Colorectal Cancer

Michael Libes, MD
Senior Physician, Carmel Medical Center, Haifa

Top 10 Cancer Types and Colorectal Statistics in the US

- The third most common cancer in men and women
- The number of deaths has ⇓ over the last 15 years due to better screening, earlier detection of polyps and cancer, improved treatment, and more effective options
- Currently ~1 million survivors in US
- 5-yr survival rate with early detection >90% (occurs in ~39% cases)
- If cancer metastasized 5-yr survival rate, <10%

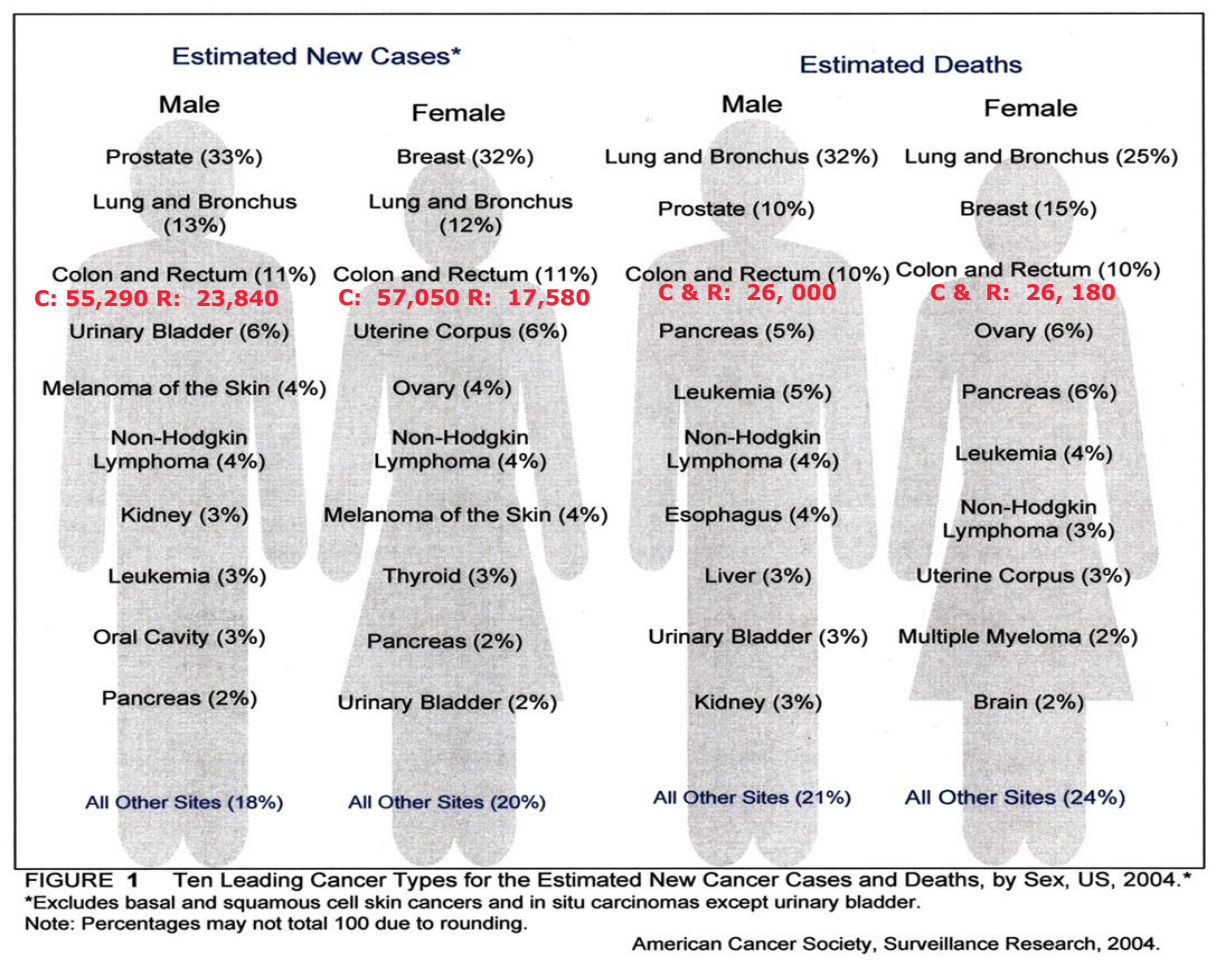
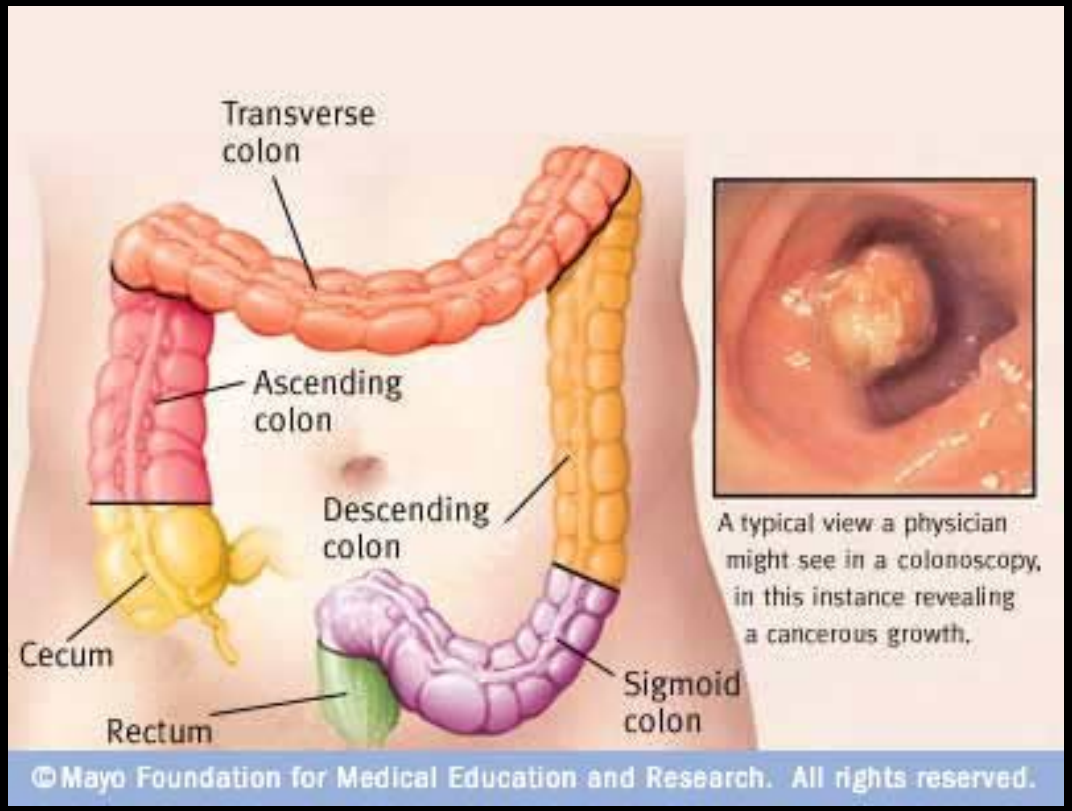


