Condensed Notes CARSEP VII and VIII Reviews Allen Kamrava, M.D. M.B.A.

Attending Staff, Colon and Rectal Surgery

Cedars Sinai Medical Center

INTRODUCTION

This is a collection of the notes I made from the CARSEP Review in preparing for the ABCRS qualifying (written) exam. It incorporates notes from both CARSEP Review VII and VIII.

In of themselves, these will be insufficient to prepare for the written boards. Nevertheless, I distinctly remember several of the questions from the CARSEP being asked verbatim during the written boards exam. I used these notes in addition to my notes on the ASCRS textbook in preparation and was successful in passing the exam.

I wish you luck in your endeavors. If you find any errors in <u>fact</u> in the following notes, please do let me know. I make no effort to correct spelling and grammatical errors when I make my study guides.

All the best, Allen

CARSEP Review VII Notes

ANORECTAL

Nerves at most risk during Sigmoid Resection:

- Superior hypogastric plexus (originates around the IMA)
- Injury: Retrograde Ejaculation

Sexual Dysfunction after Rectal Resection:

- High ligation of IMA: para-aortic sympathetic plexus
- Para-sympathetic nervi erigentes: course anterolaterally and join hypogastric nerves → Pelvic plexus
- Pelvic Plexus → branches anterior form the *periprostatic plexus*
- Pudendal nerve via dorsal nerve of the penis → sensory fibers to penis and glans
- Nerve for Sensory stimuli to Penis and Clitoris:
 - Branch of pudendal nerve
 - S2-4 → around ischial tuberosity → extrapelvic area → two branches:
 - (1) Dorsal N. of Penis
 - Motor branches to the ES
 - Sensory Fibers to Penis and Clitoris
 - (2) Perineal N.

- Superficial & deep perineal muscles & external urethral sphincter

Most common cause of injury to pelvic plexus:

- During LAR sig. posterolateral traction on rectum
- Nervi Erigentes from sacral foramina → anterolateral course → join hypogastric plexus → become Pelvic Plexus → anterior course through lateral stalks → anterior branches: Periprostatic Plexus

Anal Transition Zone:

- extends to about 1 cm cephalad to dentate line
- demarcation for lymphatic drainage
 - Proximal: pelvic lymphatics
 - Distal: inguinal lymphatics

Hirschsprung's Disease:

- emryologic failure of distal migration of neural crest cells to reach& form the distal myenteric ganglion
- Pathology: Acetylcholinesterase Staining increase in size and number of disorganized nerve fiber in lamina propria and submucosa that stain darkly for acetylcholinesterase

Deep Post-Anal Space:

- Superior: Levator Ani Muscle
- Horseshoe abscess when abscesses here communicate anteriorally

IschioAnal Space:

- Lateral border: obturator internus M., ischium and obturator fascia
- Superior: Levator Ani M.
- Inferior: Skin of perineum
- Medial: levator ani & external sphincter M

- Anterior: urogenital diaphragm & transversus perinei
 M
- Rectum is NOT a border of IschioAnal Space (Ischirectal Fossa is a misnomer, given this fact)

Internal Anal Sphincter Neuromodulation:

- Parasympathetic: from S2-4, inhibitory, causes relaxation
- Sympathetic: from L5, direct effect on 2 IS receptors - Alpha Adrenoreceptors: excitation & contraction
 - Beta Adrenoreceptors: relaxation
- Cholinergic Agonist (e.g. Bethanecol) → relaxation Anorectal Neuorsensory Function:
 - Rectal Proprioceptic Reflex: receptors in pelvic floor and rectal wall
 - Anal Sampling: proximal anal canal relaxation in response to rectal distention & mov't of contents to anal canal
 - Rectal Heat Thresholds: measurement correlate well w/ current balloon defecator desire
- *Pain Receptors*: located 5 15 mm from dentate line Stimulus and sequence of defecation:
 - Direct Stimulus for initiation: rectal distention
 - Colonic Mass Mov't → passage of material into rectum
 → Rectal Distention → Anal Canal Sampling → ES relaxation

Staple Hemorrhoidopexy (PPH):

- Best indication: Grade 3 circumferential hemorrhoids
- Grade 1 & 2: conservative measures, or traditional
- Need to reduce prolapse to place stapler so not stage 4
- SE: pelvic sepsis, rectal perf, retroperitoneal free air Anal Fissure:
 - Most become asymptomatic by 10 days of conservative Rx
 - Time to complete healing 86% by 6 months, median 8 wks
 - If patient with improving symptoms but not healed w/in this time frame → cont. conservative mgmt..

Classes of and Treatments for Anal Stenosis:

Classes:

- Mild: tight but finger and Hill-Ferguson go in
- Mod: needs forceful dilation to put in finger or HF retractor
- Severe: can't pass finger or HF retractor

Levels:

- Low: >0.5 cm distal to dentate line
- Middle: <0.5 cm distal or proximal to dentate line
- High: >0.5 cm proximal to dentate line

Therapy based on Type:

- mild: gentle dilations
- low, mild-mod: sphincterotomy
- mod-severe:
 - low: anoplasty or VY plasty (better for severe)

- High: Diamond and House Flaps
- severe High stenosis: S Flaps, bilateral U Flaps,

bilateral house Flaps, or bilateral diamond Flaps Pilonidal Disease:

- Procedure w/ quickest recovery and lowest recurrence rate:
 - Bascom procedure

 laterally placed incision left open to heal 2nd intention Anterior Fistula in a female:

- minimize sphincter transection, higher risk for incontinence
- seton may cause "keyhole" defromtiy

- Mgmt of Choice: Endoanal Advancement Flap

Most appropriate drainage of Suprlevator Abscess:

- drainage into rectum with IS division

Different types of Fistulas – note to self:

- Anteiror high: seton may cause "key hole" & incont
- Post. Midline: primary fistulotomy w/o seton
- Extrasphincteric: treat primary, deal with fistula second
- Intersphincteric: usually can drain with simple IS minimal distal division
- Ischioanal: drain as close to verge as possible, in case is fistula

Horseshoe abscess:

- Hanley Procedure -

1. enter deep postanal space from the tip of the coccyx by separating the *superficial* ES in post mid line, draining abscess.

