COLORECTAL CANCER

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Objectives

- Understand presenting symptoms based on tumor location in CRC
- Understanding management and prognosis based on stage
- Adjuvant management of high risk early-stage CRC
- Surveillance after definitive therapy of CRC

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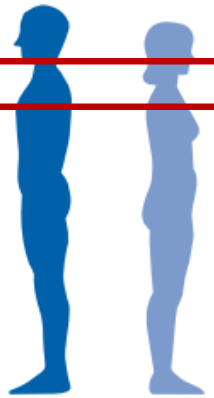
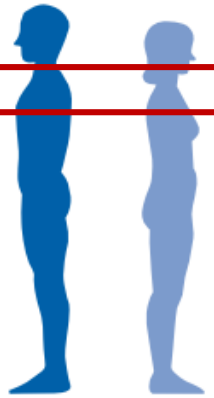
Figure 3. Leading Sites of New Cancer Cases and Deaths – 2020 Estimates



Estimated New Cases

Male			Female		
Prostate	191,930	21%	Breast	276,480	30%
Lung & bronchus	116,300	13%	Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%	Colon & rectum	69,650	8%
Urinary bladder	62,100	7%	Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%	Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%	Melanoma of the skin	40,160	4%
Non-Hodgkin lymphoma	42,380	5%	Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,380	4%	Kidney & renal pelvis	28,230	3%
Leukemia	35,470	4%	Pancreas	27,200	3%
Pancreas	30,400	3%	Leukemia	25,060	3%
All sites	**893,660**		**All sites**	**912,930**	



Estimated Deaths

Male			Female		
Lung & bronchus	72,500	23%	Lung & bronchus	63,220	22%
Prostate	33,330	10%	Breast	42,170	15%
Colon & rectum	28,630	9%	Colon & rectum	24,570	9%
Pancreas	24,640	8%	Pancreas	22,410	8%
Liver & intrahepatic bile duct	20,020	6%	Ovary	13,940	5%
Leukemia	13,420	4%	Uterine corpus	12,590	4%
Esophagus	13,100	4%	Liver & intrahepatic bile duct	10,140	4%
Urinary bladder	13,050	4%	Leukemia	9,680	3%
Non-Hodgkin lymphoma	11,460	4%	Non-Hodgkin lymphoma	8,480	3%
Brain & other nervous system	10,190	3%	Brain & other nervous system	7,830	3%
All sites	**321,160**		**All sites**	**285,360**	

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Question 1

48 yo male presents to the ER with 1 month history of abdominal pain, pencil thin stools and bleeding.

- Hg: 8.8
- FHx: No Malignancies

If this is a Adenocarcinoma; the most likely location is:

1. Ileocecal valve
2. Right Sided
3. Transverse
4. Left Sided

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- CRC mortality has been progressively declining (1.6-2.0%/yr)
- **<50 yrs**: Increase 2.1%/yr (1992-2012)
- **L sided and rectal (3.9%/yr)**
- >86% diagnosed at <50 yrs:
  - Symptomatic at diagnosis
  - Advanced stage at diagnosis
  - Poorer outcomes

