

Clinical Colon Cancer 2008

Abby Siegel MD

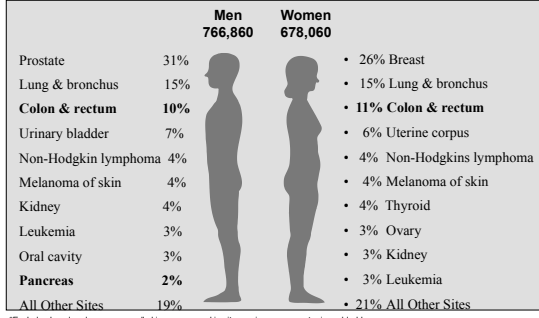
COLON CANCER

1. Epidemiology
2. Risk factors
3. Manifestations
4. Treatment

1. EPIDEMIOLOGY

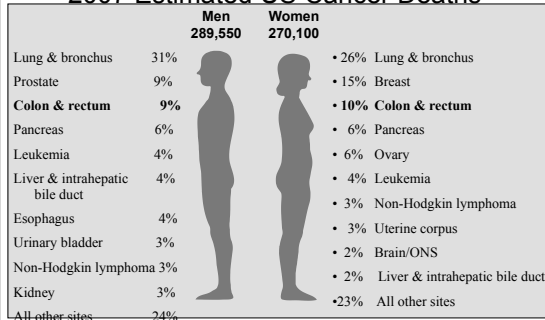
- Colorectal cancer is the third most common cancer in the United States
- About 150,000 new cases/year
- Most cases in people over 50

2007 Estimated US Cancer Cases*



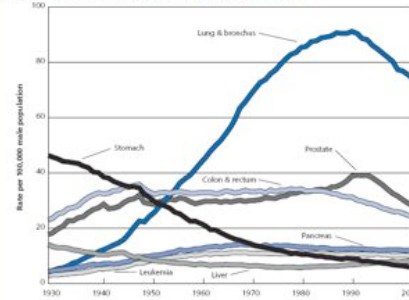
*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder. Source: American Cancer Society, 2007.

2007 Estimated US Cancer Deaths*

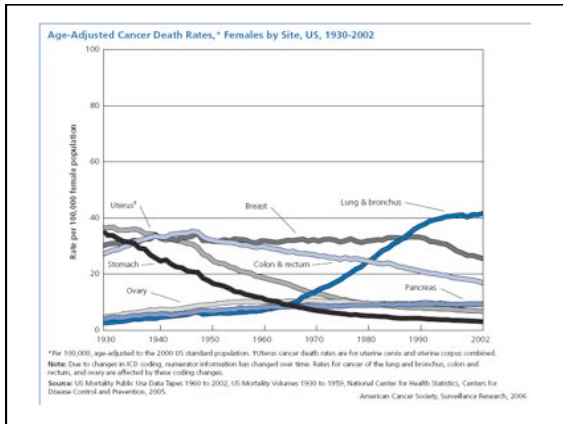


ONS=Other Nervous System. Source: American Cancer Society, 2007.

Age-Adjusted Cancer Death Rates, * Males by Site, US, 1930-2002



*Age 150,000, age-adjusted to the 2000 US standard population. Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these coding changes. Source: US Mortality Public Use Data Files 1990 to 2002, US mortality returns 1930 to 1959. National Center for Health Statistics, Centers for Disease Control and Prevention, 2005. American Cancer Society, Surveillance Research, 2006.



EPIDEMIOLOGY

- Incidence rates high in U.S., Europe, Australia
- Increasing in Japan
- Low in China, Africa

EPIDEMIOLOGY

- Changes in incidence rates over time and with migration may indicate role of environmental factors

2. RISK FACTORS:
Protective

- Folic acid
- Exercise
- NSAIDS
- ? Calcium/Vitamin D
- ? Fiber

NSAIDS

- 1) Cox-1 and Cox-2 inhibition
 - Aspirin, Ibuprofen
 - Bleeding risk
- 2) Selective Cox-2 inhibition
 - Rofecoxib (Vioxx),
 - Celecoxib (Celebrex)
 - Thrombosis risk

RISK FACTORS:
Increased risk with...