2. Distal IS divided to obliterate crypt abscess of origin.

3. counter incisions in lateral extensions for complete drainage

4. minimal ES division

MC anorectal Malformation:

- Female:
 - 1. rectovestibular Fistula
 - 2. Rectoperineal fistula
 - 3. Cloaca, short channel
 - 4. Cloaca, long channel
 - common channel <3 cm better long term fxn
- Male: Rectourethral Fistula
- associated with Down's Syndrome
- Associate malformations:
 - 1. Urinary (50%)
 - 2. sacral & spinal abnormalities
 - 3. VACTERL
- Rectovaginal Fistula repair in setting of prior XRT:
 - Transabdominal repair with coloanal reconstruction
 - need healthy tissue to interpose

Human Papillomavirus (HPV):

- virus pools at the base of the penile shaft & in vaginal introitus → condoms ineffective
- anal HPV does not require anal sex tracks along perineum from base of penis or vaginal introitus

- Causes squamous metaplasia may extend up to distal half of rectum
- metaplastic squamous epithelium at risk for CA

STD Treatment meds:

- Gonorrhea: Ceftriaxone 125 mg or Defiime 400 mg
- Chlamydia: Azithromycin and doscycycline
- Granuloma Inguinale: Bactrim

Radiation of Anal Cancer:

- can decrease in size over 3-12 months
- as along as decreasing in size, continue follow up every 6 weeks, no biopsies necessary if continues to improve
- if inguinal lymph nodes palpable, include in radiation field

Melanoma of Anal Canal:

- resistant to radiation and chemo
- no survival advantage shown for APR over WLE
- so if can do WLE, do it, otherwise APR
- APR for local recurrence as well in absence of distant disease

Chordoma:

- MC malignant neoplasm of rectorectal region
- Sx: rectal or perineal pain, aggravated by sitting and alleviated by standing or wlaking
- PE: smooth extrarectal mass w/ normal mucosa on DRE
- 4 criteria for diagnosis on PXR: expansion of bone, rarefaction or destruction, trabeculation and calcification (occasional)
- surgical resection whenever possible

Posterior Pelvic Tumors:

- only effective treatment early surgical resection
- no place for preop biopsy
- if on DRE finger can reach upper part of mass, posterior approach almost always successful
- MC cause of recurrence of benign sacrococcygeal teratomas following excision is: failure to remove coccyx

Cutaneous Paget's Disease:

- intra-epithelial adenocarcinoma w/ a long preinvasive phase
- Sx: perianal itching, bleeding, mucoid discharge, weight loss
- Dx: biopsy showing Paget's cells large, pale, vacuolated cells with hyperchromatic eccentric nuclei; periodic acid-Schiff stain; stain positive for Alcian blue and CAM 5.2
- Multiple local biopsies needed to assess local extension
- Rx: WLE

CARSEP VII and VIII Review

Lichen Sclerosus:

- thinned and wrinkled hypopigmented skin surrounding the anus and vulva
- MC women in 5th or 6th decade
- etiology unclear
- causes painful fissures
- Rx: topical glucocorticoids

Perianal Streptococcal Disease:

- consider in pediatric patient with perianal erythema and pain that doesn't improve with empiric treatment for pinworms and Candida
- -2 3 week course of antibiotics for Rx
- throat cultures negative in 40 80%

COLON AND RECTAL NEOPLASM HNPCC:

- associations: endometrial, ovarian, gastric, hepatobiliary, small bowel, transitional cell CA of ureters/renal pelvis
- "rule of 3-2-1": 3 close relative affected with an HNPCC-associated cancer, spanning 2 generations, with 1 affected before the age of 50 years.
- FAP must be excluded
- MC indication of conversion to open during lap colectomy:
- Tumor related factors size, fixation or local infiltration Risks for metachronous colon CA and polyps:
 - Polyps: 30-56%
 - Cancer: 2-8%
- Use of CEA:
 - detection of recurrent disease
 - level >5 ng/ml PPD 70-80%
 - optimal timing not known; serial not shown to help

T stage and risk of LN involvement:

T1: 12%

- T2: 22%
- T3&4: 50%

- colon CA spread MC by lymphatics

"Pseudoinvasion" in a Pedunculated Polyp: dysplastic

glands in the submucosa

- epithelium becomes misplaced into submucosa and mimics cancer.

- believed due to torsion, ischemia and architectural distortion

- can differentiate with: hemosiderin (means ischemia), retention of lamina propria, lack of morphologically invasive/malignant features

Risk factors for poor bowel prep for scope:

- later appointments
- failure to follow instructions
- Indication of constipation
- male gender
- inpatient status
- history of stroke

- dementia
- cirrhosis
- <u>Capecitabine</u>: higher risk of hadn-foot syndrome and hyperbilirubinema (vs. 5-FU)
- <u>1st Line Therapy for Stage III Colon CA</u>: 5-FU, leucovorin, Oxaliplatin (FOLFOX)
 - Irinotecan: associated with sig GI toxicity w/o improvement in survival
- MC Site of Endometriosis: rectosigmoid region
 - oophorectomy increases success of operative therapy
 - MC symptom: pelvic pain
- Primary Colorectal Lymphoma:
 - 2nd MC cancer of colon (still only 0.5% of all)
 - Sx: abdominal pain (MC), mass, weight loss
 - Prognosis: histologic grade most important
 - 5 yr survival if node positive: 12%
 - MC site of colon: Cecum (then rectum, then ascending)
 - Risk factors: IBD, immunosuppression

Solitary Rectal Ulcer Syndrome:

