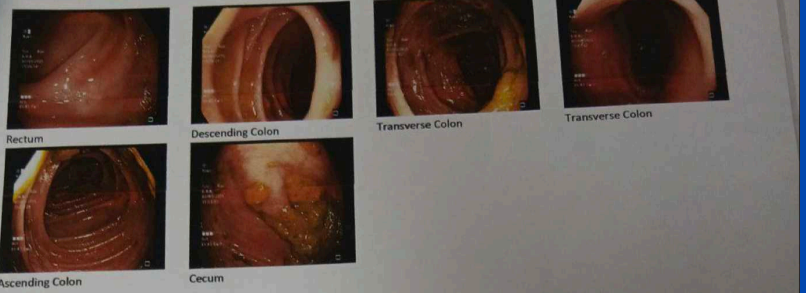
بیمار تحت درمان با ppi و escitalopram قرار گرفته و علائم بیمار کاملا از بین رفته بوده ، طوری که ایشان حدود ۶ ماه است که داروها را قطع کرده است .

بیمار به دلیل spotting به متخصص زنان مراجعه کرده و ایشان سونوگرافی و ازمایشات زیر را درخواست داده اند ، به علت افزایش cea به فوق تخصص گوارش مجددا ارجاع شده اند :

Ca125 :12.7 (in normal range)

Ca19-9:6.2(in normal range)

Cea:152 (normal less than 5)



Reason for colonoscopy: Elevated CEA

Anus: Normal

Rectum: A diminutive polyp was removed

Sigmoid: Normal

Endocrinology

Approved By: EN-5

Specimen Collection Date: 03/12/22

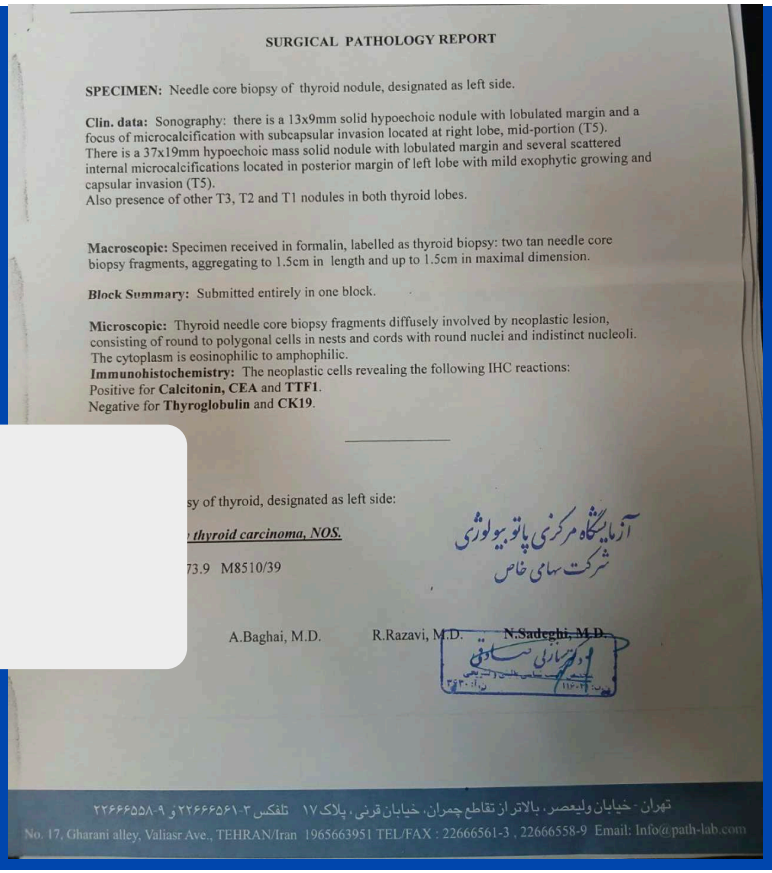
Test	Result	Units	Reference Range
T3 (ECLIA)	1.21	ng/ml	0.8 - 2.0 (Adult) 1st Trimester: 1.0 - 2.3 2nd Trimester: 1.29 -2.62 3rd Trimester: 1.3 - 2.62
T4 (ECLIA)	9.85	ug/dl	5.1 - 14.1 (Adult) 1st Trimester: 7.3 - 14.8 2nd Trimester: 7.9 - 16.1 3rd Trimester: 5.55 - 12.9
TSH (CLIA)	1.52	mIU/l	0.3-4.2 1st Trimester: 0.33 - 4.59 2nd Trimester:0.35 - 4.1 3rd Trimester: 0.21 - 3.15 >50 year : 0.17 - 8.9

