Miscellaneous Medical Protocols

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- Health Maintenance in GI
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Health Maintenance in GI

IBD and Chronic Liver Disease

INITIAL VISIT	**Check Immune Status**	**Give regardless of immunosuppression status**	**Give if not immunosuppressed nor planned immunosupressors in next 4-12 weeks**	**Review Screening**
	Hepatitis A *(total Ab)* Hepatitis B *(HBsAg & Ab, anti-HBc total)* MMR* Varicella** PPD or Quantiferon	Tdap HPV *(age 18-26)* Influenza *(injectable)* Pneumococcus Hepatitis A Hepatitis B Meningococcus***	MMR Varicella Zoster *(if =/> 60)*	Cervical Cancer Colorectal Cancer Skin Cancer Tobacco cessation Bone health Depression
F/U VISIT		**Review vaccine status and update regardless of immunosuppression**	**Give if not immunosuppressed nor planned immunosupressors in next 4-12 weeks**	**Review Screening**
		Td HPV *(age 18-26)* Influenza *(injectable)* Pneumococcus Hepatitis A Hepatitis B Meningococcus***	MMR Varicella Zoster *(if =/> 60)*	Cervical Cancer Colorectal Cancer Skin Cancer Tobacco cessation Bone health Depression Ophthalmology evaluation

*If no history of MMR vaccine, ** If no history of chicken pox nor vaccine, *** Depending on demographic risk

Fe deficiency anemia

- **Bone Marrow Bx** is “gold standard”.
- **Fasting serum Fe and transferrin saturation**:
  - correlate poorly with marrow Fe stores;
  - commonly low in “anemia of chronic disease/inflammation”
- **Fasting serum Ferritin**:
  - correlates well with marrow Fe stores,
  - falls before anemia develops;
  - Inflammation and malignancy can elevate Ferritin giving false-normal despite Fe deficiency (sTfR test can help diagnosis)
  - CKD can falsely elevate Ferritin (no good test to clarify diagnosis);
  - consider Stool HemoQuant: detects GI blood loss from any level
- **Soluble Transferrin Receptor (sTfR)**
  - Soluble transferrin receptor is high in Fe deficiency, even in presence of “Chronic Disease” (helps to interpret low-normal ferritin).
  - sTfR is low in CRF (does not help), and high in hemolysis, thalassemia, and polycythemia.

Assessment of occult GI Blood Loss (FOBT)

- **Guaiac (leuco-dye) Test:** (Hemoccult)
  - Normal blood loss in GI tract: 0.5-1 mL/d
  - Loss of 2-80 ml blood/day needed for (+)
  - 10 ml blood/day gives (+) in 50%
  - Water (diarrhea or rehydration of specimen) increases rate of (+) results (false & true positives).
  - Test should be done while on proper diet and only in **soft or formed** stool.
  - False (+): meat, radish, turnip, cantaloupe, bean sprout, cauliflower, broccoli, grapes, toilet bowl sanitizer, cimetidine, halogens, wet stools.
  - False (-): ascorbic acid, antacids, heat, acid pH, enterocolic Hb metabolism (fecal storage), dry stools.

Assessment of occult GI Blood Loss (FOBT)

- **Guaiac (leuco-dye) Test:** (Hemoccult)
  - Guaiac testing should be done evaluating 2 samples in each of 3 consecutive soft or formed stools.
  - Waiting 3 days before developing the test allows for diet restriction of red meat only (no effect on the test).
  - Hemoccult & Hemoccult II are not recommended for CRC screening.
  - Hemoccult Sensa is OK for CRC Screening.
  - Colonoscopy is recommended for all those with a FOBT(+) stool.
  - One national study has shown that only 1 in 3 patients with a guaiac(+) stool undergoes colonoscopy