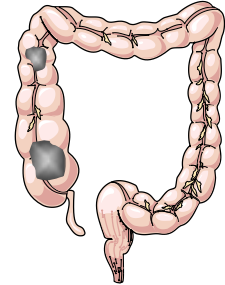
- Advanced age
- Inflammatory bowel disease
- Consumption of high-fat diet and red meat
- Personal or family history of colon cancer

FAMILIAL SYNDROMES

- HNPCC
 - Hereditary non-polyposis colon cancer
- APC
 - Adenomatous polyposis coli
- Both usually autosomal dominant

HNPCC (Lynch Syndrome) Hereditary Non-Polyposis Colon Cancer

- 2-5% of colon cancers
- Caused by mutations in mismatch repair genes
- Tend to present in the right colon
- Often associated with endometrial cancer in women
- Start screening at age 21



HNPCC Increases the Risk of Colorectal Cancer

By age 50 By age 70



	By age 50	By age 70
Population Risk	0.2%	2%
HNPCC Risk	>25%	80%

*Gastroenterology 1996;110:1020-7
Int J Cancer 1999;81:214-8*

HNPCC Increases the Risk of Endometrial Cancer

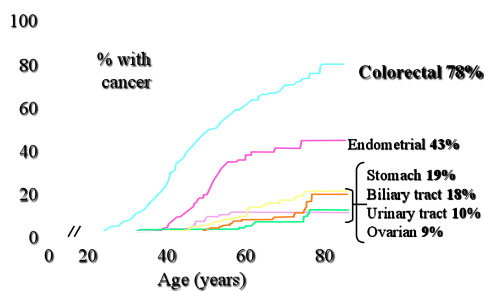
By age 50 By age 70



	By age 50	By age 70
Population Risk	0.2%	1.5%
HNPCC Risk	20%	60%

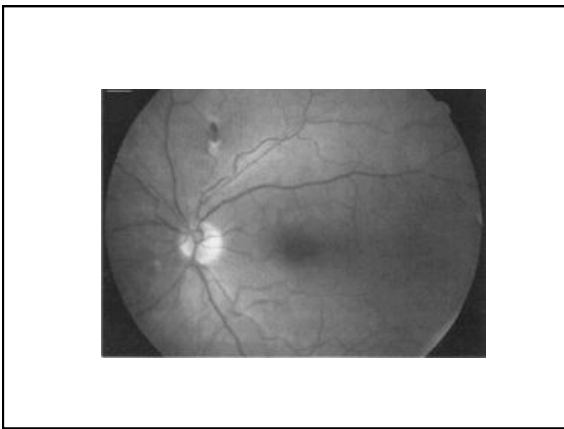
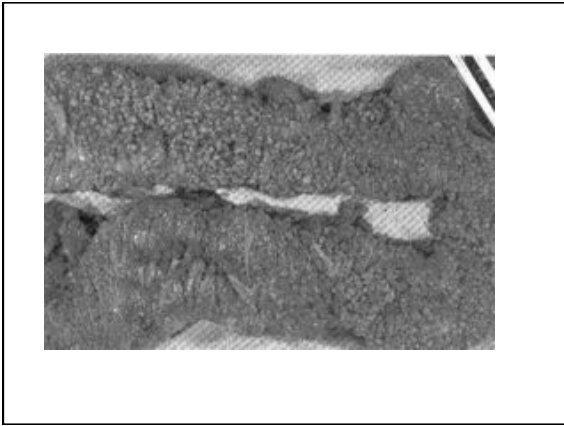
*Gastroenterology 1996;110:1020-7
Int J Cancer 1999;81:214-8*

HNPCC: Cancer Risks



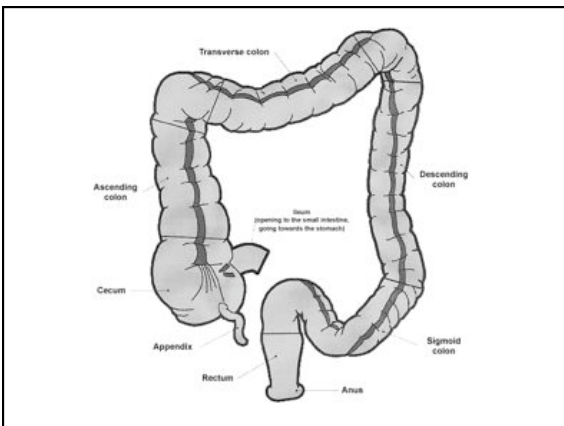
APC Adenomatous Polyposis Coli

- Less than 1% of colon cancers
- Caused by mutation of APC gene (5q21)
- Also associated with duodenal cancers, desmoid tumors, “CHRPE” (congenital hypertrophy of the retinal pigment)
- Start screening at puberty