Signed By : Dr. Zohre Alavi

آزمایشگاه مرکزی پاتوبیولوژی

تست Free Kappa / Free Lambda در این مرکز انجام می شود

آدرس :تهران-خیابان ولی عصر(عج)-بالاتر از تقاطع چمران-خیابان قرنی-پلاک۱۷-تلفن:۳-۲۲۶۶۶۵۶۱
Website: www.path-lab.com email: info@path-lab.com



SURGICAL PATHOLOGY REPORT

SPECIMEN: Needle core biopsy of thyroid nodule, designated as left side.

Clin. data: Sonography: there is a 13x9mm solid hypoechoic nodule with lobulated margin and a focus of microcalcification with subcapsular invasion located at right lobe, mid-portion (T5). There is a 37x19mm hypoechoic mass solid nodule with lobulated margin and several scattered internal microcalcifications located in posterior margin of left lobe with mild exophytic growing and capsular invasion (T5).
Also presence of other T3, T2 and T1 nodules in both thyroid lobes.

Macroscopic: Specimen received in formalin, labelled as thyroid biopsy: two tan needle core biopsy fragments, aggregating to 1.5cm in length and up to 1.5cm in maximal dimension.

Block Summary: Submitted entirely in one block.

Microscopic: Thyroid needle core biopsy fragments diffusely involved by neoplastic lesion, consisting of round to polygonal cells in nests and cords with round nuclei and indistinct nucleoli. The cytoplasm is eosinophilic to amphophilic.
Immunohistochemistry: The neoplastic cells revealing the following IHC reactions:
Positive for **Calcitonin, CEA** and **TTF1**.
Negative for **Thyroglobulin** and **CK19**.

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sy of thyroid, designated as left side:

thyroid carcinoma, NOS.

73.9 M8510/39

آزمایشگاه مرکزی پاتوبیولوژی
شرکت سهامی خاص

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دکتر نیلوفر صادقی

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No. 17, Gharani alley, Valiasr Ave., TEHRAN/Iran 1965663951 TEL/FAX : 22666561-3 , 22666558-9 Email: Info@path-lab.com

Nonmalignant	Malignant
Smoking	Tumors associated with high CEA expression
Infections	Colorectal[a]
Peptic ulcer disease	Ovarian[a]
Inflammatory bowel disease	Cervical[a]
Pancreatitis	Lung
Hypothyroidism	Oesophageal
Liver cirrhosis, hepatitis	Gastric
Benign breast conditions	Small intestinal
Other benign tumors usually	Hepatobiliary
in organs where the	Pancreatic
cancers are associated	Breast
with raised CEA	Medullary
	Other CEA-expressing tumors
	Choriocarcinoma
	Osteosarcoma
	Retinoblastoma
	Hepatoma
	Melanoma
	Lymphoma
	Urinary bladder, prostate and renal cell carcinoma

Diarrhea in DM

In 3.7% of diabetic patients, predominantly type:1

Causes;

1. drug therapy,
2. coexistent celiac disease,
3. pancreatic insufficiency,
4. BOG,
5. consumption of artificial sweeteners,

- More common in men than in women.
- It may be particularly troublesome at night.
- Mostly, poorly controlled type 1 diabetes /diabetic neuropathy.
- Associated steatorrhea is common.
- Intermittent and painless.
- No definite pathogenesis

Case 3

66 yo F with hypertension p/w 3-5 watery, non-bloody BMs a day for 4 months.

10 lb weight loss. No travel or new meds.