- Sx: rectal bleeding, mucus, difficult defecation
- Rx: Counseling to avoid straining, fiber supplements
 - biofeedback next
- if prolapse on defecation: anterior Rsxn & rectopexy Med that increases infectious complication in IBD: steroids
 - the rest no good data

Ideal cases for strictureplasty:

- multiple short jejunoileal strictures
- fibrotic strictures
- no associated phlegmon
- DO NOT do colonic strictures dysplasia risk
- Sigmoid Vaginal Fistula in CD: segmental resection

MC Sx of CD: abdominal pain & diarrhea (75%)

Radiation induced Proctitis:

- usually self limited, no transfusions needed
- significant bleeding: topical 4% formalin solution 30 seconds to 3 minutes
- other treatments: APC

Diagnosis of CMV Colitis:

- histologic staining of endoscopic biopsies inclusion bodies (pathognomic for CMV infection)
- Rx: IV Ganciclovir (can also try foscarnet)

Behcet's Disease: vasculitis of indeterminate etiology –

- results in chronic, relapsing multisystem inflammation painful oral ulcerations (hallmark)
- surgery for fistula/perforation → highest recurrence rate Ischemic Colitis:
 - in long distance runners
 - colonoscopy most useful diagnostic test
- Angiodysplasia: angiogram will show
 - "vascular tufts"
 - slowly emptying vein (earliest sign)
 - an early filling vein
 - extravasation is not specific for it

- Most sensitive test for colovesicle Fistula: CT
- air/contrast in bladder w/ adjacent thickened colon
- <u>Stercoral Ulcer</u>: pressure-induced ischemia secondary to hard bolus of stool lodged in the colon
 - MC presentation: perforation ischemia leads to ulcer then full thickness perforation
 - rectosigmoid is MC site of perforation
 - 1/3 will have other sites of these ulcers
- Total Colonic Inertia: TAC w/ IRA/ostomy
- Anastomotic Stricture most likely to be cured:
 - web-like, non-fibrotic most likely to be improved with endoscopic dilations
- Peristomal Pyoderma Gangrenosum:
 - do NOT relocate, will recur
 - infliximab has good results
- Peristomal Bleeding in setting of Cirrhosis:
 - start with direct suture ligation, pressure or epinephrine soaked pressure dressing (work in 90%)
 - if re-bleeds again consider TIPS

IPAA questions?

- rate of dysplasia at anal transition zone: 3%
- MC complication: pouchitis (30%)
- Kock Pouch MC complication: nipple valve slippage Stomas:
 - Prolapse MC w/ which type: efferent limb loop T-Colon
 - *best reduces ostomy complications*: Preop visit with a stoma nurse for counseling and marking
 - MC cause SBO w/ ostomy: adhesions
- Increases risk of parastomal hernia: long term survival
- Continence rate after anterior sphincteroplasty at 5 years: 30-50% (40%)
- <u>Common GI Complication of Cystic Fibrosis</u>: Distal intestinal obstructive syndrome
 - due to pancreatic insufficiency food becomes too viscous to pass ICV
 - treat by hydrating the luminal contents PO, PR and pancreatic enzymes
 - most will respond to aggressive hydration
 - Operative intervention: high mortality rate
 - milk through ICV
 - insert 16 g angiocath and lavage lumen
 - enterotomy and closure after removal of bolus diversion

Colonocyte Na/K ATPase Pump:

- stimulated by mineralcorticoids, glucocorticoids, and SCFAs
- sodium absorption stops if conc 15-25 mmol/L
- Potassium concentration cutoff: 15 mmol/L
- <u>ICV Competents</u>: maintained by angulation superior and inferior ileocecal ligaments

Role of colonic anaerobic bacteria

- enzymes that catabolize lipid based compounds
- vitamin K production

- ferment carbs to SCFAs butyrate
- <u>Arc of Riolan</u>: meandering mesenteric artery if enlarged may indicated SMA is occluded
- <u>Right colectomy vs. Left</u>: more likely to get diarrhea because right colon better at salt and water absorption - not due to ICV or bile salt absorption
- <u>DVT prophylaxis</u>: graded compression stockings better than intermittent pneumatic compression stockings Adrenal Insufficiency: n/v/f/abd pain
- hypoNa, HyperK, Hypotension, Tachycardia
- MC cause of bowel injury during lap case: trocar insertion
- recommend 20 lap colon cases for benign or metastatic disease before doing so for oncologic resections
- Stage of wound healing for angiogenesis: proliferative 2-4 days post incision
- platelet aggregation first during inflammatory stage Important genes:
 - Tumor Suppressor: APC, DCC, p53, SMAD4
 - onco genes: K-ras, c-myc
- APC genetic testing: Protein truncation testing
 - APC test neg, but lots of adenomas? Suspect MYH

Allen Kamrava CARSEP Review VIII

MC Nerve Damages during proctectomy & Consequences:

- High Ligation of IMA: Sympathetic nerve supply → Retrograde Ejac (if Nervi erigentes remain intact)
- Damage to Nervi Erigentes \rightarrow Erectile dysfunction
- Hypogastric N.'s: mobilization at Sacral Promontory → Retrograde Ejac.
- Isolated Nervi Erigentes: Erectile Dysfxn
- Other Nerves, unrelated to LAR, no effect on sexual Fxn:
 - Pudendal Nerve \rightarrow Ext. Anal Sphincter
 - Obturator N.: Motor to adductors of thigh, sensory to medial thigh & hip joint
- Lymphatic Drainage Anorectal
- Anal Canal distal to Dentate \rightarrow Superficial Inguinal LNs
- Rectum \rightarrow follows arterial supply
 - upper 2/3 \rightarrow para-aortic LNs via inferior mesenterics
 - lower 1/3 & Anal Canal Proximal to Dentate \rightarrow
- internal iliac LN's & inf. Mesenteric Nodes

External Anal Sphincter (EAS) Innervation:

