Clinical Evaluation of CHRONIC DIARRHEA

By

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Definition

Stool weight of more than 300 gm / 24 h more than 4 weeks

(Feldman et al 2002)

CLINICAL CLASSIFICATION

1) Large-Volume Versus Small-Volume Stools

* painless large-volume and fewer motions → right colon or small bowel source.
* frequent, small, painful stools → distal site of pathology.
* total output (patient's history, dehydration):

Normal or slightly elevated stool weight→ IBS.

If dehydration→ stool weight > 1000gm, IBS unlikely

2) Osmotic Versus Secretory (osmolarity of stool water, fasting)

4) Watery Versus Fatty Versus Inflammatory (stool tests)

3) Epidemiologic Classification

Epidemiologic Classification

Travelers:

Protozoal infections (e.g, giardiasis).

Tropical sprue

Epidemics/Outbreaks:

Protozoal infections (e.g., cryptosporidiosis)

Epidemic idiopathic secretory diarrhea

Institutionalized and *Hospitalized Patients*:

Clostridium difficile toxin-mediated colitis

Drug side effect.

Tube feeding

Fecal impaction with overflow diarrhea

Epidemiologic Classification (cont.)

Diabetic Patients:

Altered motility (increased or decreased)

Drugs (especially acarbose, metformin)

Associated diseases:

- Celiac sprue
- Pancreatic exocrine insufficiency
- Small bowel bacterial overgrowth

Initial evaluation of Chronic Diarrhea

- History
- Physical examination
- Routine laboratory tests
- Analysis of stool sample

History

1-Age (recent onset in elderly, IBS unlikely – celiac sprue – food allergy)

2-Duration of symptoms.

3- The severity of the diarrhea:

* Stool frequency is the easiest for patients to define but not necessarily correlate with stool weight
* Symptoms of dehydration.
* Acute weight loss (good marker for severity).

4- Drugs, coincidence with the onset of diarrhea.

5- aggravating and relieving factors

6-The patient's diet should be reviewed.

History (cont.)

7- Surgery or radiation.

8- Epidemiologic clues.

9- Stool characteristics:

- Blood in the stool signals the possibility of inflammatory bowel disease or malignancy.
- Watery stools suggest an osmotic or secretory process
- Oil is suggestive of malabsorption, maldigestion.
- Relationship to fasting.

Stool characteristics (cont.)

- Nocturnal diarrhea that wakes the patient from sleep strongly suggests an organic cause.
- Excess flatus: poorly absorbable carbohydrate or malabsorption.
- Other coexisting symptoms such as abdominal pain, flatulence, bloating or gaseous distention, cramps, fever.

History is essential in differentiating patients with irritable bowel syndrome, the most common cause of chronic diarrhea Current definitions of irritable bowel syndrome emphasize the presence of abdominal pain associated with defecation. A long history usually extending back to adolescence or young adulthood, passage of mucus and exacerbation of symptoms by stress. The majority have a normal stool weight.

Factors against diagnosis of irritable bowel syndrome include a recent onset, especially in older patients; Painless diarrhea, diarrhea that wakes the patient form sleep; weight loss; blood in the stool; and stool weight greater than 400 to 500 g per day. Abnormal blood tests, such as a low hemoglobin level, low serum albumin or high ESR, also are **against** this diagnosis.

Differential diagnosis of Chronic diarrhea by stool characteristics

Watery diarrhea

A - Osmotic diarrhea

1- Osmotic laxatives

(e.g., Mg^{+3}, $PO4^{-3}$, $SO4^{-2}$)

2- Carbohydrate malabsorption

B- Secretory diarrhea

Infections (Giardia, hetrophys, Coccidia, HIV)
Inflammatory bowel disease
- Ulcerative colitis
- Crohn's disease
- Microscopic colitis
  - Lymphocytic colitis.
  - Collagenous colitis.

Ileal bile acid malabsorption
Vasculitis
Drugs and poisons *eg NSAIDS, colchicine, theophylline and herbal products*
Laxative abuse (stimulant laxatives)
Disordered motility/regulation
- Irritable bowel syndrome
- Diabetic autonomic neuropathy
- Postvagotomy diarrhea
- Postsympathectomy diarrhea

Secretory diarrhea (cont.)