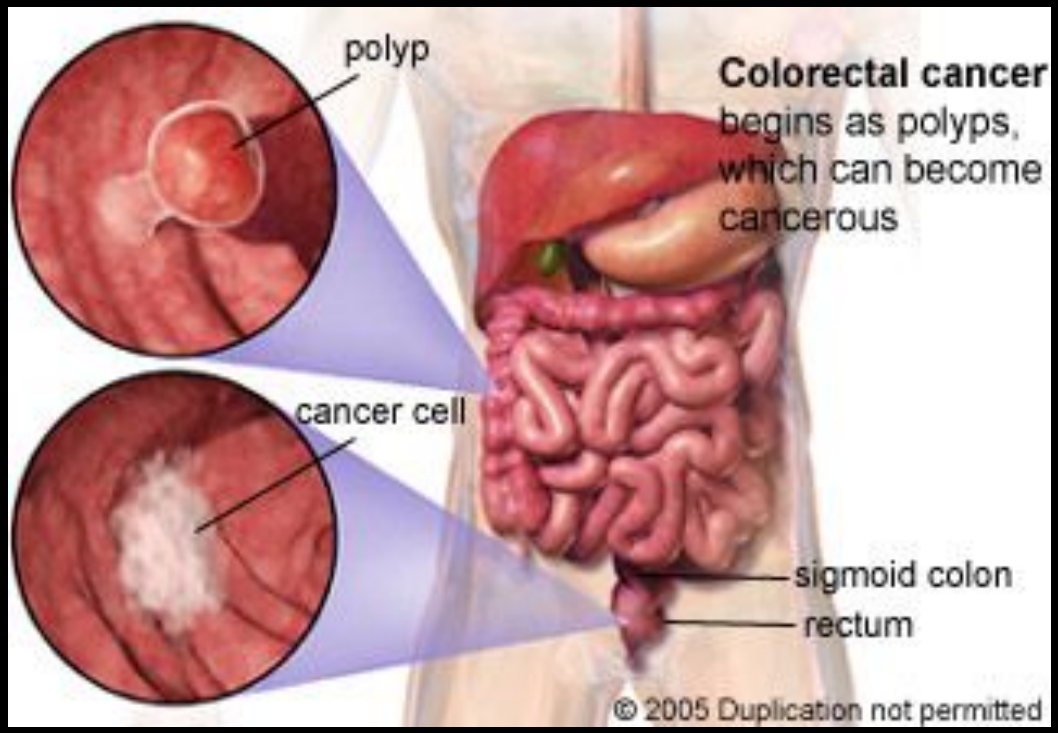
FIGURE 1 Ten Leading Cancer Types for the Estimated New Cancer Cases and Deaths, by Sex, US, 2004.*
*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.
Note: Percentages may not total 100 due to rounding.
American Cancer Society, Surveillance Research, 2004.

Anatomy of the Colon and Rectum



- The colon has four sections: ascending, transverse, descending, and sigmoid colon
- The colon absorbs water and nutrients from food and serves as a storage for waste.

Colorectal Cancer Development



- Colorectal cancer refers to cancer originating in the colon or rectum and can develop in any of the four sections
- Colorectal cancer develops slowly over a period of years (~10-15 yrs)
- Colorectal cancer begins as a polyp.

Staging of CRC

TNM system

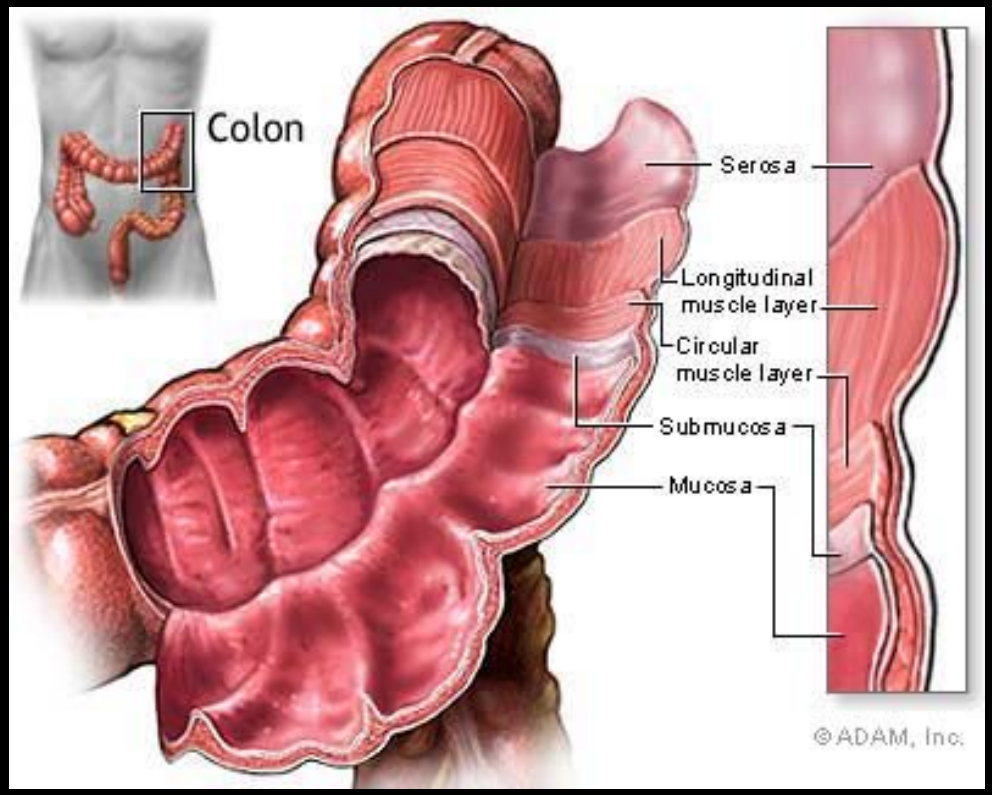
Primary tumor (T)

Regional lymph nodes (N)

Distant metastasis (M)

T Staging-American Joint Committee on Cancer system (AJCC/TNM)

- **T Categories:** Describes the extent of spread of the primary tumor (T) through the layers of tissue that form the wall of the colon and rectum
  - **Tis:** Cancer is in its earliest stage, has not grown beyond mucosa. Also known as carcinoma in situ or intramucosal carcinoma
  - **T1:** Cancer has grown through mucosa and extends into submucosa
  - **T2:** Cancer extends into thick muscle layer
  - **T3:** Cancer has spread to subserosa but not to any nearby organs or tissues
  - **T4:** Cancer has spread completely through wall of the colon or rectum into nearby tissues or organs

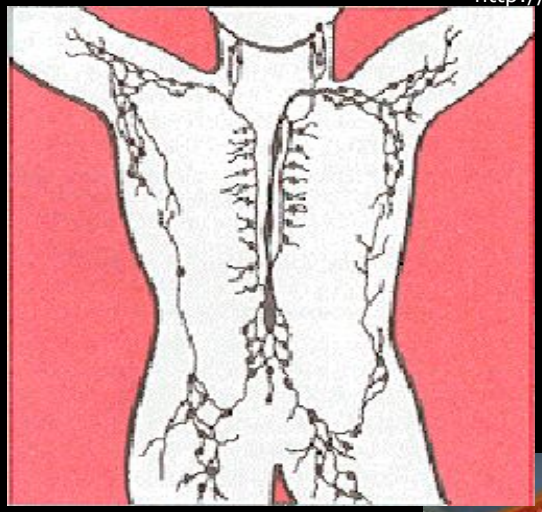


http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/19218.jpg

N and M Staging-American Joint Committee on Cancer system (AJCC/TNM)