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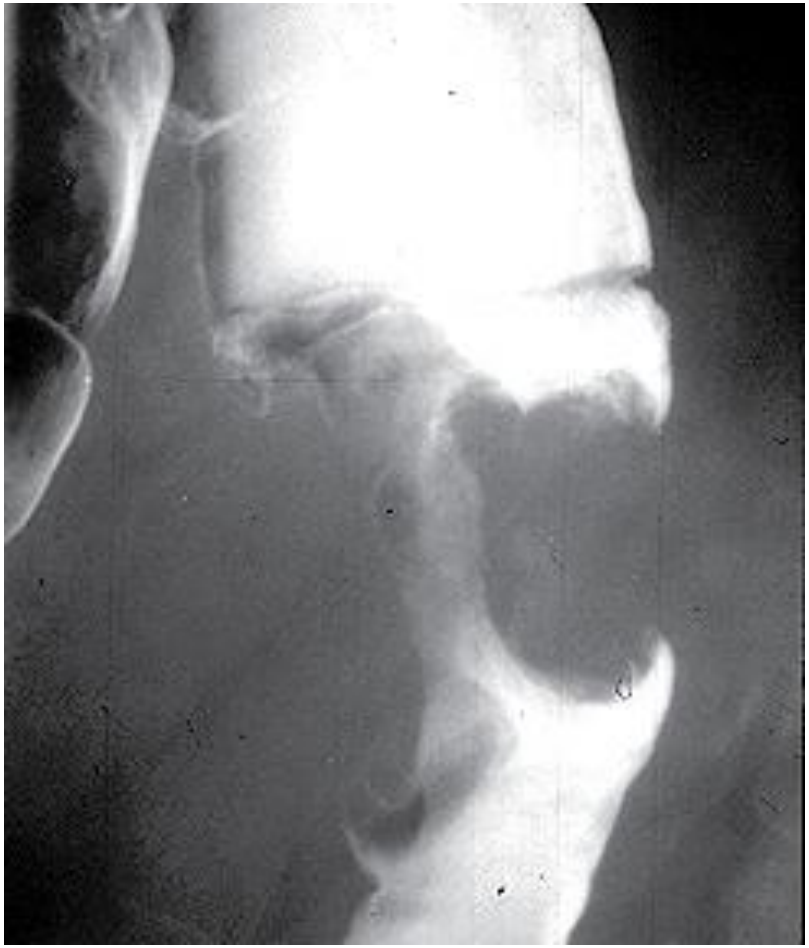
- **Screening**

- **Local Tumor Symptoms**
  - Change in bowel habits (76%)
  - Rectal Bleeding (51%)
  - Mass (25%)
  - Anemia (10%)



Courtesy : UpToDate

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Question 2

60 yo without a history of a previous colonoscopy is admitted with FUO, sepsis and abdominal pain.

- **CT:** demonstrates colonic thickening
- **Colonoscopy:** Adenocarcinoma of the sigmoid colon

Positive blood cultures can demonstrate which of the following organism(s):

1. Streptococcus bovis
2. Clostridium septicum
3. Bacteroides fragilis
4. 1&2
5. Any of the above
6. Who cares-Not an ID lecture

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Atypical Presentations

- Local invasion with malignant fistula formation

- **Sepsis**
  - Streptococcus bovis
  - Clostridium septicum
  - Bacteroides fragilis

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Question 3

67 yo newly diagnosed with non metastatic R-sided colon adenocarcinoma s/p R hemicolectomy

- Pathology: Tumor invaded the muscularis propria into pericolorectal tissue

- What is the T stage:
  1. T1
  2. T2
  3. T3
  4. T4

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Tumor (T) Staging

Colorectal cancer TNM staging AJCC UICC 8th edition

Primary tumor (T)

T category	T criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma *in situ*, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)
T1	Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
T2	Tumor invades the muscularis propria
T3	Tumor invades through the muscularis propria into pericolorectal tissues
T4	Tumor invades* the visceral peritoneum or invades or adheres¶ to adjacent organ or structure
T4a	Tumor invades* through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
T4b	Tumor directly invades* or adheres¶ to adjacent organs or structures

* Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumor on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina).

¶ Tumor that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumor is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classification should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN prognostic factor should be used for perineural invasion.

Regional lymph nodes (N)

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Question 4

In the same patient the pathology report identified negative lymph nodes but 4 ‘tumor deposits’ in the mesentery.

What is the updated staging?