Endocrine diarrhea

Hyperthyroidism — Addison's disease
Gastrinoma — VIPoma
Somatostatinoma — Carcinoid syndrome
Mastocytosis — Pheochromocytoma
Medullary carcinoma of the thyroid

Other tumors

Colon carcinoma — Lymphoma
Villous adenoma

Idiopathic secretory diarrhea

Epidemic — Sporadic

Inflammatory diarrhea

Inflammatory bowel disease

Ulcerative colitis Crohn's disease

Diverticulitis Ulcerative jejunoileitis

Infectious diseases

Pseudomembranous colitis

Invasive bacterial infections eg tuberculosis

Parasitic infections e.g. bilharziasis, strongyloides

Ulcerating viral infections e.g CMV

Ischemic colitis

Radiation colitis

Neoplasia

Colon cancer Lymphoma

Fatty diarrhea

Maldigestion

- Panceatic exocrine insufficiency
- Inadequate luminal bile acid concentration

Malabsorption syndromes

- Mucosal diseases e.g. Crohn's, Celiac disease
- Small bowel bacterial overgrowth
- Mesenteric ischemia
- Short bowel syndrome

Physical Examination:

Useful in determining the severity of diarrhea:

- Volume status (orthostatic changes in blood pressure and pulse, dehydration).
- Fever and other signs of toxicity .
- Abdominal examination (bowel sounds, abdominal distention, tenderness, masses and an enlarged liver).

Physical Examination (cont.)

Characteristic skin changes may be seen in: Celiac sprue, Addison's disease, Glucagonoma, Carcinoid syndrome.

Peripheral neuropathy and orthostatic hypotension (Amyloidosis)

A thyroid nodule with cervical lymphadenopathy (MCT).

Tremor and other systemic signs (hyperthyroidism).

Right sides heart murmurs, enlarged hard liver (Carcinoid)

Arthritis e.g inflammatory bowel disease, Whipple's disease.

Lymphadenopathy (AIDS or lymphoma).

peripheral vascular disease ± abdominal bruit

Chronic liver disease in a patient with colitis

Routine laboratory tests

CBC, serum electrolytes, calcium, albumin, liver chemistry, prothrombin time, Urea , Creatinine, ESR.

Analysis of stool sample

1- Randum stool sample or timed collected

a- Randum sample provide diagnostic clues as stool Na, K, pH, occult blood testing, WBCs, fat content, for laxatives and markers of inflammation as lactoferrin.

b- Collected samples:

- 48-72 hrs
- Regular diet with fat 80-100 gm fat.
- Withdraw any antidiarrhea medications.

2- Measurement of stool Na & K → calculate osmotic gap

Osmotic gap = 290 mOsm/Kg - 2 (Na + K)

- Small gap (< 50) = secretory diarrhea
- Large gap (> 100) = osmotic diarrhea
- Measured osmolality < 290 → addition of water or hypotonic urine.

3- pH of stool water → ↓ (< 5.5) in carbohydrate malabsorption.

4- Fecal occult blood & fecal leukocytes → inflammatory diarrhea or malignancy.

5- Stool fat measurement:

a) Quantitative on a timed (48-72 hrs): >7gm or 9% of fat intake for 24 hours --> steatorrhea. Fat excretion >14 gm/24 hr is a strong evidence of steatorrhea.

b) Qualitative estimation on a randum sample by Sudan III stain.

c) Semiquantitative: measurement of number and size of fat globules with results that correlate well with quantitative collections *(Fine et al 2000)*

Then, Categorize Diarrhea

Chronic osmotic diarrhea

Diagnostic clues:

Osmotic gap > 100

Stool volume decrease with fasting

Gas, bloating (fermentation--> fatty acids, CO2)