- Pudendal Nerve S2, S3, S4 Cross-over at the level spinal cord. Unilateral damage → EAS fxn preserved
- Congenital Deformity of Anal Canal: Proctodeum is

embryonic origin

- Imperforate Anus:
 - MC associated anomaly: urologic (50%)
 - 1st Test to do: Renal Ultrasound
 - Tethered Cord in 25%
 - *Currarino Triad*: Hemisacrum, presacral Mass, IA - Mass: Taratoma/meningocele/dermoid cysts
 - VACTERYL Anomalies: vertebral, anal atresia, cardiac, TEF, Renal, Limb

Relations of Deep Post Anal Space:

- Posterior part of ischioanal (ischiorectal) fossa
- Borders:
 - Superior: levator Ani M.'s
 - Inferior: Anococcygeal Ligament
 - Left & Right: Ischorectal Fossae
- Horseshoe Abscess via this space:
- left and right ischiorectal fossas communicate via deep post anal space
- Retrosphincteric space of Courtney (AKA)

Hypogastric Nerves:

- Risk of Injury during rectal mobilization at Sacral Promonotory \rightarrow Retrograde Ejac
- Origin: Aortic Plexus \rightarrow Lateral Lumber Splanchnic N.'s \rightarrow Sup. Hypogastric Plexus
- Mostly Sympathetic fibers froom L1 L3 nerve roots
- <u>Haustra Coli</u>: Made because colon is longer than *Taenia* $Coli \rightarrow$ haustrations result

Embryonic Formation of Hindgut:

- Terminal part of Hindgut \rightarrow forms cloaca \rightarrow
- urorectal septum forms and divides it to 2 \rightarrow

- Anterior Cloaca \rightarrow epithelial lining of bladder & urethra
- Post. Cloaca \rightarrow rectum & proximal anal canal Sacral Masses and their origins:
 - Tailgut Cysts: postanal hindgut (AKA tailgut)
 - Teratomas: primordial germ cells
 - Chordoma: ectopic rests of notochordal tissue

Pelvic Nerve Anatomy Basics:

- Sympathetic: L1-L3 hypogastric plexus
- Parasymp: S2 4 Nervi Erigentes (pelvic splanchnics)
- Both fuse in lateral pelvic Sidewall \rightarrow form 2nd plexus at base of bladder
- Injury to sympathetic plexus \rightarrow Retrograde Ejac and/or bladder dysfxn

Arc of Riolan:

- AKA meandering mesenteric artery
- if prominent \rightarrow ligate IMA distal to its take off

Vitelline Duct Remnants:

- Meckel's Diverticulum: (MC)
 - ~2% of population, ~50 cm from ICV valve
 - gastric or pancreatic tissue
- Vitelline Fistula: diagnosed early as an enterocutaneous fistula w/ drainage
- *Vitelline Ligament*: fibrous band remains from small bowel to abdominal wall → mechanical SBO

Hirschprung's Disease:

- Histology: absence of ganglion cells, thick nonmyelinated nerve fibers w/o synaptic connections
 - adrenergic & cholinergic fibers prominent
 - Staining for acetylcholinesterase is increased
- Failure of migration of neural crest cells \rightarrow absence of ganglion cells in intermuscular mucosa
- Dx: Suction biopsy 2 3 cm proximal to dentate line, should include muscularis mucosa to confirm

Considerations in Short Gut Syndrome w/ Colon Intact:

- Best Diet: High-Carb, Low-fat diet
- If colon intact: more likely to wean patients from $\ensuremath{\mathsf{TPN}}$
 - it will metabolize SCFAs into at least 1,000 Cal/day
 - If colon intact, do not force re-hydration
 - Med-CFA: absorbed as well
 - LCFA: not absorbed at all
- Glutamine: no benefit shown, needs >1/3 of bowel to be effective

Colonic Motility:

- Mass Movements: via HAPCs (AKA Giant Migrating Contractions – GMCs) – long spike, occur 3-5x a day – greater in amplitude & duration than phasic contractions
 - mostly in T-colon and Descening
- Phasic contractions: majority of colonic mobility, allow for mixing of stool in right colon

CARSEP VII and VIII Review

- LAPC: little known, related to meals & sleep-wake cycle

Dehydration & Water Absorption:

- Renin-Angio-Aldo Cascade → ↑ Aldosterone Levels → ↑ sodium resorption in colon & distal convoluted tubules
 - Sodium actively in, water follows
- Angiotensin: has effects on small bowel
- ADH: only effect on kidneys

Recto-Anal Inhibitory Reflex:

- As stool enters rectum, IAS relaxes & EAS contracts to allow for sampling → awareness of rectal filling → important part of continence
- RAIR absent in: Hirschsprung's Dz, Chagas', Dermatomyositis, Scleroderma

Obstructed Defecation Syndrome:

- increased angulation between the rectum and anal canal due to *paradoxic puborectalis contraction*
- Associations: stress, prior anal surgery, TAH
- Dx: Defecography combined w/ manometry
 - Manometry: paradoxical contraction of IAS

Biofeedback Training:

- Use of electrical/mechanical devices to increase awareness of physiologic activity
- Make information available to patients' consciousness
- Efficacy 50 70% in FI
- Associated with Success of treatment:
 - 1. Sensation of Rectal Filling,
 - 2. EAS strength during voluntary contraction

3. Coordination of Sphincters during rectal distention Immiquimod use in HIV:

- even w/ CD4 <200, shown to be equally as effective
- 5% topical, apply 3 nights a week up to 16 weeks
- 29% rate of recurrence at 14 weeks after treatment
- Induces local production of alpha-interferon
- XRT for Anal Cancer in HIV+: increased toxicity risk

- no increase in recurrence or other malignancies <u>Post-Op Cancer Surveillance Paradigm</u>:

- Check CEA Q3mo x 3 years, & then Q6mo x 2 years
- CT C/A/P: Q1yr x 3 years
- Colonoscopy: at year 3, and then Q5years - Flex Sig: Q6 mo x 5 years for rectal CAs
- H&P: Q3-6 mo x 3 years, then Q6 mo x 2 years
- LFTs, CXR not recommended