Utilization of FOBT by Primary Care

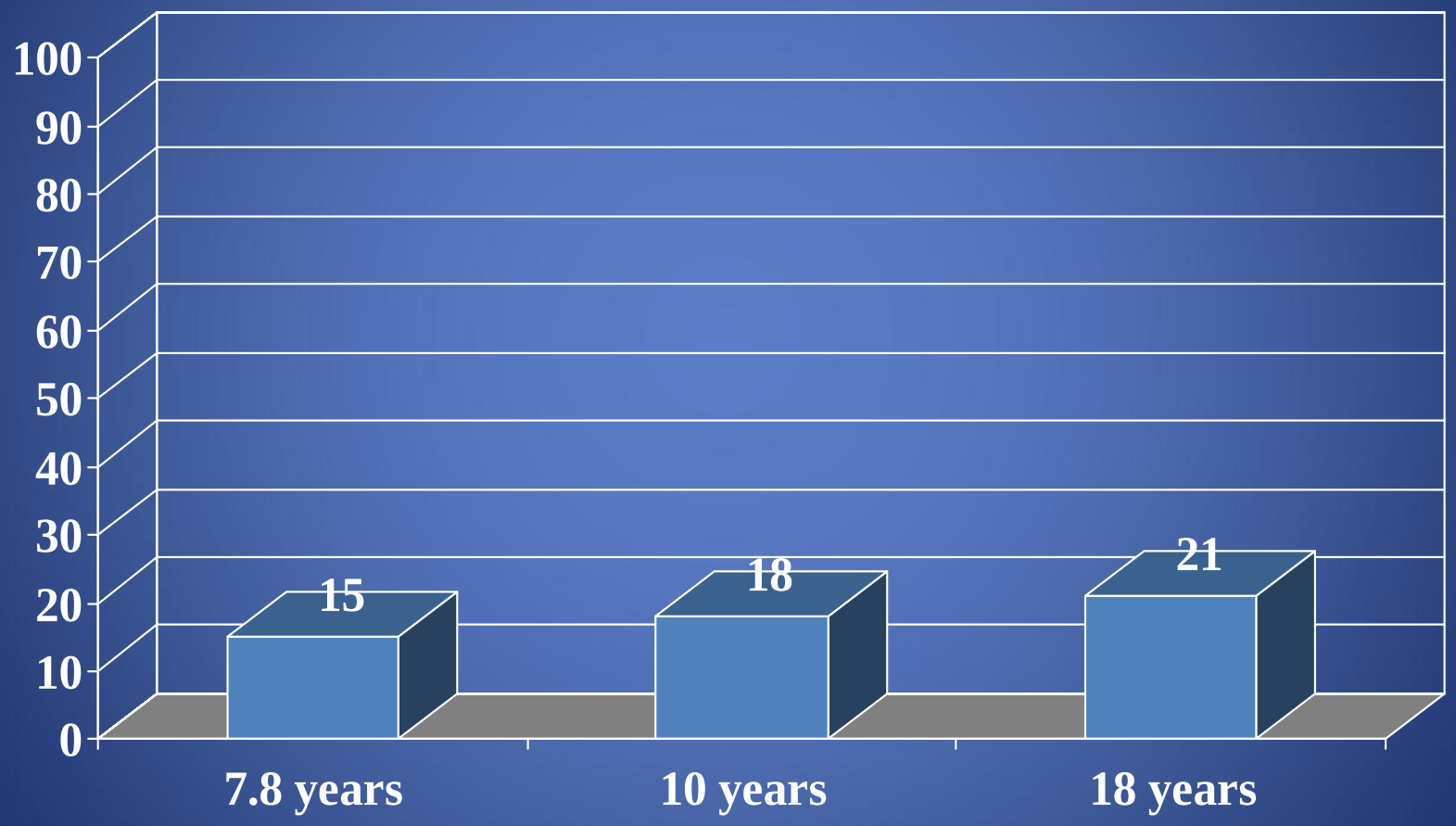
Ann. Inter. Med 2005;142:81-94,146-148

Sensitivity for:	Neoplasia (%)	Advanced Adenoma (%)	Carcinoma (%)
Single Digital FOBT	4.9	6.4	9.5
3-Card FOBT	24	30	43

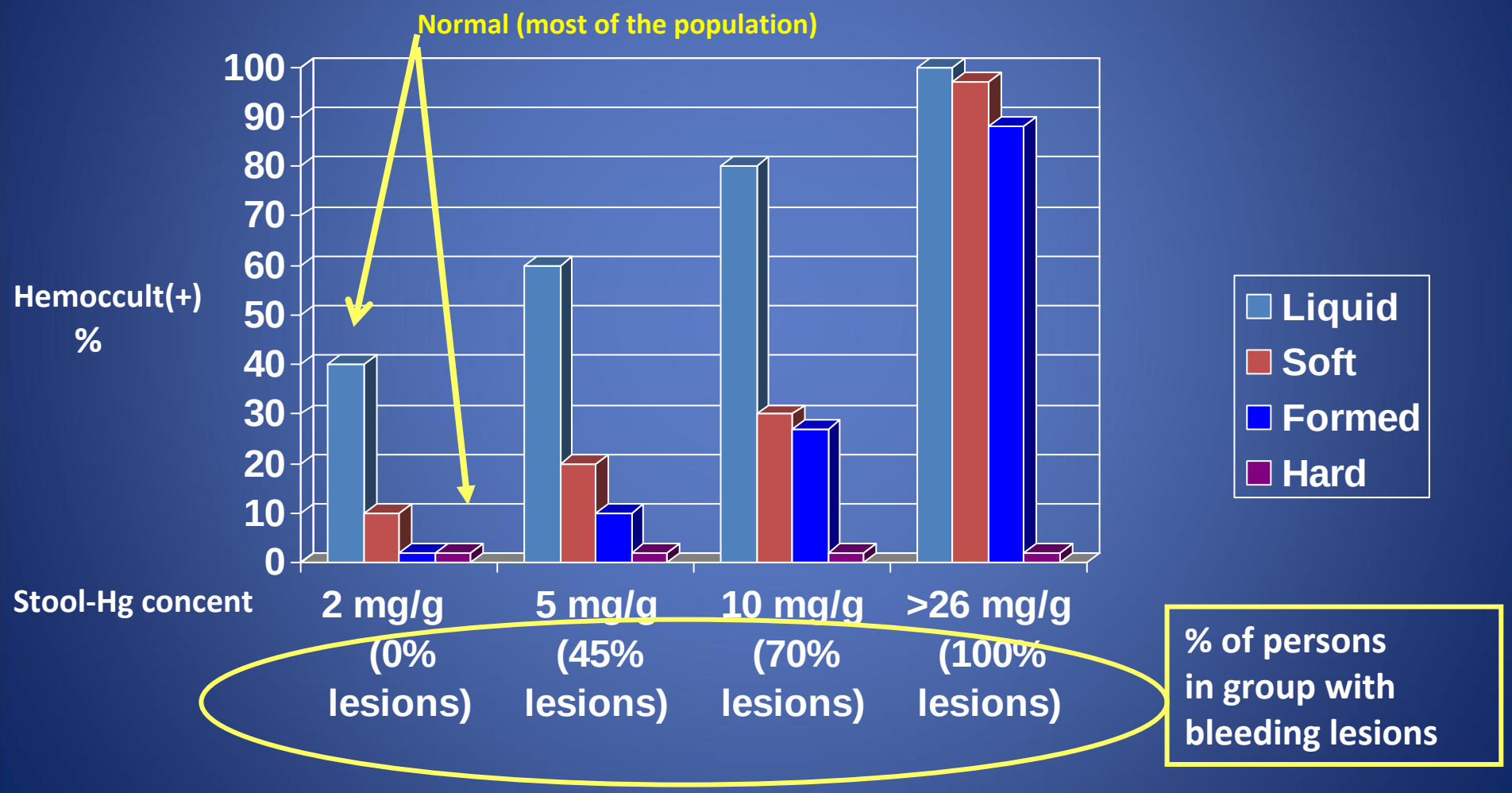
- **COLONOSCOPY ORDERED AFTER (+) FOBT:**