3. MANIFESTATIONS

1. Growth of cancer at primary site
2. Metastatic spread



MANIFESTATIONS

1. Growth of cancer at primary site
 - a. Asymptomatic/screening
 - b. Right sided syndrome
 - c. Left sided syndrome

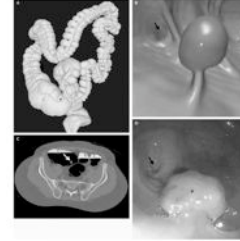
MANIFESTATIONS

1. Growth of cancer at primary site

i. Asymptomatic

- Detected by screening test
 - Fecal occult blood
 - Sigmoidoscopy
 - Colonoscopy
 - "Virtual" colonoscopy
 - Molecular techniques

Virtual Colonoscopy



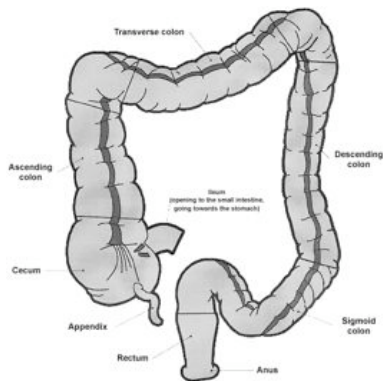
Robb et al. NEJM 359(21):2102-2109

Screening summary

- Average risk: colonoscopy every 10 years over age 50
- Family history: colonoscopy 10 years before index case
- Dysplastic polyps: repeat colonoscopy after 3 years

Screening, continued...

- APC: annual flexible sigmoidoscopy starting at age 11, colectomy when polyps develop
- HNPCC: colonoscopy at age 21, then every 1-2 years
- Inflammatory bowel disease: start 8 years after pancolitis, 12 years after distal disease



MANIFESTATIONS

1. Growth of cancer at primary site

ii. Right sided syndrome

- a) Ascending colon has thin wall, large diameter, distensible
- b) Liquid fecal stream
- c) Chronic blood loss results in iron deficiency anemia***
- d) Obstruction unlikely

MANIFESTATIONS

1. Growth of cancer at primary site
 - iii. Left sided syndrome
 - a) Descending colon wall thicker, less distensible
 - b) More solid fecal stream
 - c) Tumors tend to infiltrate
 - d) Bright red blood more common
 - e) Obstruction more common

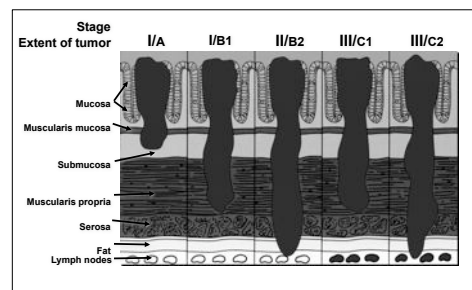
“Apple core lesion”



COMPARISON RIGHT AND LEFT SIDED COLON CANCERS

	Right	Left
Anemia	+++	+
Occult bleeding	+++	+
Gross bleeding	+	+++
Abd. Mass	++	+
Change in bowel habits	+	+++
Obstruction	+	+++

Colorectal Cancer: Staging (AJCC/ Modified Duke's)



Adapted from Skarin AT, ed. Atlas of Diagnostic Oncology. 2003.

PROGNOSIS

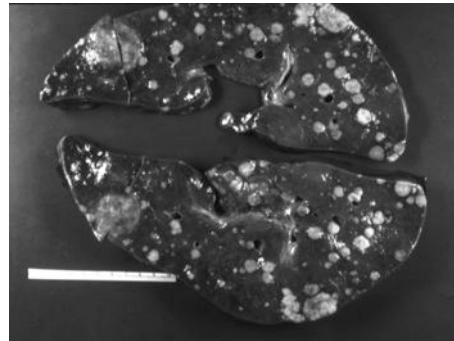
1. Histological features
 - poor differentiation
 - vascular invasion
2. Depth of invasion
3. Nodal involvement
4. Genetic alterations
 - 18q LOH (bad), MSI (good)