Condyloma Screening in HIV+: Annual DRE w/ HRA Mech of Action:

- Cetuximab: chimeric IgG1 monoclonal Ab \rightarrow binds to epidermal growth factor receptor \rightarrow inhibits tumor growth
- *Avastin*: monoclonal Ab binds to vascular endothelial growth factor receptors

Microsatellite Instability (MSI):

- in 90% of patients w/ HNPCC, 15% sporadics

- high number of DNA replication errors
- Histo: poorly differentiated,
- longer survival despite being Chemo resistant

CEA use post op:

- best used for detecting liver mets
- Not as sensitive (60%) for locoregional recurrence
- Chromosome 19q responsible
- Oxaloplatin: may cause artificial rise

Immunosuppressive Therapy in IBD: 6-MP:

- 3 4 months before clinical benefit achieved
- should be able to come off steroids once achieved
- fistula improvement in 30-40%
- Risks: Lymphoma, however low risk
- need to monitor for leukopenia regularly
 - goal is leukycte count >3,000/mm³

Anti-TNFs in IBD:

- Infliximab: chimeric monoclonal to IgG1
 - given with infusions
 - immunogenic \rightarrow allergies can form
- Adalimumab: human monoclonal IgG1
 - given SubQ
 - less immunogenic
- Contraindications for both: abscess, SBOs, fibrotic intestinal narrowing, active cancer, hx of TB (relative)

IBD and associated & linked genes:

- OCTN1/OCTN2 : IBD5 locus on Chromosome 5
- HLA Genes : IBD3 Locus on chromosome 6p
- CARD15/NOD2 : IBD1 locus on Chromosome 16 - associated with *fibrostenosing* disease
 - more likely to need surgery compared to others

Bethesda Criteria for HNPCC:

- 1. CR CA in pt. younger than 50
- 2. presence of synchronous/metachronous CAs
- 3. CR CA w/ MSI-H histology in age <60
- 4. 1st degree relative w/ HNPCC type CA < age 50
- HNPCC related CR CA in 2 or more 1st/2nd relatives regardless of age

Genetic Testing in HNPCC:

- patient w/ CA is tested for MSI or Immunohistochemical (IHC) staining for MLH1 or MSH2 proteins.
 - Normal: protein is identified
- Abnormal: protein is NOT identified

FAP and the APC Gene:

- germline mutation on chromosome 5q
- APC is tumor suppressor gene, it is deleted/truncated IBD Tumor Markers:
 - Anti-Saccharomyces cerevisiae (ASCA) Crohn's Dz
- antineutrophil cystoplasmic antibodies (p-ANCA) UC

Heparin Induced Thromobcytopenia:

- 1st Step: Stop All Heparin
- administer Argatroban thrombin inhibitor
- typically occurs between post op day 3 14
- OK to continue SCDs

- do NOT do platelet transfusion

Sodium Phosphate Bowel Preparation - Adverse Events:

- Risk of Acute Phosphate Nephropathy
- At risk people: >55 yo, hypovolemia, baseline kidney disease, bowel obstruction, active colitis, Diuretic medications, ACE-I, ARBs, NSAIDs
- Nutrient Deficiencies:
 - Zing: 3-4 mg daily alopecia, dermatitis, wound healing
 - Copper: Hypochromic Anemia (Bone Marrow problems)
 - Chromium: glucose intolerance
- <u>Refeeding Syndrome</u>: hypokalemia, hypophosphatemia, thiamine deficiency, CHF (from rapid extracellular volume expansion)
 - in severely starved, give thiamine supplement before refeeding to prevent Wenicke's encephalopathy
- <u>Alvimopan</u>: peripherally acting antagonist of the µ-opiod receptor that has limited ability to cross the blood-brain barrier
 - seems to work for reducing the length of post op ileus, while not affecting post op pain control (12 mg dosing)
- methylnatrexone: similar peripheral acting medication
- <u>Max dose Lidocaine</u>: 300 mg @ 1% w/o epi \rightarrow 30 mL max

Medications for Moderation Sedation:

- Meperidine (Demerol): decreases seizure threshold;
 5min onset of action, 2 4 hour duration
- *Fentanyl*: Does not lower seizure threshold, 1min onset, 30 60 min duration
- Midazolam: 1-2.5min onsent, 2 6 hours duration, ok w/ hx of seizures
- *Propofol*: 30-60sec onset, 3 10 min duration severe cardiopulmonary effects, so only by anesthesia team

<u>Normothermic Post op Shivering</u>: AVSS \rightarrow Rx: meperidine <u>Ureteral Injuries – 4 MC points of injury</u>:

- 1. High ligation of IMA \rightarrow primary repair over stent
- 2. Sacral Promontory → primary or Boari/Psoas/Tunneled
- 3. Division of lateral stalks \rightarrow tunneled ureteroneocysto-

4. Perineal Phase of APR \rightarrow ureteroneocystostomy

- Nosocomial Pneumonia: MC due to pseudomonoas start antibiotics for gram negative coverage
- CO₂ Gas Embolism During Laparoscopy:
 - millwheel/machinery murmur in heart
 - hypotension and bradycardia
 - Steep Trendelenburg w/ left lateral decub, & FIO2 max'd

<u>Argon Beam</u>: high-frequency monopolar current <u>Emergency Stoma</u>: higher risk of necrosis <u>Kock Pouch Complications</u>:

- MC Nipple Valve Slippage; causes:
 - Fecal incontinence

- difficulty intubating pouch
- can sometimes be salvaged by making new nipple from afferent limb (saving pouch)
- Risks: Male, >40yo, s/p IPAA or EI 1st
- Evaluating a patient w/ seepage/incontinence Sx's:
 - Anoscopy 1st must rule out hemorrhoidal disease which can give symptoms of FI.
- <u>Autonomic Dysreflexia</u>: in patients with T6 level or higher lesions → HTN, sweating, HA, Hot/cold flashes during anorectal procedures
 - Lidocaine anal block will decrease the response
- <u>Anorectal Infxns in the presence of neutropenia</u>: duration of neutropenia most indicative of prognosis
 - Aminoglycoside, flagyl, zosyn/3rd gen ceph
 - MCs: E. Coli, Group D Strep
- Mgmt of RectoVag Fistula s/p pregnancy:
 - even if "continent" assume sphincter defect $\rightarrow 1^{st}$ best procedure is sphincteroplasty (before flaps)

Anal Fissure Treatment:

- Acute, less than 4 wks: fiber, NSAIDs, topical antiinflammatory local anesthetics
- Chronic Fissure w/ low normal tone: if NTG fails, then Diltiazem, then botox
- Fissure in HIV/AIDS: always rule out infectious or neoplastic disorder
- Chronic Fissure that failed LIS: repeat EUS & Manometry – if still high tone → Rx: Contralateral LIS
 Pt's at risk for FI: Rx: anoplasty
- NO relaxes smooth muscle of IAS

Infectious colitides/proctitis:

CMV: watery Diarrhea, bloody stools in patients w/ AIDS

- can progress to toxic megacolon
- 40% colitis will only be on right side (so COY not flex)
- Dx: must be done by biopsy (mucosa may look normal)
 → lymphocytic infiltrate w/ mucosal cells containing intranuclear inclusions "owl's cells"
- Rx: Ganciclovir
- Enterobius Vermicularis: (Pinworm)
 - live in proximal colon, migrate to rectum at night
 - deposit ova on perianal skin
 - tape to anal area in morning & look under microscope
 - Rx: Mebendazole

Gonorrhea:

- Sx: severe anal pain, tenesmus, mucopurlent discharge
- Exam: thick purulent d/c from multiple anal crypts w/ pressure on the perineum
- Culture: Thayer Martin or Modified NY City media <u>before</u> doing procto/anoscopy/DRE
- Rx: Ceftriax IM one x1/Cipro 500 x1/Levo 250 x1/ Ofloxacin 400 x1/Cefexime 400 x1
 - treat chlamydia as well: Azithro 1 g x1 or doxy 100 mg bid x 7 days

CARSEP VII and VIII Review

Chlamydia Trachomatis Proctitis:

- Serovars D through K

Chlamydia Trachomatis – Lymphgranulma Venereum:

- Servars L1 – L3

- Mucosal ulcerations of the peri-anal area, anus & rectum; may seem like Crohn's disease – crypt abscesses and granulomas
- Inguinal Lymph nodes matted (not in CD)
- Oral doxycycline x21 days

- No sex until 7 days after abx completed Herpetic Proctitis:

- Sx: anal pain, tenesmus, rectal d/c, BRBPR
- Exam: several ruptured vesicles around anal verge, diffuse friability to rectum, 50% b/l tender inguinal LAD
- Dx: Viral culture (M4 media) or serologic tests
- Rx: Acyclovir x 10 days
 - not ganciclovir \rightarrow used for CMV

Syphillis:

- Primary Stage: w/in 2-10 wks from exposure
- Sx: chancre: small papule which ulcerates eventually, single or multiple, perianal or anorectal; painless but prominent LAD

Lichen Planus:

- ex: skin disorder, most idiopathic, some related to medications
- Sx: shiny, flat-topped papules w/ darker pigmentation; mouth may have white plaques w/ small gray lines (Wickham's striae)
- Rx: moist dressings, sitz-baths, low concentration steroid cream
- Lichen Sclerosus et Atrophicus: ivory colored, atrophic papules that may break down to red raw surface w/ intense pruritis → replaced w/ chronic inflammation
- *Psoriasis*: scaling plaques, bleeding results if scales removed.
- $\begin{array}{l} \textit{Pemphigus: a systemic disease, begins as bulla \rightarrow \\ \textit{pustules} \rightarrow \textit{blisters} \rightarrow \textit{warty vegetation} \end{array}$
- Molluscum Contagiosum: poxvirus \rightarrow pearly, flesh coloured firm, umbilicated nodules;
 - localized mass of hypertrophied epidermis; benign
 - spreads by direct contact
 - If immunocompotent, will spontaneously regress in 2-3 months. Progression based on immune status, even after destruction will recur if immunocompromised
 - \rightarrow Rx: treat immunosuppression (protease inhibitors HIV) will usually improve in 3 4 months
 - if want removed, same treatments as HPV, but main stay of therapy is restoring immunocompotence so it will spontaneously regress

Human Papilloma Virus (HPV) Vaccine - Gardasil:

- Vaccine: for 6, 11, 16, 18 (70% of CAs, 90% of warts)
- No evidence has effect on pre-existing HPV infxn
- No known serious side effects

- Ideally give before onsent of sexual activity
- Calymmatobacterium Granulomatis:
 - casuses Granulom Inguinale ulcerative skin disease, cauliflower like appearance, pustules & papules
 healed areas can be devoid of pigment
 - formally known as Donovania Granulomatis
 - Dx: hx and Donovan bodies on microscopy

Levator Syndrome:

- Hx: deep-seated rectal pain, radiates from coccyx and left buttocks, worse w/ sitting, relieved by ambulation/recumbancy
- Dx: detailed hx, anorectal exam, flex sig; pain reproducible during DRE w/ TTP on puborectalis M.
 Exclude: PID in women, Prostatitis in men
 - Pelvic floor studies not really indicated
- Rx: digital massage of levators, prostaglandin inhibitors, muscle relaxants, heating pads, electrogalvanic stimulation (EGS)
- if all above fail, then do pelvic floor testing

Solitary Rectal Ulcer:

- Trauma, repeated prolonged & excessive straining
- Dx: histology must show obliteration of lamina propria
 - glands misplaced within submucosa
 - immunostain for smooth muscle actin w/in lamina propria to clarify
 - if unclear, need to do operative bx to ensure not CA
- Rx: symptomatic; operative is rectopexy/High Ant Rsxn
 - local therapy will recur, so only use if acutely bleeding is a temporizing measure.