- **30 %**

Effect of Biennial Guaiac Testing Without Rehydration on CRC Mortality



Effect of stool-Hb-concentration & stool-consistency in Hemoccult



Assessment of occult GI Blood Loss (FOBT)

- **Immunochemical (HemeSelect & Hemoccult ICT)**
  - Anti-Hb or anti-albumin (human only); no special diet.
  - May miss < 100 ml UGI blood;
  - Very poor for UGI source; only fair for proximal colon.
  - False (-) from enterocolic Hb metabolism & long storage (Hb degradation).
  - Recommended for CRC screening.
- **Heme-porphyrin (HemoQuant)**
  - Detects heme-derived porphyrins (human or animal) (detects 88% of ingested blood). Avoid meat.
  - Hb-equivalent /g-stool > 2 mg/g is abnormal.
  - Good for upper & lower GI sources.
  - Can help to guide work-up in menstruating women, post-gastrectomy patients, vegeterians, and when unable to differentiate “Fe deficiency” from “chronic disease” or CRF anemia.

Assessment of occult GI Blood Loss (FOBT)

- **High Sensitivity** FOBT is indicated for:
  - Screening for CRC in asymptomatic, average risk person older than 50, with proper diet (45 for African-Americans ?)
  - Fe defic. anemia with (-) Colon & EGD+SB bx (to get approval for capsule enteroscopy)
  - Best: HemeSelect & Hemoccult ICT
  - Second choice: Hemoccult II Sensa
  - Not recommended: Hemoccult & Hemoccult II
- FOBT is **not** indicated for:
  - Person younger than 50 (45 for African-Americans)
  - Person who has not follow proper diet if using guaiac based test (admission or clinic visit)
  - Nasogastric aspirate or vomit.
  - Person with Fe deficiency **[unless colon & EGD+SB Bx (-)]**
  - Melena, hematochezia, “coffee ground” emesis, hematemesis.
  - Person in a “colonoscopy surveillance” program.

Assessment of Overt Blood Loss

- **Melena:**
  - Ingestion of 200 ml of blood consistently causes melena.
  - Infusion of 150 ml blood in cecum gives melena or hematochezia, depending in transit time.
  - Indicates bleeding from upper source, small bowel, or less often from right colon.
  - Sudden drop (1 day) of Hb of 1.5 gm or more, in person having daily, non-melanotic stools, makes GI source very unlikely; give laxative and look at the stool.

Assessment of Overt Blood Loss

- **Hematochezia:**
  - more than 100 ml blood from Lt colon, or
  - more than 150 ml from Rt colon.
  - only 11% have an upper source (above ligament of Treitz)
  - patients with upper source are usually orthostatic by syst BP drop > or = 10 mm Hg and/or pulse increase > 20 bpm at 3 minutes (> 20% blood volume loss [> 1,000 mL])

Signs of GI Blood Loss
Summary

- Hematemesis (above ligament of Treitz)
- Coffee ground emesis (above lig. Treitz)
- Melena: may be upper or lower source
  - > 200 mL blood in stomach, or
  - </= 150 mL blood in cecum)
- Hematochezia: usually lower; sometimes upper
  - > 100 mL blood in Lt colon, or
  - > 150 mL blood in Rt colon, or
  - > 1000 mL upper bleed (orthostatic =/> 10 mmHg).
  - Upper source in 11%.
- Guaiac (+) stool: 2-80 ml blood/day (mean 10 ml)

Tube Feeding

Indications

- Feeding difficulty due to:
  - Poor volitional Intake
  - Neurologic impairment
  - Oro-pharyngeal dysfunction
- Major Trauma
- Difficulty meeting Nutritional needs due to:
  - Severe burn,
  - Severe alcoholic hepatitis,
  - Severe acute pancreatitis (jejunum, 60 cm distal to LOT (?), is preferred)
- Non-critically ill, eutrophic, unable to eat =/> 10 days
- BMI < 20, or weight < 80% IBW
- Unintentional weight loss:
  - > 5 % in 1 month, or
  - > 10 % in 6 months.