- **N categories:** describes the absence or presence of metastasis to nearby lymph nodes (N)
  - **N0:** No lymph node involvement
  - **N1:** Cancer cells found in 1-3 regional lymph nodes
  - **N2:** Cancer cells found in 4 or more regional lymph nodes

http://www.ricancercouncil.org/img/hodgkins.gif



Lymph nodes are small, bean shaped structures that form and store white blood cells to fight infection

- **M Categories:** describes the absence or presence of distant metastasis (M)
  - **M0:** No distant spread
  - **M1:** Distant spread is present

An iceball in a patient with a metastases from a colon cancer receiving cryosurgery treatment

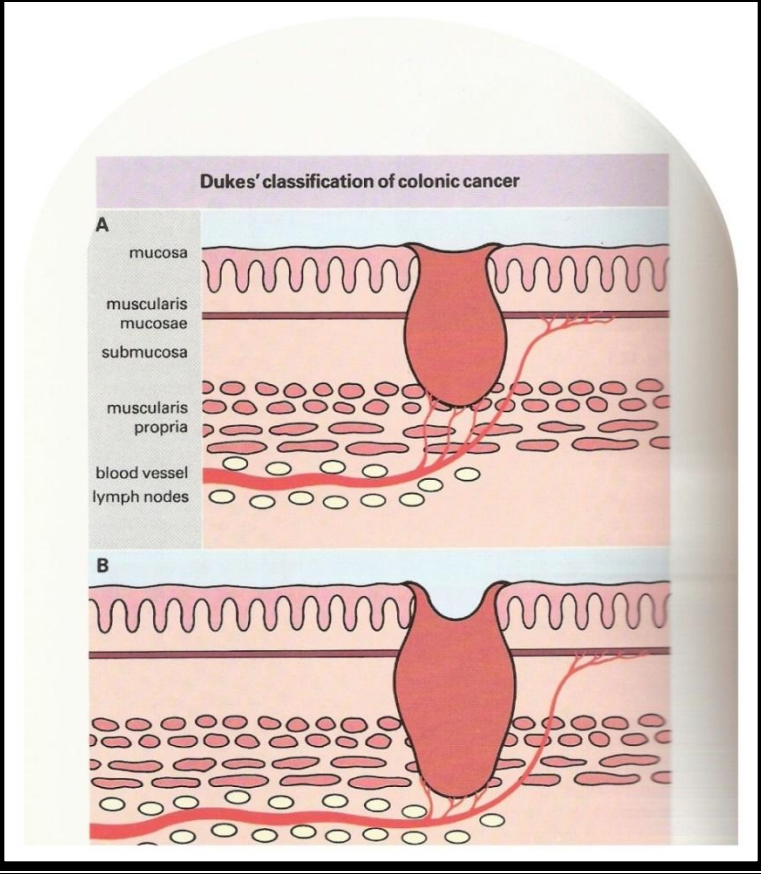
http://www.livercancer.com/treatments/images/cryo.jpeg

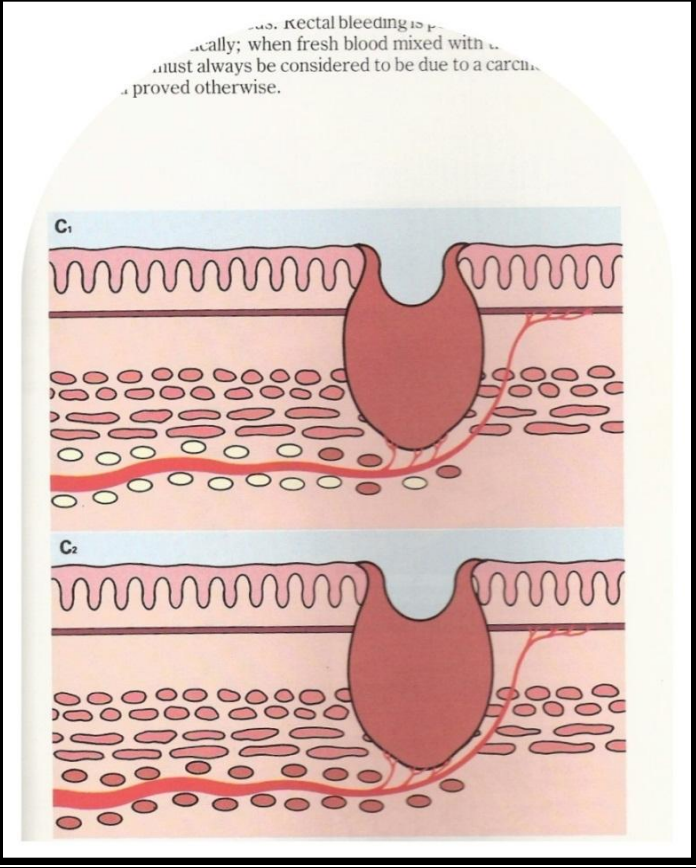
Staging-American Joint Committee on Cancer system (AJCC/TNM)

- **Staging is an indicator of survival**
- **Stage grouping:** From least advanced (stage 0) to most advanced (stage IV) stage of colorectal cancer

Stage	TNM Category	Survival Rate	
Stage 0:	Tis, N0, M0		The earliest stage. Has not grown beyond inner layer (mucosa) of colon or rectum.
Stage I:	T1, N0, M0 T2, N0, M0	93%	Has grown into submucosa (T1) or muscularis propria (T2)
Stage IIA: Stage IIB:	T3, N0, M0 T4, N0, M0	85% 72%	**IIA:** Has spread into subserosa (T3). **IIB:** Has grown into other nearby tissues or organs (T4).
Stage IIIA: Stage IIIB: Stage IIIC:	T1-T2, N1, M0 T3-T4, N1, M0 Any T, N2, M0	83% 64% 44%	**IIIA:** Has grown into submucosa (T1) or into muscularis propria (T2) and has spread to 1-3 nearby lymph nodes (N1) **IIIB:** Has spread into subserosa (T3) or into nearby tissues or organs (T4), and has spread to 1-3 nearby lymph nodes (N1) **IIIC:** Any stage of T, but has spread to 4 or more nearby lymph nodes (N2).
Stage IV:	Any T, Any N, M1	8%	Any T or N, and has spread to distant sites such as liver, lung, peritoneum (membrane lining abdominal cavity), or ovaries (M1).