Colonoscopy demonstrates:

What is the most appropriate next step?

a) Perform random biopsies throughout the colon during the colonoscopy

b) Upper endoscopy with biopsies of the small bowel

c) Diagnose irritable bowel syndrome and reassure the patient

d) Schedule a capsule endoscopy

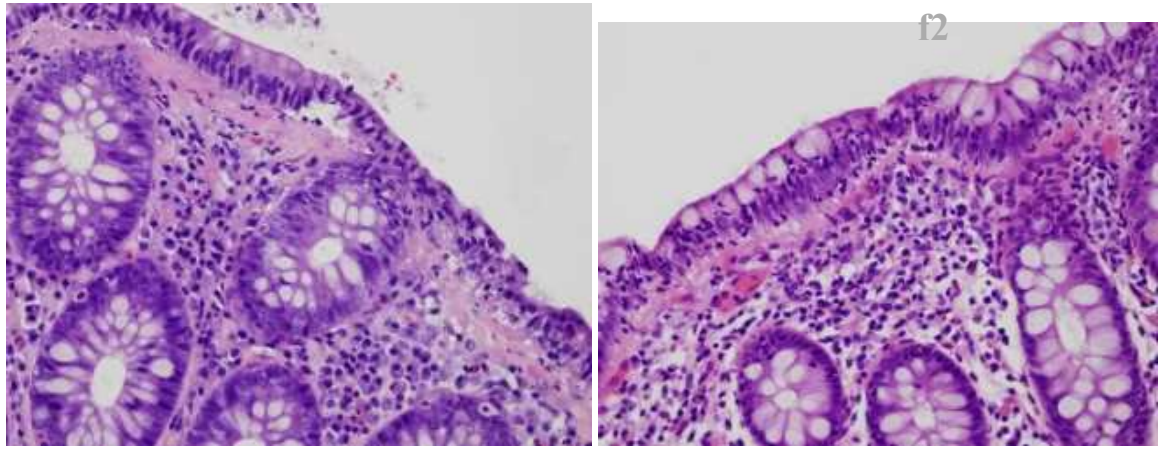
Microscopic colitis

Two different types :

1.Lymphocytic colitis

2:Collagenous colitis without lymphocytic infiltration of the surface epithelium

- The diagnosis can be made with colonoscopy with random biopsy specimens taken from both sides of the colon.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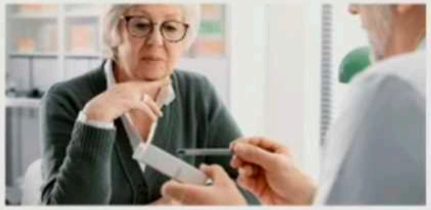
Microscopic colitis : watery diarrhea

- **Symptoms**
  collagenous colitis and lymphocytic colitis

- Symptoms and signs :
  watery diarrhea
  no blood or pus
- Diarrhea chronic,
  may come and go
- Bowel incontinence
- Abdominal cramps
- Nausea
- Abdominal bloating fatigue.

- **Complications**
  collagenous colitis and lymphocytic colitis

- Without treatment, dehydration
- Malabsorption nutrients very rare
- Malnutrition very rare
- Weight loss very rare



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    - NOT specific!!!

Faecal elastase:

has been well characterised as a sensitive biomarker for moderate to severe pancreatic insufficiency with sensitivities of 73–100%and specificities of 80–100%.

However, faecal elastase is not useful in cases of mild pancreatic insufficiency

Step-Wise Approach to Diarrhea

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Schiller LR, et al. CGH 2017;15:182-93

Other components of wheat may potentially be responsible for symptoms seen in **NCGS**, leading to the broader term of **NCWS**, include alpha-amylase trypsin inhibitors (ATIs), wheat germ agglutinins (WGAs) and Fructans, a type of fermentable oligo-, di-, mono-saccharide and polyol (FODMAP).