Tube Feeding
Contraindications/Withholding

- Withhold/do not start tube feeds until cause investigated and patient stabilized in:
  - Hypotension: sustained BPs < 70 mm Hg.
  - Need for accelerated doses of pressor agents
  - Increasing ventilatory support.
  - Worsening signs of GI intolerance.
  - Overt regurgitation or aspiration
  - Gastric residual volume (GRV) 400-500 mL
    - GRV < of 500 mL should be returned to patient.

Tube Feeding

- **Start**: within 48 h of injury/admission, or meeting indication threshold.
- **Gastric feeding**: OK once NGT output =/< 1200 mL/d (30% of saliva + gastric input)
- **Post-pyloric feeding**: at anytime, unless SB obstructed or SB ileus (seen as A/F level in AAS; but remember that gastroenteritis/lactulose/sorbitol can give "false(+) A/F level")
- **Rate**:
  - **Order total volume to be given** (not only rate)
  - Better to order feeds over 20 h or 12 h, to prevent delivery of < 100% of planned volume.
  - Start at 35-40% goal rate and increase q 4h, to reach goal in 8 h (more slowly if at risk of re-feeding syndrome)
- **Formula strength**: Always give "full strength" feeds.

Tube Feeding

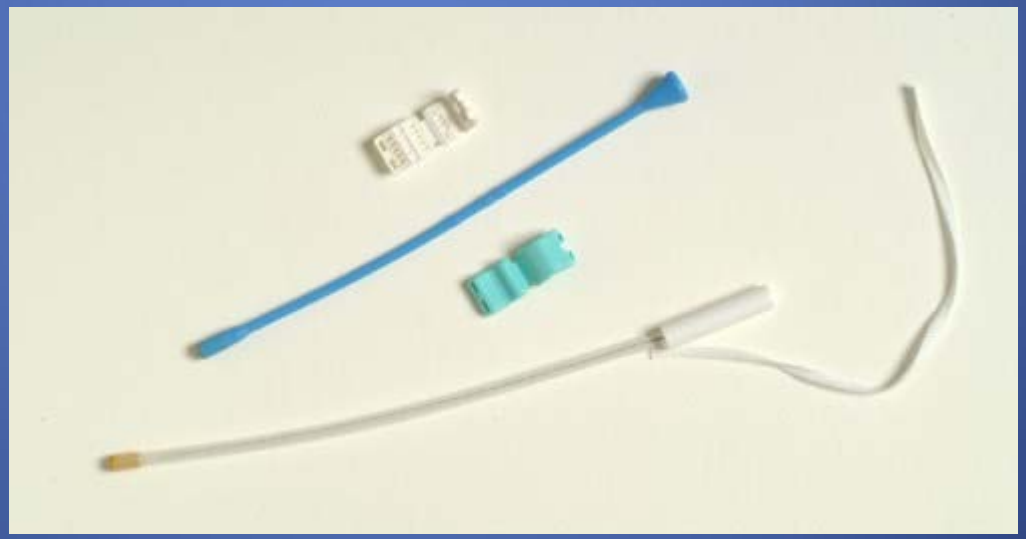
- Keep 45^0 “head of bed” elevation all the time.
- Order **not to check** “residual volume” in small bowel feed.
- Order “hold feeding” only for residual > 400 ml, in gastric feeding.
- Theoretical “maximal absorption capacity” of “intact bowel” is 375-400 mL/hour.
- Remember possibility of “re-feeding syndrome”
  - Follow closely K, P, and Mg BID, and replace.
  - Advance feeding rate more slowly

Bridle

- Indication: Risk of pulling naso-enteric tube.
- Technique:
  - Local anesthesia with lidocaine jelly in both nares.
  - Place 9 Fr or smaller feeding tube with one end entering each nare, into pharynx.
  - Pull both ends out of the mouth and tie them (or suture them) together with silk.
  - Rotate until tied ends are in front of nose; tie both arms of tube close to the septum.
  - Tape or tie naso-enteric tube to bridle.

NGT Retaining Loop
(AMT Bridle)

Applied Medical Technology



Simple Colon Transit Time

- **DAY 1**: Take 1 capsule of Sitzmarks (24 markers) under office observation.
- Instruct not to take laxatives, enemas, nor suppositories for 5 days.
- **DAY 5**: KUB
- **Interpretation**: if 19 or more markers were expelled, transit is normal.
- If 5 or more markers are retained:
  - Give bulking agent and encourage fluid intake.
  - Consider doing "Segmental Colon Transit Time" study in a few weeks.