Examples:

lactase deficiency

laxative abuse

poorly absorbed CHO

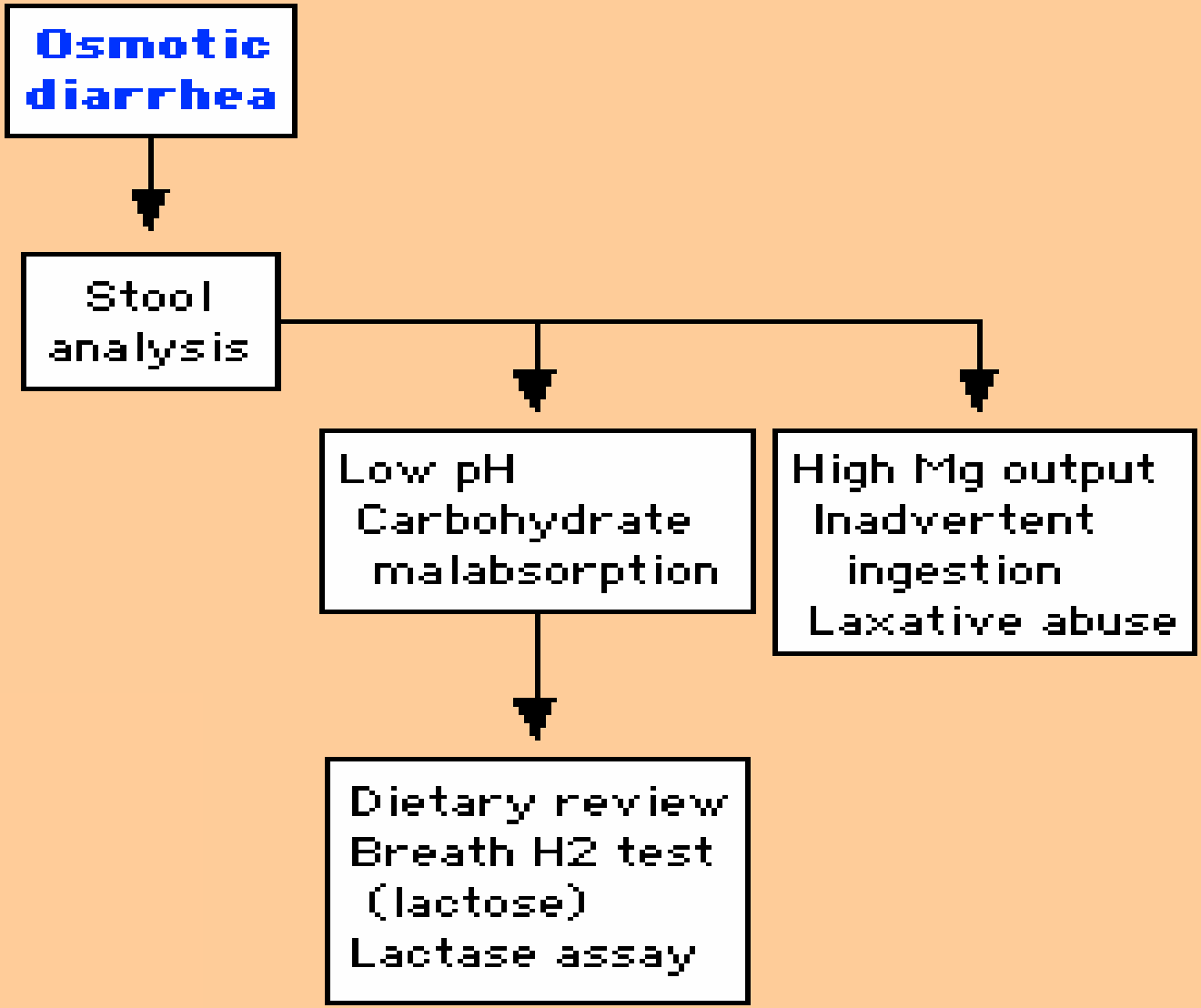
Stool analysis

Stool pH

Laxative screen eg Mg,

Carbohydrate malabsorption:

- Dietary review
- Breath hydrogen test with lactose as sugar substrate.
- Therapeutic trial of an elimination diet.


Osmotic diarrhea
Stool analysis
Low pH
Carbohydrate malabsorption
High Mg output
Inadvertent ingestion
Laxative abuse
Dietary review
Breath H2 test (lactose)
Lactase assay

Chronic secretory diarrhea:

Diagnostic clues:

- Large volume (> 1 litre)
- Little change with fasting
  (except bile salt diarrhea)
- Normal osmotic gap

Diagnostic approach

1) **Exclude infection** (bacterial culture + special tests).
2) **Small bowel radiography** by Barium follow-through or enteroclysis → detect structural diseases
3) **CT abdomen detect** structural small intestinal or colonic disease and pancreatic tumours.
4) **Endoscopy or enteroscopy + biopsy** for Mucosal diseases (usually steatorrhea) eg Crohn s disease, celiac sprue.
5) **Small bowel aspirate** → $> 10^6$ bacteria on culture denote bacterial overgrowth syndrome.