SYMPTOMS

Intestinal
- Abdominal pains (68%)[a]
- Diarrhoea (33%)[a]
- Nausea
- Body mass loss
- Bloating, flatulence

Cutaneous 40%[a]
- Erythema
- Eczema

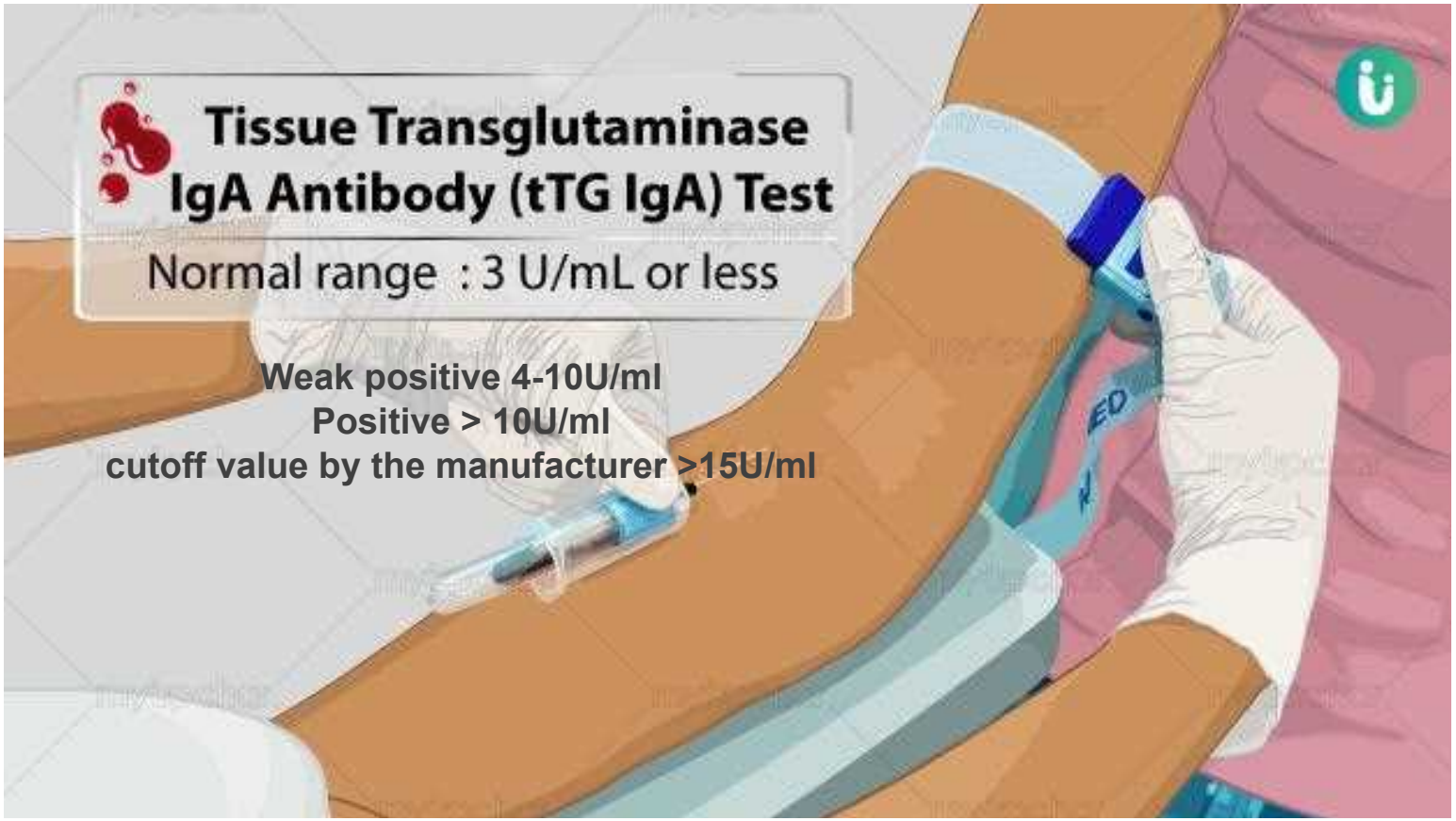
General
- Headache (35%), bone and joint pain (11%)[a]
- Muscle contractions (34%)[a]
- Numbness of hands and feet (20%)[a]
- Chronic tiredness (33%)[a]

Haematological
- Anaemia (20%)[a]