Staging of colorectal cancer





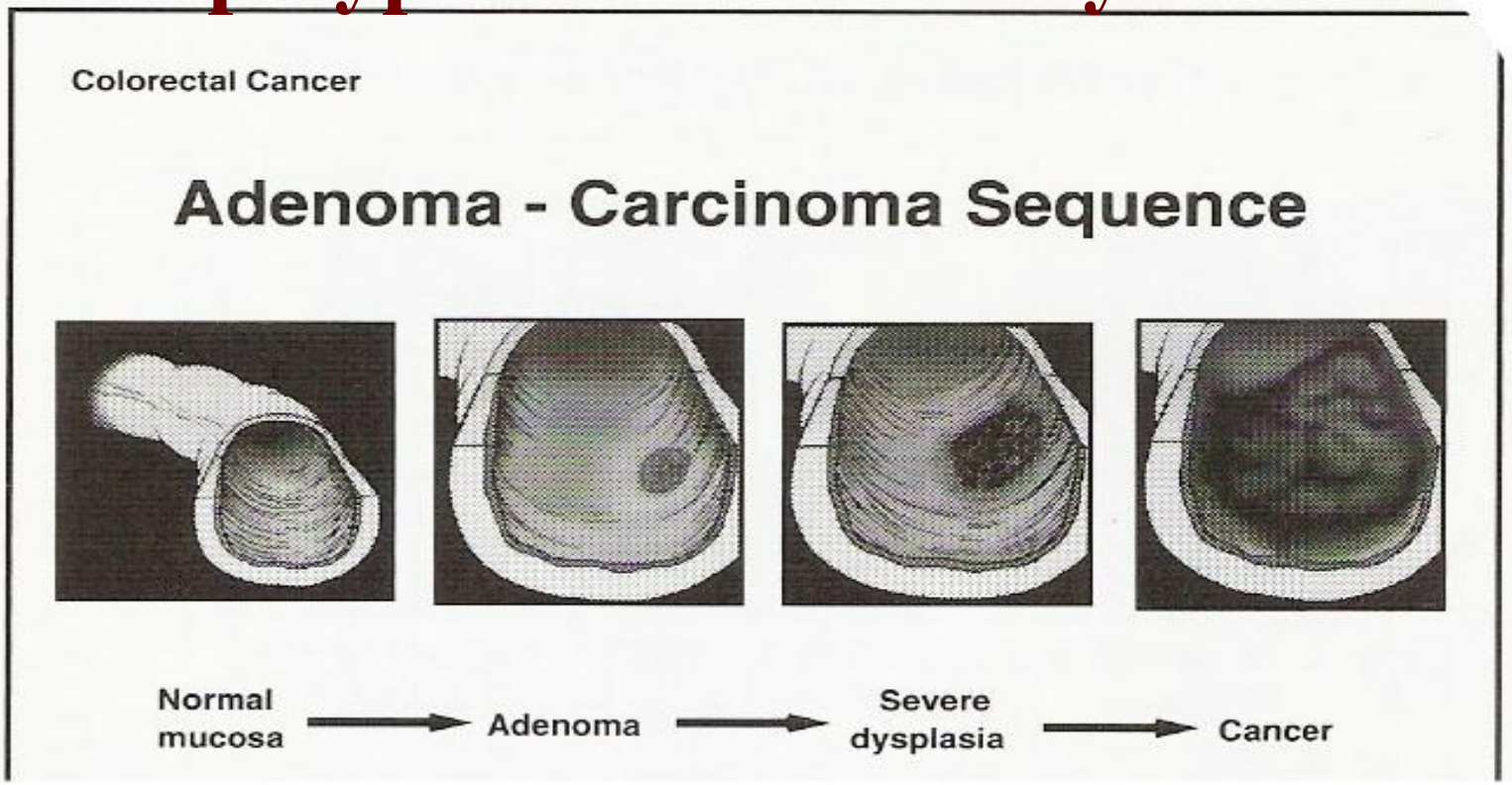
Staging of colorectal cancer

Table 3. Colorectal cancer staging[15]

Dukes' stage (modified)	Definition	Approximate frequency at diagnosis	5-year survival
A	Cancer localised within the bowel wall	11%	83%
B	Cancer penetrating the bowel wall	35%	64%
C	Cancer in lymph nodes	26%	38%
D	Distant metastases (most often in the liver)	29%	3%

[15] Frequency and survival statistics based on data from 777 patients derived from St Vincent's Hospital colorectal cancer database, Dublin. (Mulcahy, 1997, personal communication.) Note that stage frequency and survival figures vary widely between published series from different centres.

90 % cancers arise from polyps
polyp – cancer 8 – 10 yrs



Symptoms of Colorectal Cancer

- Early colon cancer usually presents with no symptoms. Symptoms appear with more advanced disease.
- Symptoms include:

  -a change in bowel habits (diarrhea, constipation, or narrowing of the stool for more than a few days)

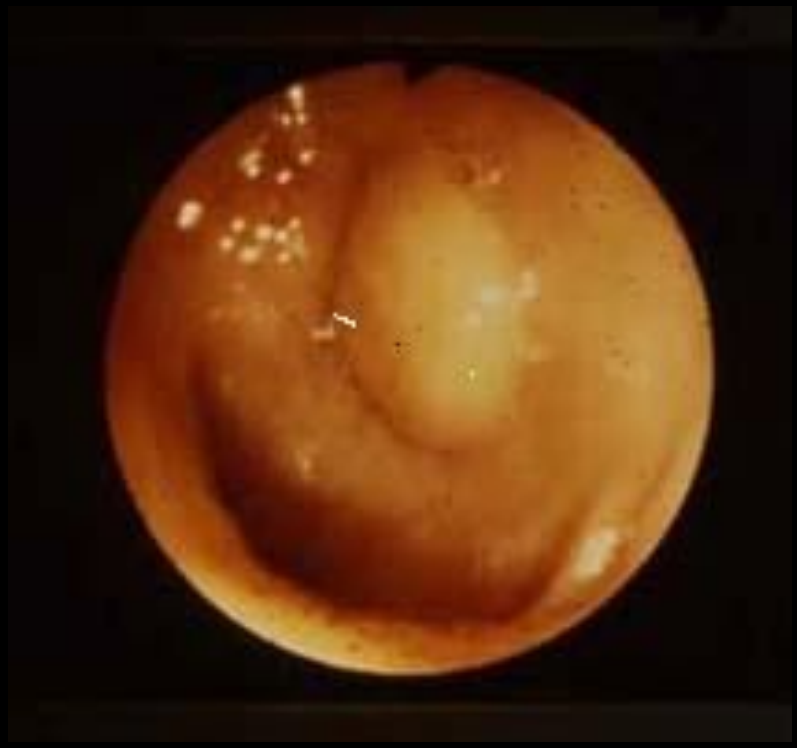
  -a constant urgency of needing to have a bowel movement

  -bleeding from the rectum or blood in the stool (the stool often looks normal)