Segmental Colon Transit Time
(Metcalf Protocol)

- **Sitzmarks capsules with 24 radiopaque rings each.**
  - **Capsule 1: "O" rings,**
  - **Capsule 2: "DD" rings,**
  - **Capsule 3: "Mercedes" rings)**
- **No laxatives, enemas, nor suppositories for the duration of the Test**
- **Protocol:**
  - **Day 1: give capsule 1;**
  - **Day 2: give capsule 2;**
  - **Day 3: give capsule 3;**
  - **Day 4: take KUB X-ray;**
  - **Day 7: repeat KUB only if more than 50 rings present in day-4 KUB**
- **Segmental times (hours):**
  - **a) Rt colon (Nl </= 11): # rings in Rt colon in day 4 + day 7.**
  - **b) Left colon (Nl </= 11): # rings in Lt colon in day 4 + day 7.**
  - **c) Rectosigmoid (Nl </= 12): # rings in Rectosigmoid in day 4 + day 7.**
  - **d) Total time (Nl </= 35): Rt colon + Lt colon + Rectosigmoid**
  - **e) If total time is > 70, then transit in any segment is abnormal only if > 30 hours.**

Contrast-induced Nephropathy Prevention Protocol

(JAMA 2004; 291:2328-2334)

- NAC 1200 mg BID p.o. starting 2 d before, and continue 2 days after.
- D5 Na-bicarbonate (154 mEq/L) solution:
  - 3 mL/kg IV 1 hour before contrast.
  - 1 mL/kg/hour x 6 hours during & after contrast.

Chronic Pancreatitis Anti-oxidant Cocktail

- The antioxidant supplementation included daily doses of
  - 600 μg of organic selenium,
  - 0.54 g of ascorbic acid,
  - 9,000 IU of β-carotene,
  - 270 IU α-tocopherol, and
  - 2 g of methionine.

The Narcotic Bowel Syndrome: Clinical Features, Pathophysiology and Management

Clin Gastroenterol Hepatol. 2007 October ; 5(10): 1126–1122.

- Chronic or intermittent colicky abdominal pain that worsens when the narcotic effect wears down.
- Narcotics may are helpful at first, over time the pain-free periods become shorter and tachyphylaxis occurs, leading to increasing narcotic doses. Ultimately, increasing dosages enhance the adverse effects on pain sensation and delayed motility, thereby initiating the development of NBS.
- Although pain is the dominant feature, nausea, bloating, intermittent vomiting, abdominal distension and constipation are common.
- Eating can aggravate the symptoms, so when the condition lasts for weeks, mild weight loss may occur due to anorexia or a willful restriction of eating out of fear of aggravating the pain (sitophobia).
- The symptoms may correlate with delayed gastric emptying and intestinal transit.

The Narcotic Bowel Syndrome: Clinical Features, Pathophysiology and Management

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- Abdominal X-rays may show signs suggestive of a partial intestinal obstruction, which in fact is due to an adynamic ileus or pseudoobstruction. There may also be large amounts of fecal retention seen.
- Laboratory tests including blood count, amylase, lipase, liver chemistries and urinalysis are usually normal.
- PATHOPHYSIOLOGY: The evidence for the enhanced pain perception is based on:
  - a) activation of excitatory anti-analgesic pathways within a bimodal opioid regulation system,
  - b) descending facilitation of pain at the Rostral Ventral Medulla and pain facilitation via dynorphin and CCK activation, and
  - c) glial cell activation that produces morphine tolerance and enhances opioid induced pain.

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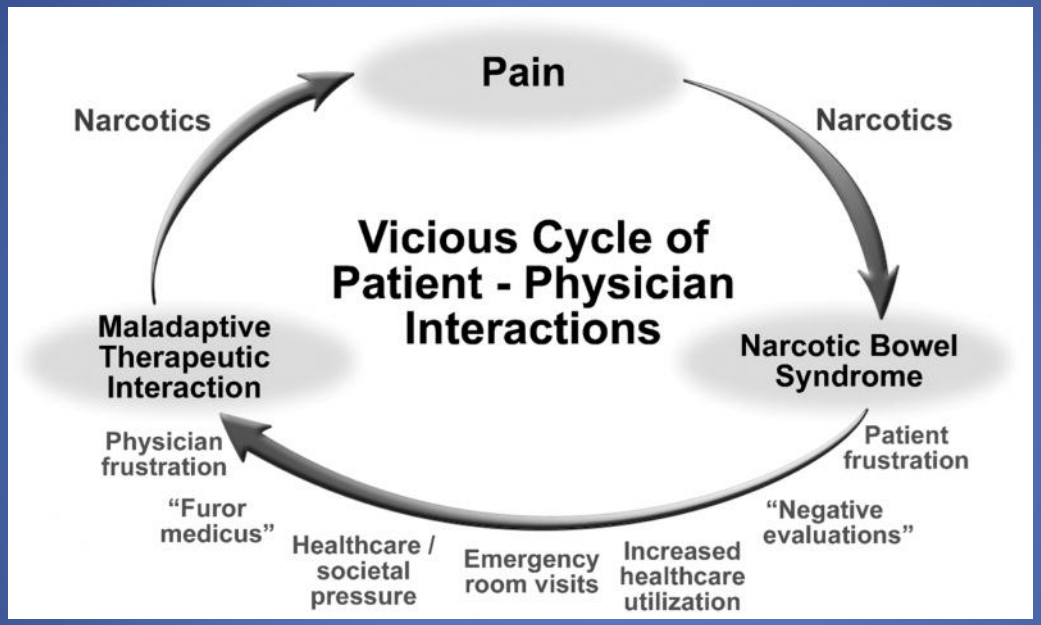