6) Sigmoidoscopy or colonoscopy + biopsy e.g. IBD

-Colonosocpy is preferable if bloody stool, suspicion of right colonic or ileal disease.

-Normal colonic mucosa on endoscopy + abnormal histology in microscopic colitis, Whipple's disease, oesinophilic colitis and amyloidosis.

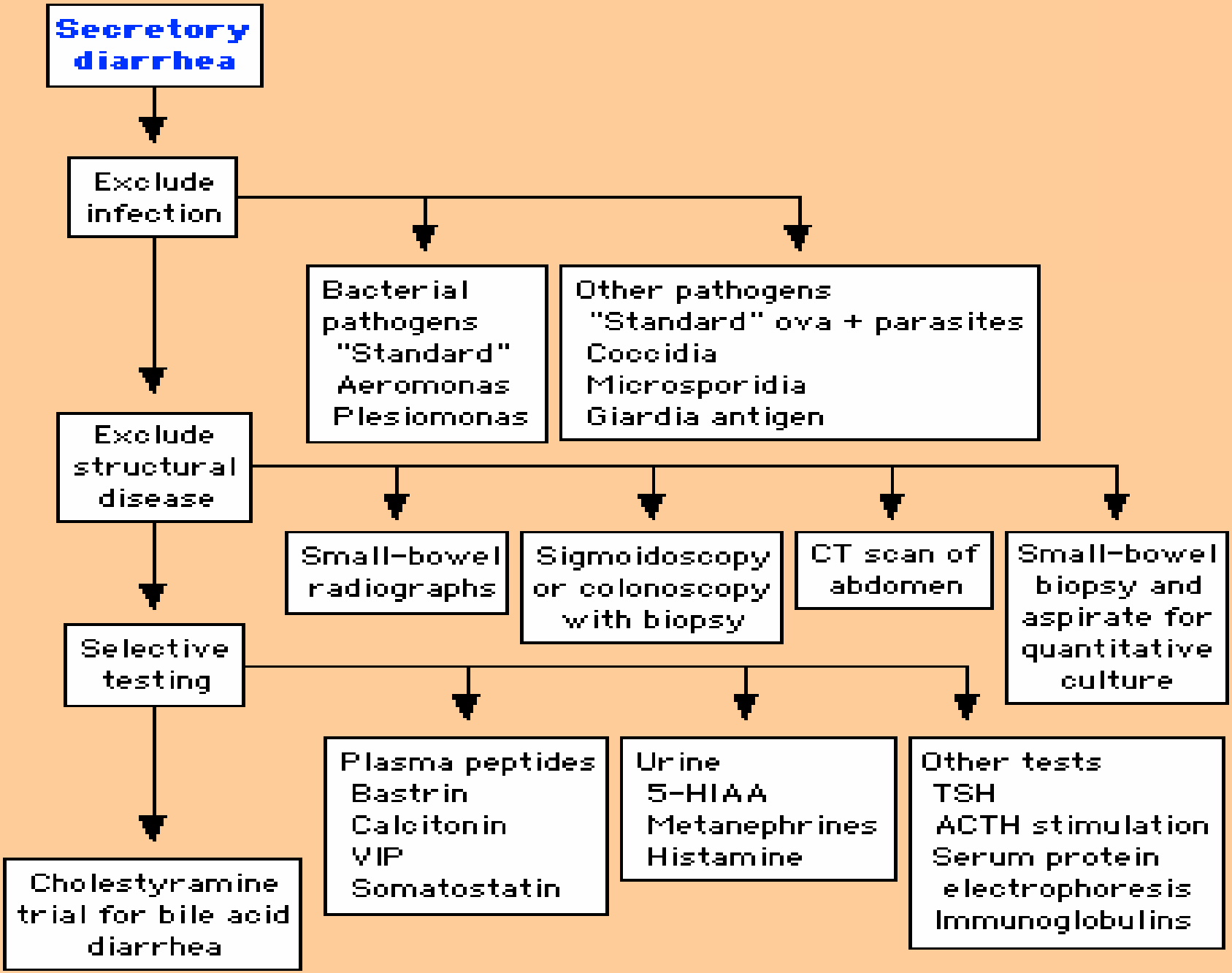
7) Cholestyramine trial for bile acid diarrhea.