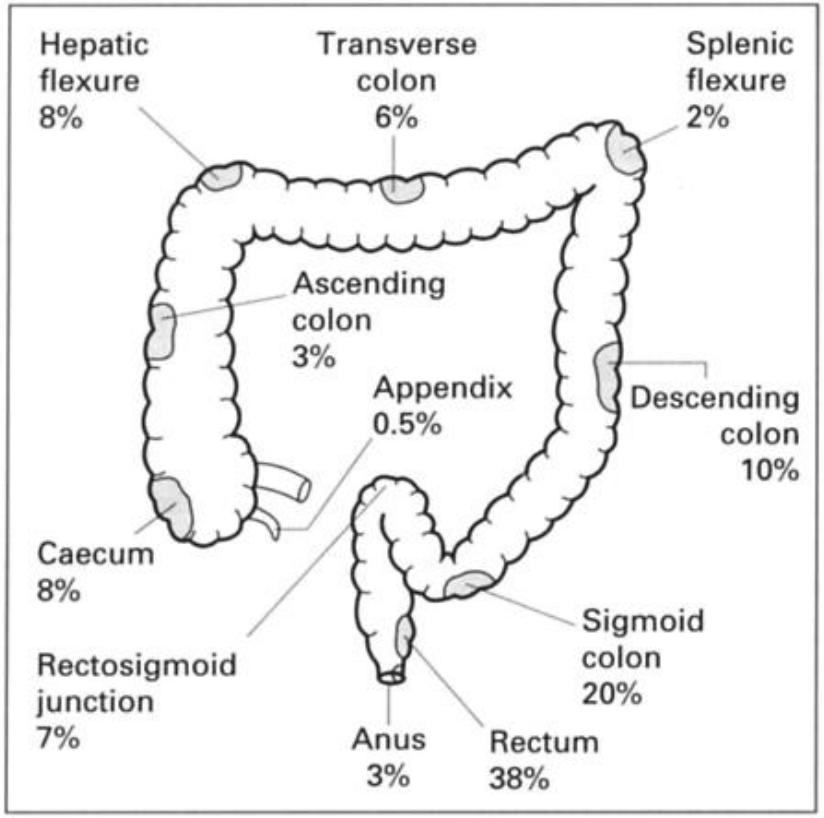
  -cramping or steady stomach pain

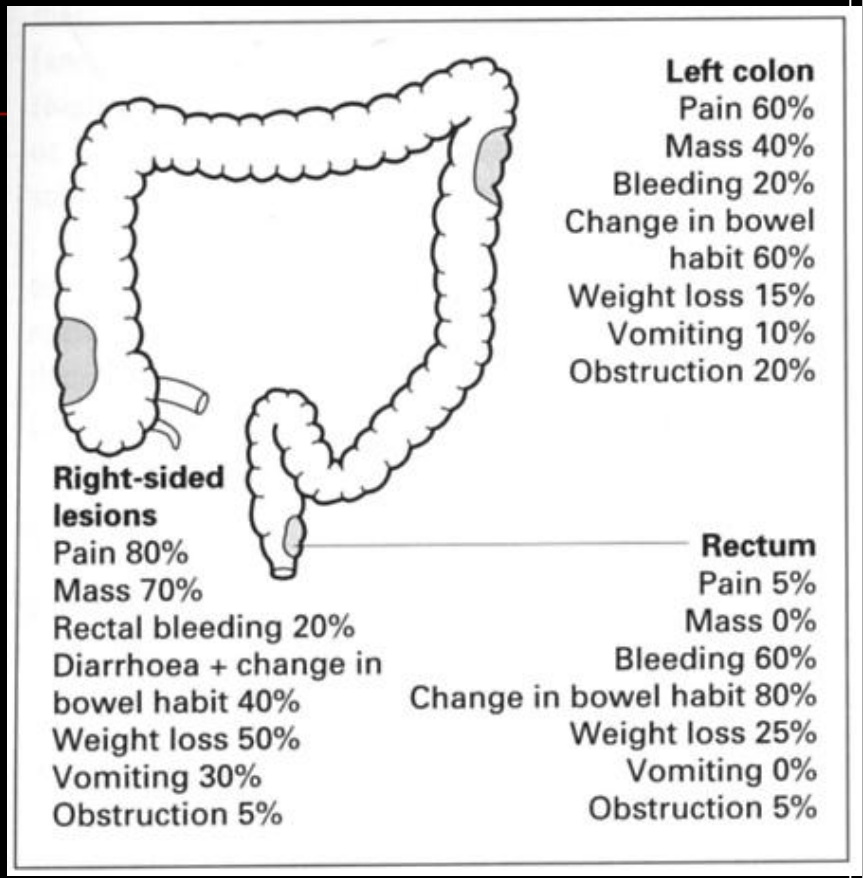
  -weakness and fatigue or anemia

  -unexplained weight loss



A polyp as seen during colonoscopy


Hepatic flexure 8%
Transverse colon 6%
Splenic flexure 2%
Ascending colon 3%
Appendix 0.5%
Descending colon 10%
Caecum 8%
Rectosigmoid junction 7%
Sigmoid colon 20%
Anus 3%
Rectum 38%


Left colon
Pain 60%
Mass 40%
Bleeding 20%
Change in bowel habit 60%
Weight loss 15%
Vomiting 10%
Obstruction 20%
Right-sided lesions
Pain 80%
Mass 70%
Rectal bleeding 20%
Diarrhoea + change in bowel habit 40%
Weight loss 50%
Vomiting 30%
Obstruction 5%
Rectum
Pain 5%
Mass 0%
Bleeding 60%
Change in bowel habit 80%
Weight loss 25%
Vomiting 0%
Obstruction 5%

Sites of metastasis

Via blood	Via lymphatics	Per continuitatem
Liver	Lymph nodes	Abdominal wall
Lung		Nerves
Brain		Vessels
Bones		

Risk Factors

Risk Factor	Description
Age	9 out of 10 cases are over 50 years old
History of polyps	⇑ risk if large size, high frequency, or specific types
History of bowel disease	Ulcerative colitis and Crohn's disease (IBDs) ⇑ risk
Certain hereditary family syndromes	Having a family history of familial adenomatous polyposis or hereditary nonpolyposis colon cancer (Lynch Syndrome) ⇑ risk
Family history (excluding syndromes)	Close relatives with colon cancer ⇑ risk esp. if before 60 years (degree of relatedness and # of affected relatives is important)
Other cancers and their treatments	Testicular cancer survivors ⇑ risk
Race	African Americans are at ⇑ risk
Ethnic background	Ashkenazi Jew descent ⇑ risk due to specific genetic factors

Risk Factors (cont'd)

Risk Factor	Description
Diet	High in fat, especially animal fat, red meats and processed meats ⇑ risk
Lack of exercise	⇑ risk
Overweight	⇑ risk of incidence and death
Smoking	-⇑ risk of incidence and death -30-40% more likely to die of colorectal cancer
Alcohol	Heavy use of alcohol ⇑ risk
Diabetes	30% ⇑ risk of incidence and ⇑ death rate
Night shift work	More research is needed but over time may ⇑ risk

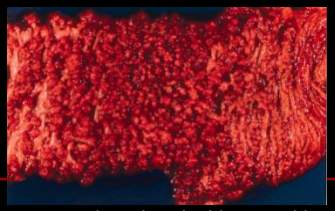
Risk factors – Hereditary Family Syndromes

- **The development of colorectal cancer is a multi-step process involving genetic mutations in the mucosal cells, activation of tumor promoting genes, and the loss of genes that suppress tumor formation**

- ***Tumor suppressor genes*** constitute the most important class of genes responsible for hereditary cancer syndromes
  --Familial Adenomatous Polyposis (FAP): A syndrome attributed to a tumor suppressor gene called Adenomatous Polyposis Coli (APC)
  -- Increased risk of colon and intestinal cancers

- ***Tumor suppressor genes*** are normal genes that slow down cell division, repair DNA mistakes, and promote apoptosis (programmed cell death). Defects in tumor suppressor genes cause cells to grow out of control which can then lead to cancer