Vicious cycle of patient-physician interaction in narcotic bowel syndrome. Patient presents with a pain, either due to a structural condition (e.g., IBD), post-surgery or functional GI disorder and narcotics are started. Patient develops symptom of Narcotic Bowel Syndrome. Subsequent evaluation is unrevealing and the narcotics are escalated to treat the abdominal pain with worsening of NBS. This prompts the patient to increase health care utilization or make emergency room visits, which leads to physician frustration and "furor medicusw" leading to a maladaptive therapeutic interaction with additional use of narcotics. The cycle continues until the syndrome is recognized and treatment initiated.

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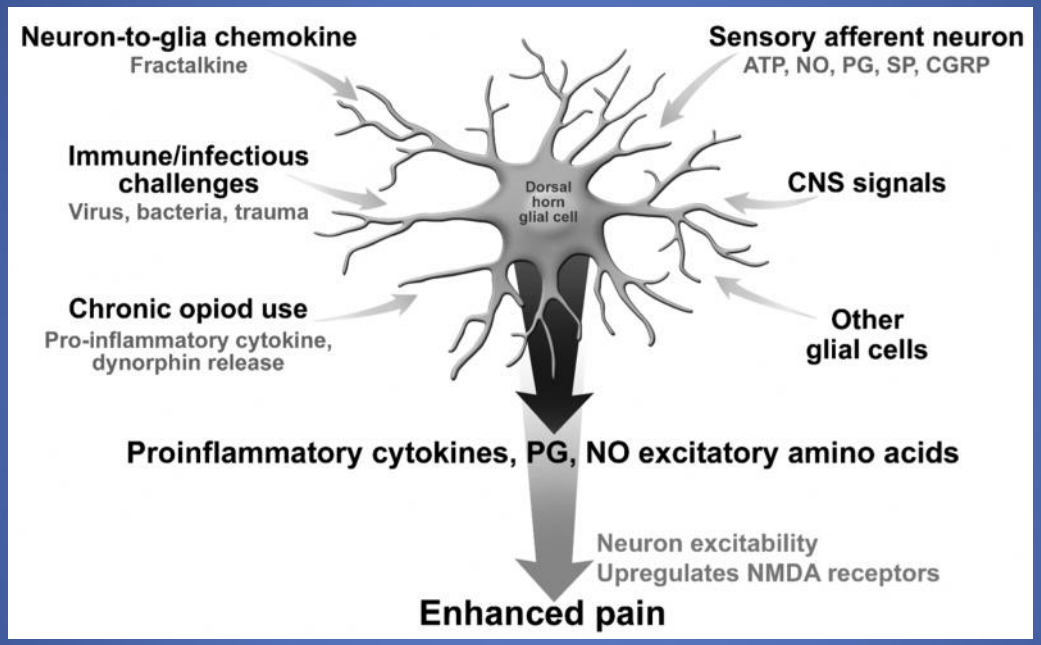

Activation of Dorsal Horn Glial Cells. The activation of spinal cord glial cells leads to hyperalgesia. This process is enabled via stimulation of glial cells to produce proinflammatory cytokines, prostaglandin, nitric oxide and excitatory amino acids, which increase neuron excitability and upregulate NMDA receptors leading to enhanced pain.

Factors that activate this mechanism include. :

a) release of Adenosin triphosphate (ATP), nitric oxide (NO), prostaglandins, substance P and calcitonin g-related polypeptide (CGRP) from sensory afferent neurons,

b) descending signals from the CNS,

c) a vicious cycle with activation from other activated glial cells,

d) immune challenges or infections, and e) release of a neuron to glia chemokine, fractalkine. Importantly chronic opioid use also activates this system via release of pro-inflammatory cytokines and endogenous dynorphin release. Thus chronic opioid use in addition to these other factors can lead to hyperalgesia via this mechanism.