Behavioural
- Disturbance in attention[a]
- Depression (22%)[a]
- Hyperactivity
- Ataxia

Dental
- Chronic ulcerative stomatitis

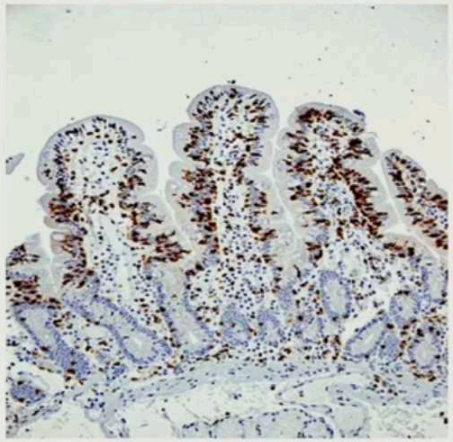
Clinical Nutrition 34 (2015) 189-194


Tissue Transglutaminase
IgA Antibody (tTG IgA) Test
Normal range : 3 U/mL or less
Weak positive 4-10U/ml
Positive > 10U/ml
cutoff value by the manufacturer >15U/ml

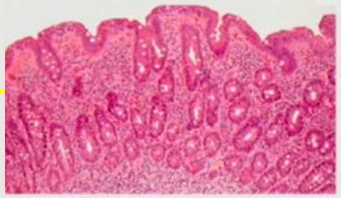
Mistakes in celiac disease

diagnosis based on minimal lesion (Marsh 1) at histopathology

- Marsh 1, i.e. IEL >25/100, does not indicate CD
- A wide array of conditions may show Marsh 1:
  - Hp infection / Giardiasis
  - Autoimmune diseases
  - Drugs (NSAIDs)
  - Lactose intolerance
  - Allergy
  - NCG / WS
  - …



- Pts with Marsh 1 with +ve serology, +ve HLA-DQ2 /DQ8 are potential CD (about 10% of all Marsh 1)



Non gluten-dependent villous atrophy

Disease	Histological features
Whipple disease	Macrophages in lamina propria (LP)
Eosinophilic gastroenteritis	Eosinophils infiltrate
Viral, mycotic, parasitic infections (giardiasis)	Identification of microbial agent
Autoimmune enteropathy	Normal γ/δ lymphocytes
Common variable immunodeficiency	Absence of plasmacells in LP lymphoid hyperplasia
NSAIDs enteropathy	-
Olmesartan villous atrophy	

35 yo F with no PMHx referred for LFT abnormalities. Denies use of alcohol or recreational drugs. No family history of liver disease. Not on any medications. Review of systems only notable for intermittent diarrhea. Initial work-up detailed below:

ALT 60	HAV IgG: pos	HIV 1/2 assay: neg	Ferritin: 199
AST 45	HBV S Ab: pos	Hgb 11.0	TIBC: 510
Alk phos 54	HBV S Ag: neg	Hct: 31.9	% sat: 18
Tbil 0.3	HBV c Ab: neg	MCV 78.3	Iron: 48
Albumin 3.4		HCV Ab: neg	

What is the most appropriate next step?