8) Lastly, selective testing for peptide secreting tumours:

-Low pretest probability in a patient with chronic diarrhea

- Examples: Urinary 5-HIAA, Metanephrine and histamine.

- More common endocrine diseases → DM, hyperthyroidism and addison → blood sugar, TSH, cortisol.


Secretory diarrhea
Exclude infection
Bacterial pathogens
"Standard"
Aeromonas
Plesiomonas
Other pathogens
"Standard" ova + parasites
Coccidia
Microsporidia
Giardia antigen
Exclude structural disease
Small-bowel radiographs
Sigmoidoscopy or colonoscopy with biopsy
CT scan of abdomen
Small-bowel biopsy and aspirate for quantitative culture
Selective testing
Plasma peptides
Bastrin
Calcitonin
VIP
Somatostatin
Urine
5-HIAA
Metanephrines
Histamine
Other tests
TSH
ACTH stimulation
Serum protein electrophoresis
Immunoglobulins
Cholestyramine trial for bile acid diarrhea

Chronic Inflammatory diarrhea

Diagnostic clues:

- Fever
- Hematochezia
- Abdominal pain
- Weight loss

Diagnostic approach

- Sigmoidoscopy or colonoscopy + biopsy

  - Sigmoidoscopy: simple preparation, can detect most causes

  -Colonoscopy examine the entire colon and terminal ileum especially if fecal occult blood test is positive

- Exclude infection that can cause or exaggerate diarrhea by BIOPSY, SEROLOGY and appropriate CULTURE

Chronic Fatty diarrhea

Diagnostic clues:

- Weight loss
- Fecal fat > 7-10 gm/ 24 hr
- Anemia
- Hypoalbuminemia

Diagnostic approach

1- Exclude structural disease involving **small intestine** by **small bowel radiograph, CT abdomen, enteroscopy and small intestine biopsy.**

2- **Small intestine aspirate for culture** to exclude **small bowel bacterial overgrowth**

3- If no structural diseases are discovered, **pancreatic exocrine insufficiency** should be considered.

Pancreatic exocrine insufficiency

Suggestive features:

1- smaller stool volume and higher fat concentration / 100 gm stool. Fat concentration > 9.5 gm / 100 gm in patients with suspected maldigestion suggest pancreatic or biliary dysfunction.

2- Oil is seen in stool.