Familial Adenomatous Polyposis (FAP)



http://www.nature.com/modpathol/journal/v16/n4/images/3880773f1.jpg

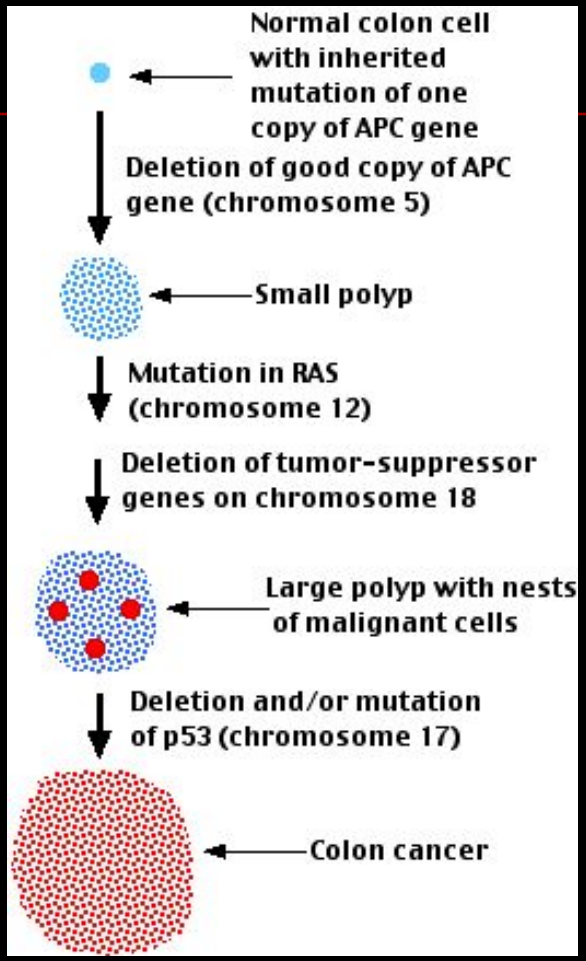
- **FAP:**
  - Multiple colonic polyps
  - Patients with an APC mutation have a 100% lifetime risk of colorectal cancer if patient fails to undergo total colectomy
  - Adenomas (>100) occur in: colorectum, small bowel & stomach
  - Cancer onset ~39 years
  - Screening recommendations:

  - DNA testing for APC gene mutation

  -Annual colonoscopy starting 10-12 yrs old until 15-20 yrs

  -Upper endoscopy (scope through mouth to examine the esophagus, stomach and the first part of the small intestine, the duodenum). Frequency of 1-3/year when colonic polyps are detected

  -Older than 20 years annual upper endoscopy and colonoscopy needed



http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/C/ColonCancer.png

Juvenile Polyposis Syndrome (JP)

- **Juvenile Polyposis:**

-occurs in children with sporadic juvenile polyps (benign and isolated, occasionally are multiple lesions)

-Criteria for JP:

1. ≥5 hamartomatous (disordered, overgrowth of tissue) polyps in colorectum
2. Any hamartomatous polyps in the colorectum in a patient with a positive family history of JP
3. Any hamartomatous polyps in the stomach or small intestine

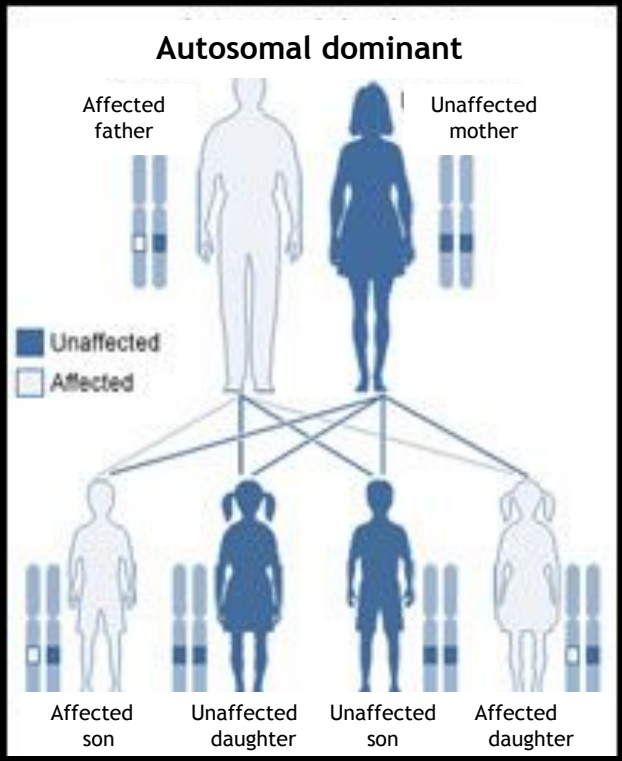
-JP occurs in 1:15,000-1:50,000 individuals whereas sporadic juvenile polyps occurs in ~2% of children

http://www.altcancer.com/images/polyposis.jpg

Lynch Syndrome (also known as HNPCC)

- **Lynch syndrome:**
- Also known as hereditary nonpolyposis colorectal cancer (HNPCC)
- A rare inherited condition that increases risk of colon cancer and other cancers
- 2-3% colon cancers attributed to Lynch Syndrome
- Increase risk for malignancy of: endometrial carcinoma (60%), ovary (15%), stomach, small bowel, hepatobiliary tract, pancreas, upper uro-epithelial tract, and brain
- Caused by autosomal dominant inheritance pattern (if one parent carries a gene mutation for Lynch syndrome, then 50% chance mutation passed to child)
- Cancer occurs at younger age <45 years
- Accelerated carcinogenesis: a small adenoma may develop into a carcinoma with in 2-3 yrs as opposed to ~10 yrs in general population
- Screening:

  -Colonoscopy every other year starting in 20s, and every year once reach 30s
- Education and genetic counseling recommended at 21 years