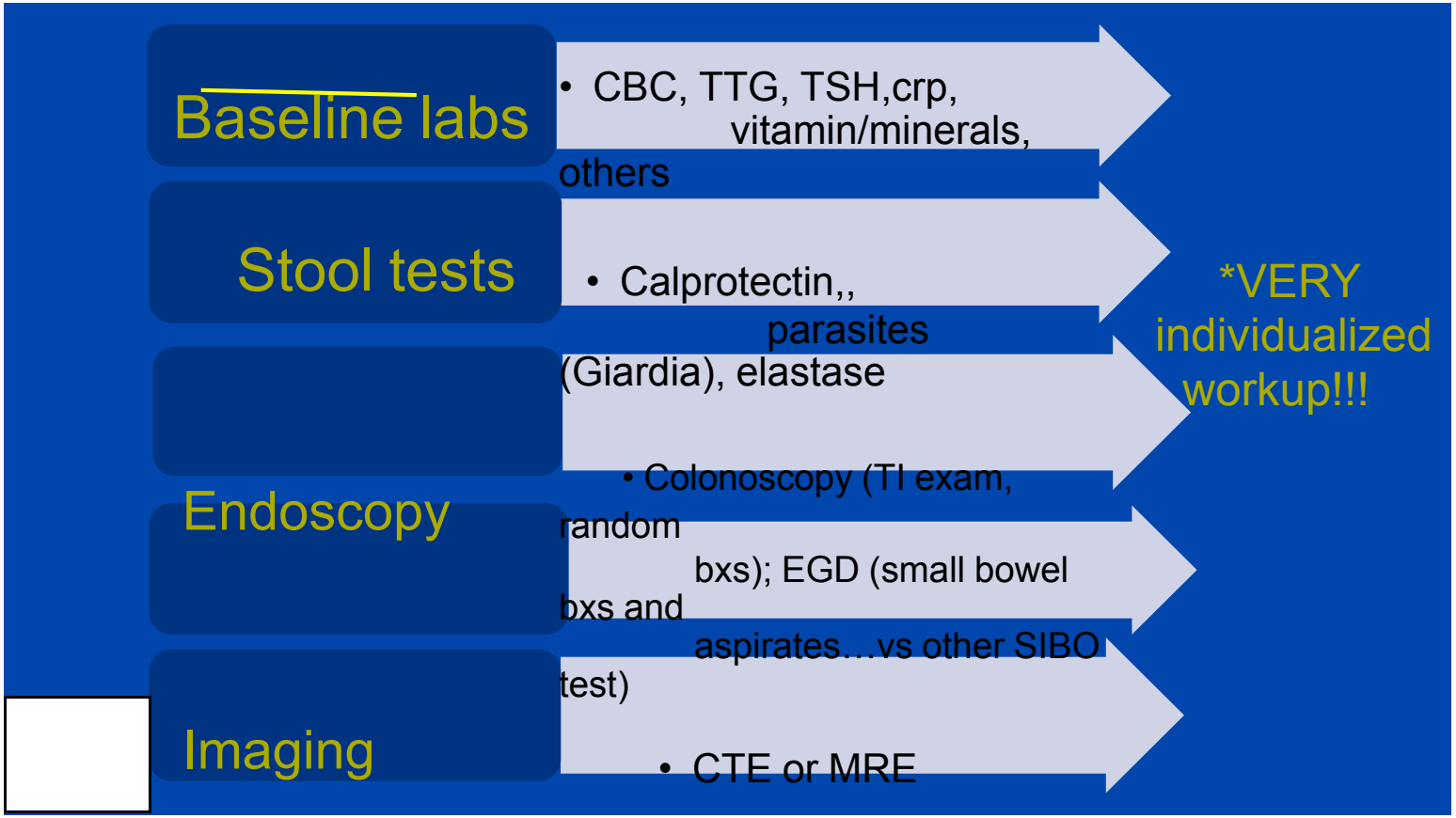
a) Liver biopsy

b) Anti-gliadin IgG

c) Anti-tTG IgA and total IgA

d) MRCP

	Osmotic	Secretory
Testing Strategy	•Dietary review •Carb malabsorption •-Breath tests •-Avoidance •Stool magnesium	•Cultures •Structural evaluation •Colon biopsies •Cholestyramine •Hormonal levels


Baseline labs
• CBC, TTG, TSH,crp, vitamin/minerals, others
Stool tests
• Calprotectin,, parasites (Giardia), elastase
Endoscopy
• Colonoscopy (TI exam, random bxs); EGD (small bowel bxs and aspirates…vs other SIBO test)
Imaging
• CTE or MRE
*VERY individualized workup!!!

Summary

- Diarrhea is common, and many etiologies for diarrhea can be deciphered from a careful history and exam.
- A step-wise approach for diarrhea is important:
  - 1) Patient truly has diarrhea?
  - 2) Chronic in nature?
  - 3) Characterized into a specific type?
  - 4) Historical clues to the diagnosis?
  - 5) Diet or medication-induced?
  - 6) Possible factitious component?


Thank you!!