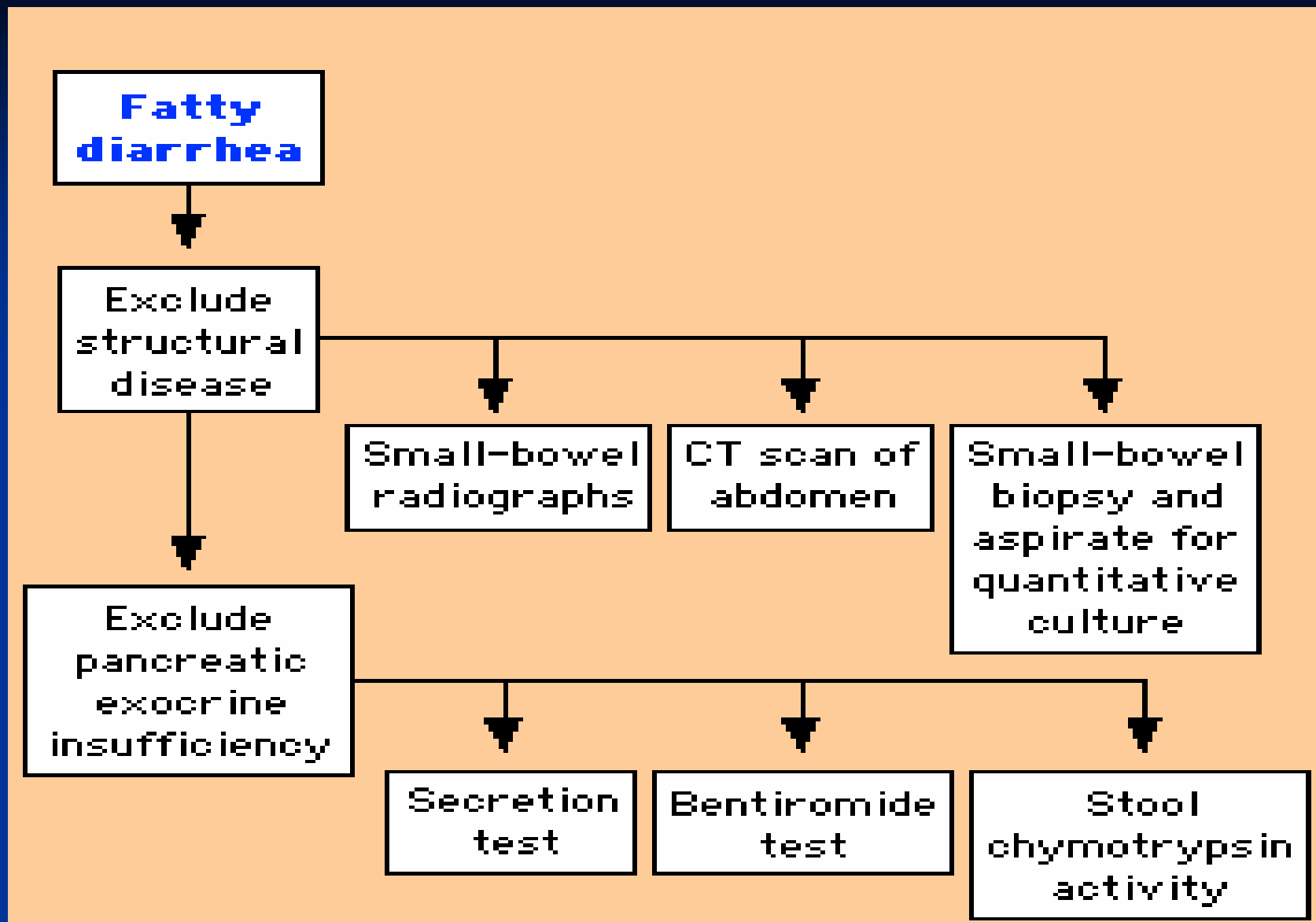
3- Fewer problems with vitamin deficiencies.

4- Lower frequency of hypocalcemia (more common in small bowel mucosal diseases.

Pancreatic exocrine insufficiency (cont.)

Tests for diagnosis:

- **Bentiromide test**
- **Secretin test**
- **Therapeutic trial** of pancreatic enzyme supplementation in high dose and monitor weight gain & fecal fat excretion.
- **Pancreatic endosonography**


Fatty diarrhea
Exclude structural disease
Small-bowel radiographs
CT scan of abdomen
Small-bowel biopsy and aspirate for quantitative culture
Exclude pancreatic exocrine insufficiency
Secretion test
Bentiromide test
Stool chymotrypsin activity

Frequent diagnoses in patients with diarrhea of obscure origin

- Functional diarrhea, irritable bowel syndrome
- Iatrogenic diarrhea (drugs, surgery, radiation)
- Surreptitious laxative ingestion
- Microscopic colitis syndrome
- Bile acid-induced diarrhea
- Small bowel bacterial overgrowth
- Pancreatic exocrine insufficiency
- Carbohydrate malabsorption
- Peptide-secreting tumors
- Chronic idiopathic secretory diarrhea

Bile acid deficiency

1. **Causes**: chronic cholestatic liver disease as primary biliary cirrhosis, ileal resection or dysfunction.
2. **Diagnosis:**
    1. measuring conjugated bile acid in postprandial duodenal aspirate.
    2. Therapeutic trial
3. **Treatment:**
    1. **supplementation** of the diet **with conjugated bile acid**
       ↓ steatorrhea (? ileal disease).
    2. **Bile acid** binding resin

Empiric therapy of chronic diarrhea

Indication:

- as temporary or initial treatment before diagnostic testing
- failure of diagnostic testing to confirm diagnosis
- no available or failure of specific treatment

Empiric therapy of chronic diarrhea (cont.)