Colitis Cystica Profunda:

- Ulcer
- Dx: mucous cysts deep to the muscularis mucosa - normal appearance of glands in submucosa
- Colon Cancer Mutations: APC early mutation in path, p53 and k-ras late

Anal Cancer Staging:

- T: 1 <2 cm; 2 <5 cm; 3 > 5cm; 4 Invades organ (vagina/bladder but not sphincter)
- N: 0: none, 1: peri-rectal; 2: unilat Inguinal; 3 b/l ing or an N1 & N2
- M: x: unknown, 0: none, 1: present

Benefits of Chemotherapy for Stage III Colon CA: 30% reduction recurrence, 22-32% mortality reduction - unkown benefit for stage II

- Chemotherapy for Colon CA:
 - FOLFOX: 5-FU, Leucovorin, Oxaliplatin x 6 months
 - Capecitabine (Xeloda): adjuvant in older pts, taken by mouth as single agent, well tolerated, seems equivalent to 6 months of FOFLOX
 - Oxaliplatin: high incidence of peripheral neuropathy

Nigro Protocol:

- Complete tumor response rates from 68 100% at 5 yrs
- XRT dose: 45 59 Gy ↑ response rate w/ doses >54
- work up: COY, CT A/P & CXR(CT); [PET not standard]
- Follow up 6 8 wks post XRT; bx suspicious lesions
- As long as continues to regress, can cont. to obs
- if stops regressing or starts growing $\rightarrow \mathsf{APR}$
- Follow up exam: DRE, Anoscopy, Groin Exam Q3mo x 1 yr, Q6mo x 1 year, and then Q1yr x 5years
- 5 yr survival for salvage APR: 28 60%
- <u>Anal Margin Squamous Cell CA</u>: if not invading sphincters, treat like Squamous Cell CA of skin

Perianal Paget's Disease:

- intraepithelial adenocarcinoma from apocrine glands
- 50% associated w/ other CA \rightarrow do COY in all to eval
- WLE ok if not invasive (in situ) but always do COY
- Anal Melanoma:
 - Neoadjuvant Chemo: NO role
 - APR: for locally recurrent or advanced disease that can't be treated locally (use standard melanoma margins)

Bethesda Criteria:

- 1. CRC in individual under age 50
- 2. presence of synchronous/metachronous CRC or other HNPCC associated tumor, regardless of age
- 3. CRC w/ the MSI-H histology
- 4. CRC in 1 or more 1st degree relatives w/ one <50 yo
- 5. CRC in 2 or more 1st/2nd regardless of age
- HNPCC tumors: endometrial, ovarian, gastric, urothelial, pancreatic, brain/small bowel.
- Screen Q2 yrs in family members

Genetic Testing:

- FAP: test for APC gene, 80% sensitivity
- HNPCC: Test for MSH2&MLH1, 50% sensitivity GIST Pearls:
 - 2 cm, mitotic rate
 - c-kit, CD117, tyrosine kinase
 - hematogenous spread (not lymphatic)

- Imatinib (Gleevec) – tyrosine kinase inhibitor <u>Cetuximab</u>:

- block epidermal growth factor receptor (EGFR)
- EGFR active in 80% of cancers
- K-ras mutation predicts resistance to Cetuximab
- Contraindications to salvage exenterations:
 - extensive pelvic sidewall involvement
 - tumor encasement of iliac vessels
 - extension of tumor into sciatic notch
- invasion proximal to S2-S3 jxn

Rectal Carcinoids - features dictating LAR:

- invasion of muscularis propria
- mitotic rate 2/50hpf
- lymphovascular invasion

- perineural invasion

Differentating Pre-sacral Masses on the exam:

- *Teratoma*: other anomalies, can become infected, encapsulated
- Chordoma: not encapsulated

Dermoid Cyst: squamous epithelium & skin appendages

Ant. Sacral Meningocele: communicates w/ dural sac; associated w/ headaches; Scimitar Sacrum(smooth concave border w/o invasion); need to ligate dural defect during resection

Bony Destruction: Ewing's, Chordoma, Osteosarcoma Calcifications: taratoma, dermoid cysts, cystic hamartomas

Sacrectomy Nerve Fxn: at least one S3 nerve root must be preserved to preserve bladder/bowel fxn

- Diverticular disease w/ hx Rental Tranpslant or PKD: high risk for complications, do surgery if even 1 attack of uncomplicated diverticulitis.
- Endometrial rectal disease: disc excision if < 3 cm in size
- <u>Alosetron</u>: 5-hydroxytrypatmin-3 receptor antagonist used for diarrhea type IBS. Associated with ischemic colitis
- <u>Hycosamine</u>: antimuscarinic → antispasmodig agent → reduces in pain in patients w/ postprandial abd pain
- <u>Lupiprostone</u>: for constipation type IBS; locally acting chloride channel
- Chaga's Disease Megacolon:
 - Rx: Retrorectal pull through (majority need surgery)
 - Minority of pt's treated w/ laxatives & enemas
 - Duhamel-Haddad vs. Habr-Gama techniques to bypass rectum, since acts as fxnl obstruction
 - recurrence rates are high

Incidental Small Bowel Intussusception: no further work up needed if: transient, non-obstructing, Asympt., <3.5 cm