The Narcotic Bowel Syndrome: Clinical Features, Pathophysiology and Management

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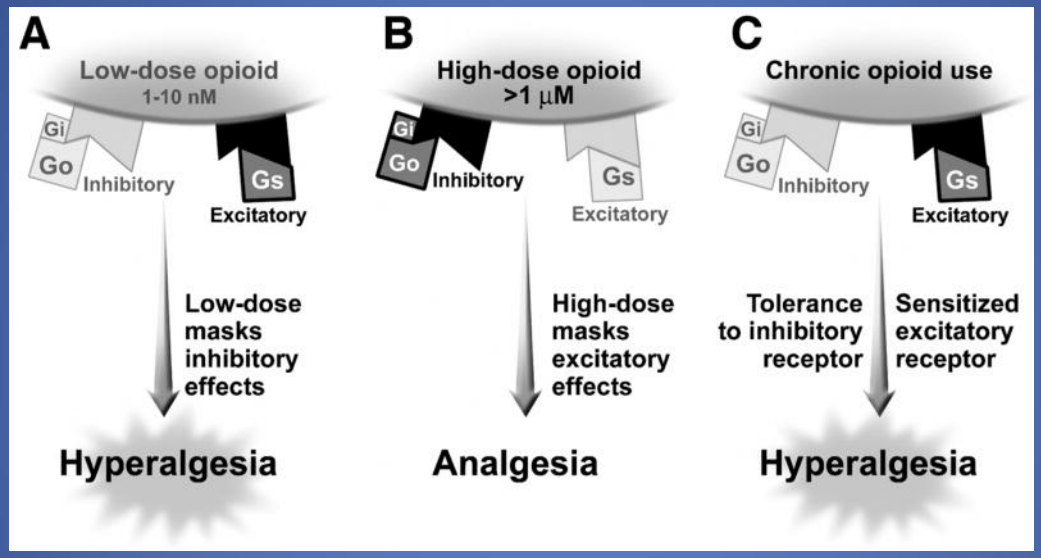

Opioids appear to have differential effects on the opioid receptor in the dorsal root ganglion based or whether it activates the traditional GI/GO protein inhibitory mode leading to analgesia or a newly identified Gs protein excitatory receptor that can produce hyperalgesia.

Figure 2a shows the effect of low dose opioids (1–10 nM), which preferentially activates the excitatory (Gs coupled) mode and masks the inhibitory (Gi/Go) mode leading to hyperalgesia.

Figure 2b More typically high dose opioids are used where there is preferential activation of the inhibitory mode and masking of the excitatory mode.

Figure 2c With the chronic use of opioids there is again sensitization and unmasking of the excitatory mode and tolerance of the inhibitory mode leading to hyperalgesia. Low doses of opioid antagonists like naltrexone, naloxone or buprenorphone have selective inhibitory effects on the excitatory pathways which enhances morphine activity.

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Table 1

Diagnostic Criteria for Narcotic Bowel Syndrome

Chronic or frequently recurring abdominal pain that is treated with acute high dose or chronic narcotics and all of the following:
• The pain worsens or incompletely resolves with continued or escalating dosages of narcotics.
• There is marked worsening of pain when the narcotic dose wanes and improvement when narcotics are reinstituted ("Soar and Crash").
• There is a progression of the frequency, duration and intensity of pain episodes.

The Narcotic Bowel Syndrome: Clinical Features, Pathophysiology and Management

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Table 3

Overview of Treatment of Narcotic Bowel Syndrome

1. Physician-Patient Relationship
   a. Accept the pain as real
   b. Provide information through dialog with the patient
      i. The physiological basis for the pain
      ii. The effects of narcotics on pain and GI function
   c. Discuss the rationale for withdrawal
   d. Present the withdrawal program
   e. Elicit the patient's concerns and expectations
   f. Gauge the patient's willingness to undergo the program
   g. Discuss the treatment plan with a family member
2. Specific Treatment Guidelines
   a. Narcotic withdrawal protocol
   b. Concomitant medications
      i. antidepressant
      ii. benzodiazepine

Explain:

a) the patient has a bona fide disorder that needs to be treated rather spending more money doing studies, but the clinician will stay vigilant to evaluating new findings should they emerge,

b) clarify that the treatment is based on a gradual withdrawal of narcotic as other treatments are substituted, so the patient will not be abandoned in pain, and

c) that the physician will be available to address any side effects or flare ups with the patient if they occur.

Treatments for Narcotic Bowel Syndrome

- Antidepressants
  - TCAs- Desipramine or nortriptyline: 50mg qhs titrated to 150mg qhs,
  - SNRIs – Duloxetine: 30mg qd titrated to 60mg qd, Venlafaxine: 37.5mg qd titrated to 225 mg qd
- Sympatholytics
  - Clonidine: Start 0.1–0.2mg q4hrs as titrated by orthostatic blood pressure
- Anxiolytic
  - Lorazepam: Start 1mg q6hrs or
  - Clonazapam: Start 0.25mg q8hrs
- Spasmolytic
  - Hyoscyamine: 0.25mg sublingual q4hrs prn
- Cathartic
  - Polyethylene glycol solution (PEG)
  - Consider Lubiprostone
- Psychological Treatment
  - Cognitive-Behavioral Therapy
  - Relaxation methods
- Future therapies
  - Alvimopan
  - N-methylnaltrexone
  - Atypical antipsychotic?