1) Empiric antibiotic therapy (metronidazole, flouroqinolone, less useful, no supporting data).

2) Therapeutic trials of pancreatic enzyme supplementation, conjugated bile acids, bile acid binding resins.

3) Symptomatic treatment with opiates eg diphenoxylate, loperamide. Also, lactobacillus and octreotide (endocrine diarrhea) and clonidine (diabetic diarrhea).

4) Stool modifying agents as psyllium alter stool consistency (patients with coexisting fecal incontenence).

Diagnostic approach of chronic diarrhea

Meticulous history (severity, diet, drugs, aggravating, surgery, radiation, fasting, stool characters)

Physical examination (severity, characteristic features)

Stool analysis **(parasites, leucocytes, RBCs, Weight/24 hr, Osmotic gap, Fecal fat).**

Fecal WBCs, RBCs

Inflammatory diarrhea

- Sigmoidoscopy or colonoscopy
- Barium radiograph

Normal Osmotic gap

Increased Stool weight

Secretory diarrhea

- Barium enema
- Sigmoidoscopy or colonoscopy
- Small bowel radiography&biopsy
- Small bowel aspirate & Culture
- Lastly, screen for endocrine tumours

Normal Stool weight

Irritable bowel syndrome
Facticious diarrhea.

Increased Osmotic gap

Fecal WBCs, RBCs

Normal Osmotic gap

Increased Osmotic gap

Increased fecal fat

Fatty diarrhea

- Small bowel radiography
  - Ba. Follow through
  - Enteroclysis
- Small intestinal biopsy
  - By endoscopy
  - Crospy capsule
- Small bowel aspirate & Culture
- If all are negative→ test for pancreatic exocrine insufficiency

Normal fecal fat

Osmotic diarrhea

- Stool pH
- Laxative screen
- Elimination diet

Diagnostic approach of chronic diarrhea

- Meticulous history
- Physical examination
- Stool analysis **(parasites, leucocyte, RBCs, Weight/24 hr, Osmotic gap, Fecal fat).**

Fecal WBCs, RBCs → Inflammatory diarrhea → - Sigmoidoscopy or colonoscopy
- Barium enema

Increased fecal fat, Increased Osmotic gap → Fatty diarrhea

- Small bowel radiography
  - Ba. Follow through
  - Enteroclysis
- Small intestinal biopsy
  - By endoscopy
  - Crospy capsule
- Small bowel aspirate & Culture
- If all are negative→ test for pancreatic exocrine insufficiency

Normal fecal fat, Increased Osmotic gap→ Osmotic diarrhea

→ Stool pH, Laxative screen, **Elimination diet**

Normal Osmotic gap, Normal Stool weight

→ Irritable bowel syndrome, Factitious diarrhea.

Normal Osmotic gap, Increased Stool weight→ Secretory diarrhea

* **Sigmoidoscopy or colonoscopy, Barium enema**
* **Small bowel radiography & biopsy**
* **Small bowel aspirate & Culture**
* **Lastly, screen for endocrine tumours**

Diagnostic approach of chronic diarrhea

Meticulous history (severity, diet, drugs, aggravating, surgery, radiation, fasting, stool characters)

Physical examination (severity, characteristic features)

Stool analysis **(parasites, leucocyte, RBCs, Weight/24 hr, Osmotic gap, Fecal fat).**

Fecal WBCs, RBCs

Inflam. diarrhea

- **Sigmoidoscopy or colonoscopy**
- **Barium radiograph**
- **Exclude infection**

Increased fecal fat

Fatty diarrhea

- Small bowel radiography by Ba. Follow through, Enteroclysis
- Small intestinal biopsy by endoscopy or Crospy capsule
- Small bowel aspirate & Culture
- If all are negative→ test for pancreatic exocrine insufficiency

No Fecal WBCs, RBCs or fecal fat

Normal Osmotic gap

Secretory diarrhea

- **Barium enema**
- **Sigmoidoscopy or colonoscopy**
- **Small bowel radiography & biopsy**
- **Small bowel aspirate & Culture**
- **Lastly, screen for endocrine tumours**

Thank you