http://media.npr.org/programs/atc/features/2006/dec/pgd/dom200.jpg

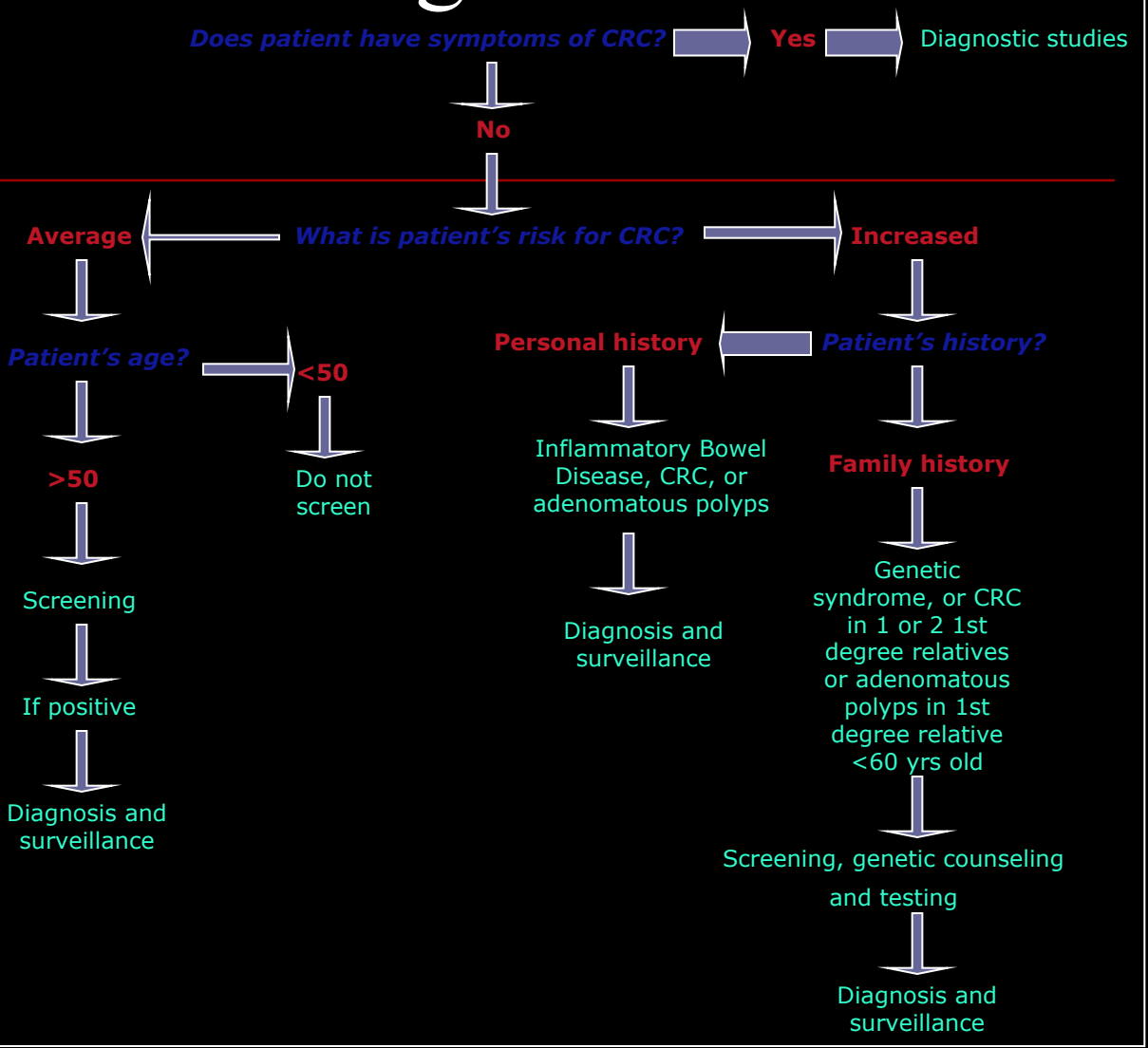
Factors that may reduce risk

Method	Description
Screening	Regular screening can prevent colon cancer completely (it usually takes 10-15 years from the time of the first abnormal cells until cancer develops). Screening can detect polyps and remove before cancerous, or early detection with a better prognosis.
Diet and Exercise	Fruits, vegetables, whole grains, minimal high-fat foods and 30-60 minutes of exercise 5 times per week help ⇓ risk
Vitamins, calcium w/D, magnesium	Aid in ⇓ risk
NSAIDs (Non-steroidal anti-inflammatory drugs)	20-50% ⇓ risk of colorectal cancer and adenomatous polyps; however, NSAIDs can cause serious or life threatening implications on the GI tract and other organs
Female Hormones	HRT (hormone replacement therapy) may ⇓ risk esp. amongst long term users, but if cancer develops, it may be more aggressive. HRT ⇓ risk of osteoporosis, but may ⇑ risk heart disease, blood clots, breast and uterine cancers

Screening

- **Medical History and Physical Exam:**

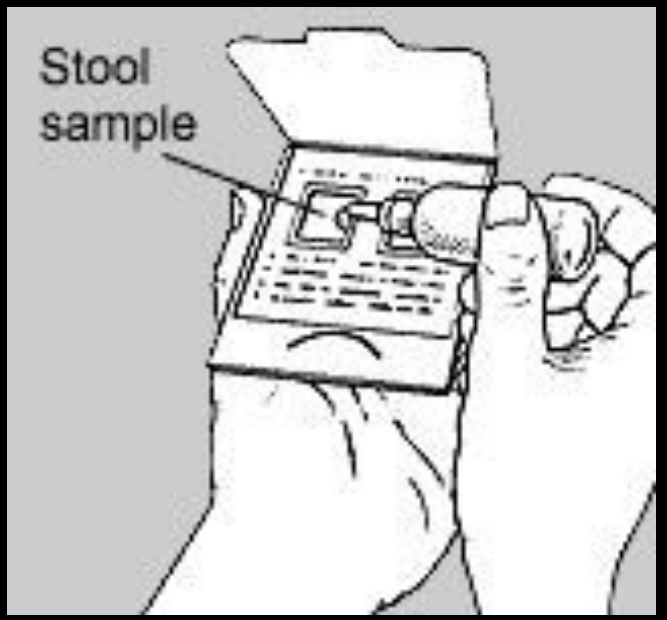
A history (symptoms and risk factors) and DRE (digital rectal exam) is performed for patients thought to have colon cancer. An abdominal exam is performed to feel for masses or enlarged organs.



Screening Options: Fecal Occult Blood Test

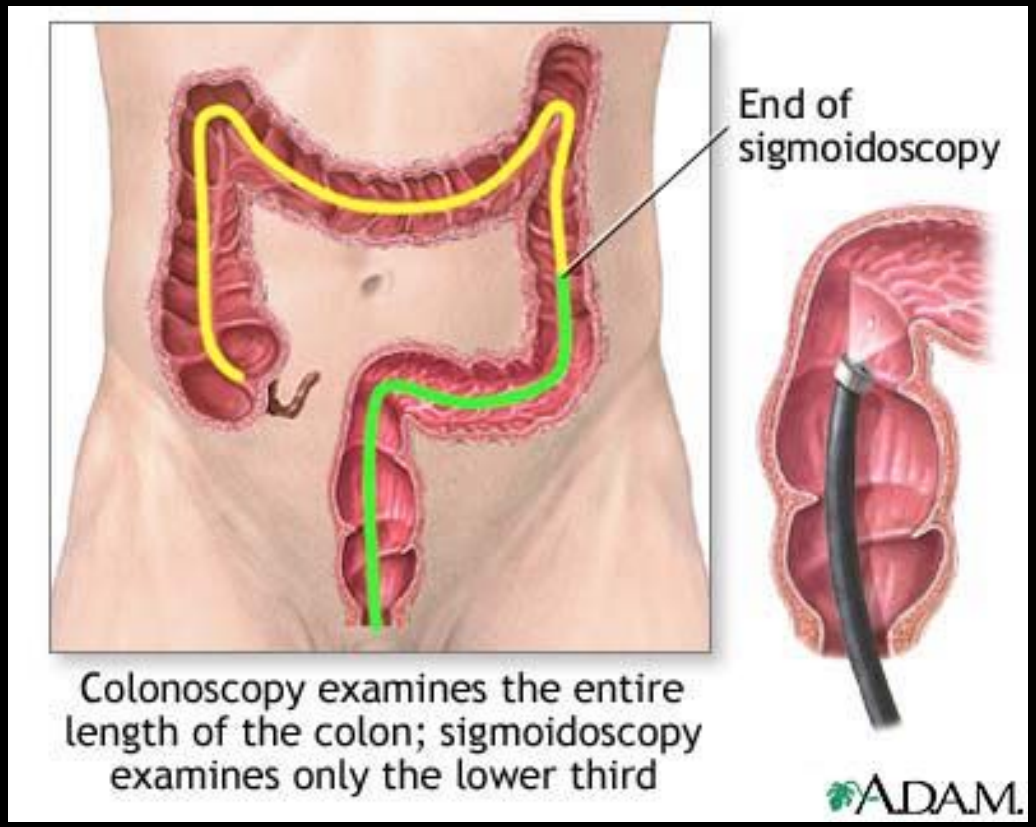
- **Stool Blood Test (FOBT or FIT):** Used to find small amounts of blood in the stool. If found further testing should be done.

http://www.owenmed.com/hemoccult.jpg



http://digestive.niddk.nih.gov/ddiseases/pubs/dictionary/pages/images/fobt.gif

Screening: Flexible Sigmoidoscopy



http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/1083.jpg

- **Flexible Sigmoidoscopy:** A sigmoidoscope, a slender, lighted tube the thickness of a finger, is placed into lower part of colon through rectum
- It allows physician to look at inside of rectum and lower third of colon for cancer or polyps
- Is uncomfortable but not painful. Preparation consists of an enema to clean out lower colon
- If small polyp found then will be removed. If adenoma polyp or cancer found, then colonoscopy will be done to look at the entire colon