- <u>Neutropenic Colitis</u>: usually right sided, no clear cut standard. Right colectomy if operate, GSF, abx, fluids to start. Surgery *seems* to be better, but poor data.
- Microscopic Colitides:
 - Grossly normal on COY, but bx's show:
 Lymphocytic Colitis: >10 lymph per 100 epithelial cells.
 Collagenous Colitis: abn thick sub-epithelial band
 - Mgmt: Anti-diarrhea meds & diet changes
 - caffeine, alcohol, diary, NSAIDs, simvastatin, ticlopidine, carbamazepine, lansoprazole
 - 2nd line Rx: mesalamine, sulfalazine, cholestyramine
 - 3rd line Rx: Corticosteroids; 4th: 6-MP
 - Last line: operation
- <u>Peutz-Jeghers Syndrome</u>: perioral/<u>buccal</u> pigmentation w/ GI <u>hamartomatous</u> polyposis; autosomal dominant
 - hamartomas mostly small intestinal \rightarrow not cancerous, either cause bleeding or intussusception
 - risk of other malignancies increased: colon CA, gastric, pancreatic, breast, ovarian, testicular, cervical

Angiographic findings Angiectasia:early filling dilated submucosal veins during arterial phase w/ persistence as slow-emptying veins in the late phase

Dieulafoy's Lesion: rare rectal \rightarrow can cause massive bleed

- visibly protruding vessel typically w/o ulcer/erosion w/ surrounding normal mucosa

- Histo: solitary mucosal defect w/ erosion of an underlying large-caliber tortuous submucosal artery

- Rx: oversewing/suture ligation
- Imperforate Anus: Site for diversion descending colon/sigmoid colon w/ mucous fistula → colostogram
- Portal Vein Thrombosis s/p TPC w/ IPAA: needs anticoagulation only. If asymptomatic, probably doesn't need treatment - being evaluated.

Crohn's Disease:

- smoking independent RF of recurrence
- no correlation w/ younger age, gender, extra-GI sympt.
- Improve w/ Rsxn: erythema nodosum, oral apthous ulcers, episcleritis, some peripheral arthritis
- do NOT improve w/ Rsxn: pyoderma gangrenosum, uveitis, spondyloarthropathy, PSC
- Dysplasia-Associate Lesion or Mass (DALM): indication for surgery - TPC w/ IPAA vs. EI
 - When can observe: complete polypectomy of ALM, 4 separate bx specimens of surrounding mucosa normal, no dysplasia anywhere else in colon $\rightarrow 6$ month f/u COY and close surveillance (no dysplasia at all)
- How to image/work up Duodenal-Colonic Fistula: Enema study - upper GI low sensitivity due to itraluminal pressure in colon ↑ than in duo
- MC reason for surgery in CD of Duo: obstruction - MC op: GastroJejunostomy
- Pyoderma Gangrenosum: 1st step is punch bx of leading edge of lesion \rightarrow if histology confirms, then topical and systemic steroids for treatment
- <u>Pouchitis</u>: \uparrow pANCA levels $\rightarrow \uparrow$ Risk for chronic Pouchitis
 - Smoking is protective;
 - Rx: Cipro and/or flagyl
 - 2nd line: budenoside (when above failed)
 - Last resort: pouch excision
- Probiotics: once intial inflammation treated
- Permanent Stomas and Fluid Changes:
 - Serum electrolytes: remain normal
 - Stool Volume ↑'d and urine volume ↓'d
 - \downarrow urine sodium, \uparrow urine potassium
 - chronically \1'd mineralcorticoids \1 serum aldosterone
- Rx Pseudomyxoma Peritonei: open cecectomy, w/ heated intraoperative intraperitoneal chemotherapy, early post-operative intraperitoneal chemotherapy and cytoreductive surgery

Most reliable indicator or reaching cecum during COY:

- 1st: ICV, 2nd: AO, 3rd: Trans-illumination

SCIP Peri-op Measures:

- 1. Abx w/in 1 hour of incision & d/c'd w/in 24 hours
- Clipping instead of shaving
- normothermia > 36C/96.8F
- cont. beta blockade if on it at home
- DVT prophylaxis before and after surgery
- Clinical Equipoise: uncertainty as to whether the treatment being tested will be beneficial.

Beneficience: researcher's oblication to protect human research subjects from harm while maximizing benefit

- Statistical Tests:
 - Analysis of Covariance (ANCOVA): evaluation of normally distributed variables with adjustment for risk factors
 - Fischer Exact Test: evaluation of binary (dichotomous) data
 - Logistic Regression: evaluating dichotomous data with adjustment of risk factors
 - Log-Rank Test: time to event analysis
 - t-Test: evaluation of continuous data w/ no adjustment for risk factors
 - Mann-Whitney test: used for evaluating ordered discrete data sets
- Absolute Risk Reduction (ARR): proportion in the control group w/ event minus proportion in intervention group w/ event
- Relative Risk Reduction (CRR): ARR ÷ proportion in control group w/ event

Number Needed to Treat (NNT): 1 ÷ ARR

Type of error:

Type I: rejecting null hypothesis when it is true Type II: accepting null hypothesis when it is false

Phases of trials for drug testing:

- Phase I: test in a small group to eval for safety Phase II: test in a larger group to eval for safety Phase III: larger group to confirm effectiveness, monitor side effects and compare to the standard treatment
- Phase IV: post-marketing studies to evaluate risks, benefits, and optimal use of the drug/treatment
- Best test when can't complete COY: CT (virtual) COY - more sensitive than the other options
- Endoscopic Optical Coherence Tomography (OCT): imaging method for evaluating IBD. Very low depth of penetration \rightarrow not effective for GISTs, CAs, etc

COY Narrow Band Imaging light: blue

- Botox for anal fissure:
 - decreases mean resting pressure
 - also decreased squeeze pressure
 - high rate of recurrence

Anti-tumor necrosis factor (TNF) Antibodies:

Adalimumab: fully human monoclonal antibody to TNF Natalizumab: humanized IgG4 monoclonal antibody to

alpha4-integrin \rightarrow blocks adhesion & migration of leukocytes to the <u>gut</u>

Infliximab: chimeric antibody w/ murine sequences

Certolizumab-pegol: humanized Fab fragment linked to polyethylene glycol