Dukes Stage*	Description	5-Year Survival**
A	Confined to bowel wall	80-90%
B	Extending through bowel wall	60-70%
C	Lymph node metastases	20-30%
(D)	Distant Metastases	5-10%

MANIFESTATIONS

Metastatic Spread

1. Lymphatics
 - Mesenteric nodes
 - Virchow's node
2. Hematogenous spread
 - Liver via portal circulation



LIVER METASTASES

MANIFESTATIONS

1. Pain (stretching capsule)
2. Hepatomegaly, nodular surface
3. Elevated liver function tests

4. TREATMENTS

1. Surgery
 - Localized disease (Stage I, II, III)
 - Try to remove isolated metastases
2. Radiation therapy
 - Rectal cancer-helps prevent local recurrence
3. Pharmaceuticals
 - Stage III and IV disease

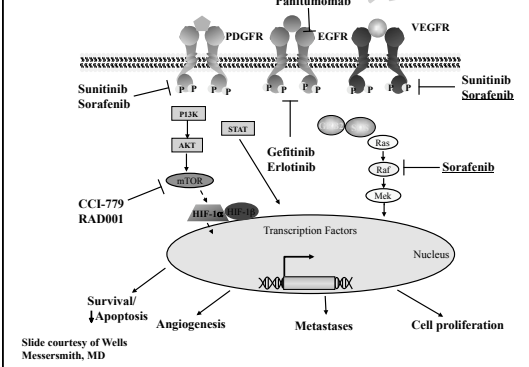
TREATMENT: Pharmaceuticals

1. 5-Fluorouracil
 - pyrimidine antimetabolite
2. Irinotecan
 - topoisomerase inhibitor
 - prevents re-ligation after cleavage of DNA by topoisomerase I
3. Oxaliplatin
 - alkylating agent, causes formation of bulky DNA adducts

Exciting new biologics...

4. Bevacizumab
 - Antibody against VEGF
 - May block angiogenesis and also stabilize leaky vasculature
5. Cetuximab, Panitumomab
 - Antibody against EGFR
 - Binds to EGF receptor on tumor cells and prevents dimerization and cell signaling

Molecularly Targeted Therapy in Oncology



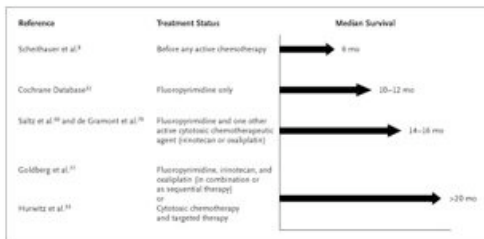
TREATMENT

- Pharmaceuticals
1. “Adjuvant” (after surgery)
 - Curative goal in patients after complete resection
 2. Palliation in patients with gross metastatic disease
 3. “Neoadjuvant” (before surgery)
 - Shrink tumors, then try to resect in limited metastatic disease

TREATMENT: Metastatic disease

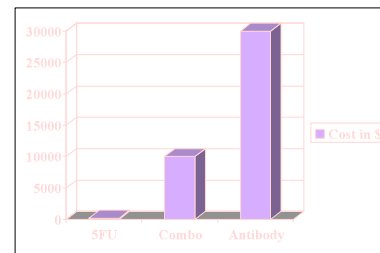
- Systemic chemotherapy now has improved survival for those with metastatic disease to about 2 years
- We now sometimes treat neoadjuvantly (before surgery), shrinking metastases and then surgically removing them
- This is important, because some of these “limited metastases” patients are cured!

Trends in the Median Survival of Patients with Advanced Colorectal Cancer



Meyerhardt, J. A. et al. N Engl J Med 2005;352:476-487

Estimated drug costs for eight weeks of treatment for metastatic colorectal cancer



Schrag, D. N Engl J Med 2004;351:317-319

Conclusions:

- Know HNPCC and APC—these may help you prevent cancers in others
- Understand how colon cancer commonly presents (right versus left-sided), and common sites of spread
- Think about colon (or other GI) cancer in an older person with iron-deficiency anemia—don't just give them iron!
- Don't give up on those with metastatic disease with new treatment options and occasionally cures

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- Many thanks to Tom Garrett for many slides!