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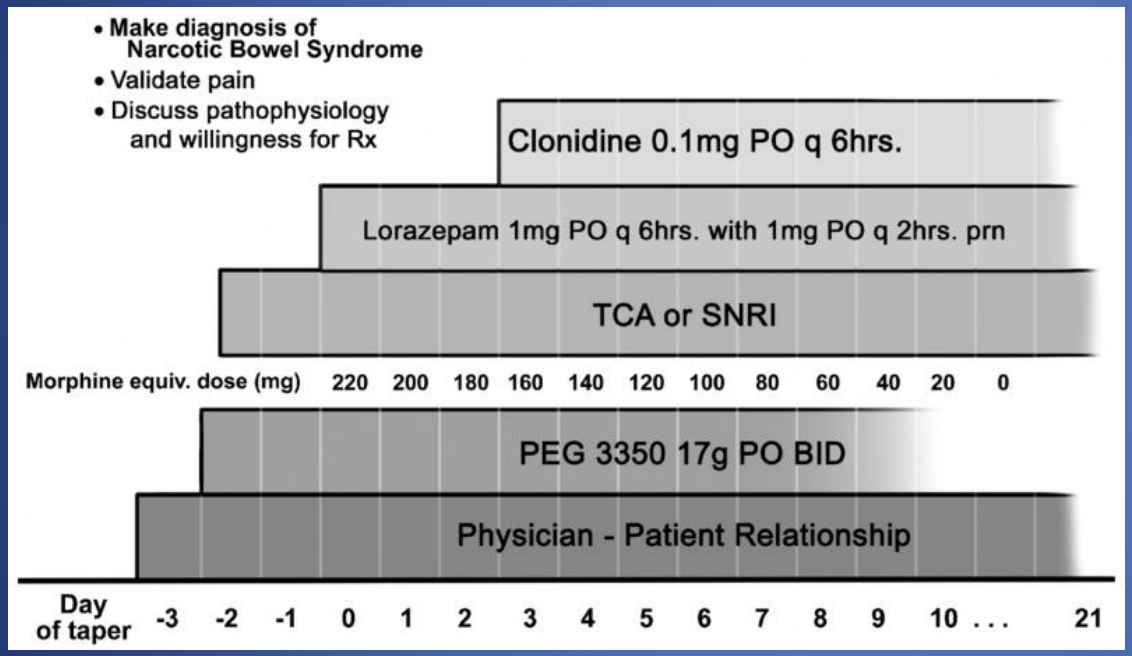

Up to 0.6 mg/d

Or Clonazepam

Desipramine 50-75 or nortriptiline; duloxetine

May need Tegaserod or Lubiprostone, Or Methylnaltrexone

Narcotic dose is reduced **10** to 33% per day. May give Ketorolac to help.

Hypercoagulability Workup

- Check with CT of abdomen for: cirrhosis, Cancer, or inflammatory focus.
- Look for presence of: Pregnancy, Oral contraceptive use, Bechet's disease, Ulcerative colitis, or Celiac Sprue.
- Myeloproliferative dz:
  - Granulocyte V617F JAK2 mutation
  - Bone marrow Bx: clusters of dystrophic megakariocytes or endogenous erythroid colonies in culture
  - Splenomegaly + Plat count > 200000 highly suggest MPD.
- PNH:
  - Flow cytometry of Peripheral Blood Cells for CG55 and CD59
  - Ham-Dacie and sucrose tests where flowcytometry is unavailable
- Antiphospholipid S:
  - High anticardiolipin Ab
  - Lupus anticoagulant
  - Antibeta2 glycoprotein 1
- Factor V Leiden:
  - R605Q factor V mutation (useful even in cirrhosis)
  - Increased protein C resistance

Hypercoagulability Workup

- Plasminogen deficiency
- Factor II gene mutation:
  - G20210A mutation (useful even in cirrhosis)
- Inherited antithrombin deficiency:
  - Decreased antithrombin III plus
    - Normal PT, or
    - Family Hx of Antithrombin deficiency
- Inherited Protein C deficiency
  - Decreased protein C level, plus
    - Family Hx of Protein C deficiency (check 1st degree relatives), or
    - Normal prothrombin level.
- Inherited Protein S deficiency:
  - Decreased protein S level, plus
    - Normal prothrombin level, or
    - Family Hx of Protein S deficiency (check 1st degree relatives)
- Hyperhomocysteinemia:
  - High serum homocysteine prior to disease (check also serum Vit B12 level & RBC folate level)
  - TT677 MTHFR genotype (useful even in cirrhosis)
  - Uncertain value of C677T homozygous polymorphism

Local Risk Factors for Portal Vein Thrombosis

- **Cancer**
  - Any abdominal organ
- **Focal inflammatory lesions**
  - Neonatal omphalitis, ombilical vein catheterization
  - Diverticulitis, Appendicitis
  - Pancreatitis
  - Duodenal ulcer
  - Cholecystitis
  - Tuberculous lymphadenitis
  - Crohn's disease, Ulcerative colitis
  - Cytomegalovirus hepatitis
- **Injury to the portal venous system**
  - Splenectomy
  - Colectomy, Gastrectomy
  - Cholecystectomy
  - Liver transplantation
  - Abdominal trauma
  - Surgical portosystemic shunting, TIPS, Liver transplantation
- **Cirrhosis**
  - Preserved liver function with precipitating factors (splenectomy, surgical portosystemic shunting, TIPS dysfunction, thrombophilia)
  - Advanced disease in the absence of obvious precipitating factors