Screening: Barium Enema

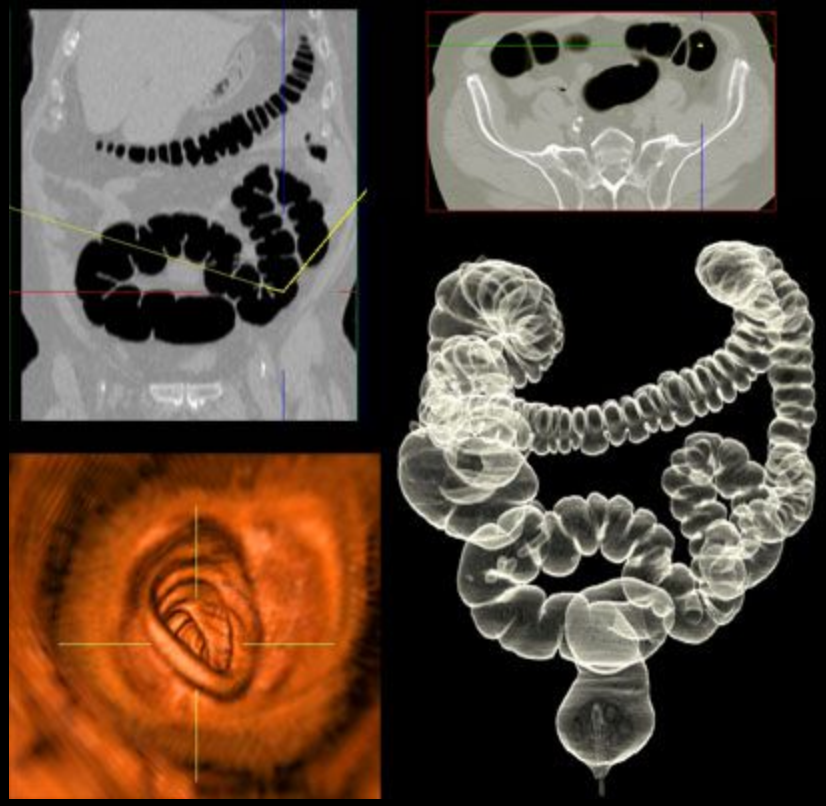
http://www.acponline.org/graphics/observer/may2006/special_lg.jpg

- **Barium enema with air contrast:** A chalky substance is used to partially fill and open up the colon
- Air is then pumped in which causes the colon to expand and allows clear x-rays to be taken
- If an area looks abnormal then a colonoscopy will be done
- Now is practically not used

A cancer of the ascending colon. Tumor appears as oval shadow at left over right pelvic bone

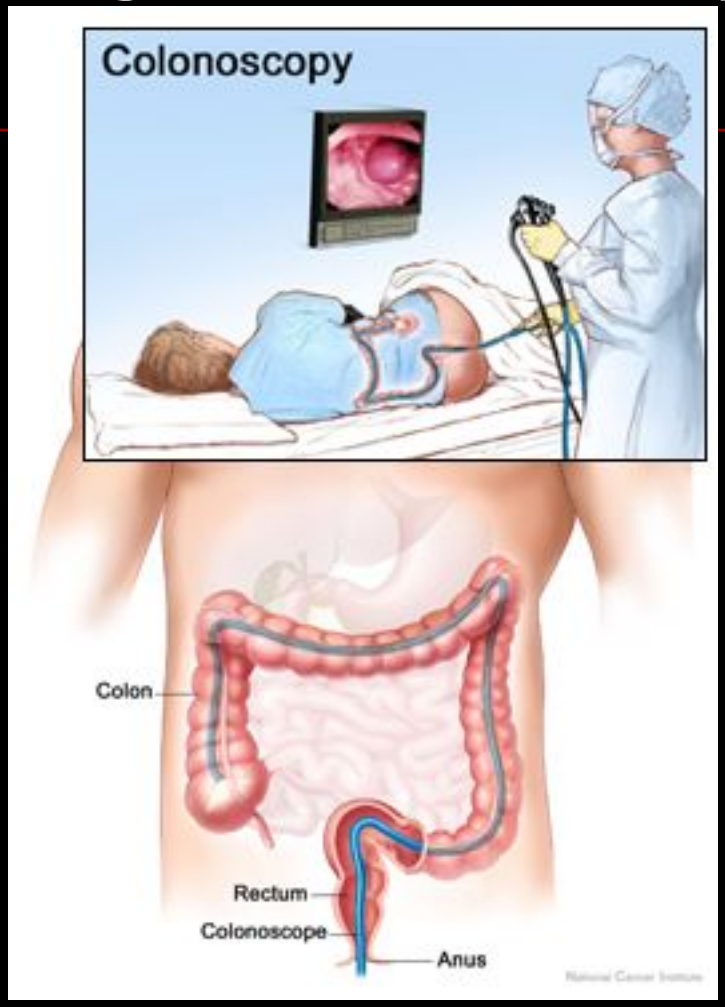
Screening: Virtual Colonoscopy

- **Virtual Colonoscopy:** Air is pumped into the colon in order for it to expand followed by a CT scan which takes hundreds of images of the lower abdomen
- Bowel prep is needed but procedure is completely non-invasive and no sedation is needed
- Is not recommended by ACS or other medical organizations for early detection. More studies need to be done to determine its effectiveness in regard to early detection
- Is not recommended if you have a history of colorectal cancer, Chron's disease, or ulcerative colitis
- If abnormalities found then follow-up with colonoscopy



Screening: Colonoscopy

- **Colonoscopy:** A colonoscope, a long, flexible, lighted tube about the thickness of a finger, is inserted through the rectum up into the colon
- Allows physician to see the entire colon
- Bowel prep of strong laxatives to clean out colon, and the day of the procedure an enema will be given
- Procedure lasts ~15-30 minutes and are under mild sedation
- Early cancers can be removed by colonoscope during colonoscopy



http://www.cadth.ca/media/healthupdate/Issue6/hta_update_mr-colonograpy2.jpg

Screening Guidelines, Advantages, and Disadvantages

Screening	Guidelines	Advantages	Disadvantages
Fecal Occult Blood Test (FOBT)	Annually starting at age 50	-Cost effective -Noninvasive -Can be done at home	-False-positive/false-negative results -Dietary restrictions -Duration of testing period
Flexible Sigmoidoscopy (FS)+FOBT	Every 5 years starting at age 50	-Cost effective -Can be done w/o sedation -Performed in clinic -Any polyps can be biopsied	-Examines only portion of colon (additional screening may be done) -Discomfort for patient -Bowel cleansing
*** Colonoscopy (preferred method b/c polyps can be biopsied and removed)**	Every 10 yrs starting at age 50	-Patient sedated -Outpatient screening -Views entire colon and rectum -Polyps can be removed and biopsied	-Bowel cleansing -Sedation may be a problem for some -Cost if uninsured -Risk of perforation
Virtual Colonoscopy (a.k.a. computed tomography colonography-CT)	Every 10 yrs starting at age 50	-Relatively noninvasive -No sedation needed -Can show 2- or 3-D imagery	-Small polyps may go undetected -Bowel cleansing -Cost -If polyps found, colonoscopy required -Exposure to radiation -Patient discomfort

***American Cancer Society Recommendation**

Therapy

Surgical resection the only curative treatment

Likelihood of cure is greater when disease is detected at early stage

Early detection and screening is of pivotal importance