1. T3M1
2. T3N1c
3. T3N2
4. Missed my path lecture

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Nodal (N) Staging

N category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative
N1a	One regional lymph node is positive
N1b	Two or three regional lymph nodes are positive
N1c	No regional lymph nodes are positive, but there are tumor deposits in the: • Subserosa • Mesentery • Nonperitonealized pericolic, or perirectal/mesorectal tissues
N2	Four or more regional nodes are positive
N2a	Four to six regional lymph nodes are positive
N2b	Seven or more regional lymph nodes are positive

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis by imaging, etc; no evidence of tumor in distant sites or organs. (This category is not assigned by pathologists.)
M1	Metastasis to one or more distant sites or organs or peritoneal metastasis is identified
M1a	Metastasis to one site or organ is identified without peritoneal metastasis
M1b	Metastasis to two or more sites or organs is identified without peritoneal metastasis
M1c	Metastasis to the peritoneal surface is identified alone or with other site or organ metastases

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Staging

When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1, T2	N0	M0	I
T3	N0	M0	IIA
T4a	N0	M0	IIB
T4b	N0	M0	IIC
T1-T2	N1/N1c	M0	IIIA
T1	N2a	M0	IIIA
T3-T4a	N1/N1c	M0	IIIB
T2-T3	N2a	M0	IIIB
T1-T2	N2b	M0	IIIB
T4a	N2a	M0	IIIC
T3-T4a	N2b	M0	IIIC
T4b	N1-N2	M0	IIIC
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB
Any T	Any N	M1c	IVC

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

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Survival by Stage

Stage	Description	Approximate 5-Year Disease-Free Survival
I	Tumor does not invade the full thickness of bowel wall (T1, T2); lymph nodes not involved (N0)	90%-95%
II	Tumor invades full thickness of the bowel and may invade into pericolonic or perirectal fat (T3, T4); lymph nodes not involved (N0)	70%-85%
III	One or more lymph nodes involved with cancer (N1, N2); any T stage	25%-70%
IV	Metastatic tumor spread to distant site (M1); any T stage; any N stage	0%-10%

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Question 5

45 yo female undergoes a Rt hemicolectomy for a large non-obstructive T3 poorly differentiated adenocarcinoma. No LVI or PNI. 0/35 LN. Margins –ve.

- Staging:

1. Stage I
2. Stage II
3. Stage III
4. Stage VI

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Question 6

In the previously mentioned patient…

Which statement is accurate:

1. RAS mutation analysis can guide adjuvant therapy decision
2. Stage II MSI high tumors have an excellent prognosis and don't req adjuvant Rx
3. Most cases of MSI-H tumors occur as a manifestation of Lynch syndrome

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Management

- **Stage I:** surgery alone
- **Stage II:**
  - low risk vs. high risk

  Surgery +/- Adjuvant chemo
- **Stage III:** Surgery plus adjuvant chemotherapy
- **Stage IV:** Palliative Chemotherapy (except oligometastatic disease)

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High Risk Stage II

- Perforated or obstructed primary tumor
- T4 or close/positive margins
- <12 LN's resected
- MSI Status
- PNI or LVI
- Poorly differentiated histology
- Assessment of comorbidities and life expectancy

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What about MSI and Stage II

- MSI-H:
  - Hypermutability that occurs due to a deficiency in the DNA MMR
  - DNA Replication with accumulated errors
  - Microsatellites aka repeated sequences of DNA
  - MSI can be
    - **Sporadic**-15%; due to hypermethylation of the MLH1 gene promoter
    - **Genetic**-Lynch syndrome; germline mutation in MLH1, MSH2, MSH6, PMS2

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- MSI-H (IHC or PCR) portends to a better prognosis and don't respond to 5-FU based regimens*
- Popat et al# in a systematic review of 32 studies of CRC demonstrated that MSI-H pts derived no benefit from adjuvant FU-containing chemotherapy
- Sargent et al^ demonstrated that MSI-H pts treated with chemotherapy was associated with a reduced OS

*Ribic CM, NEJM,2003; #Popat S, JCO,2005;^Sargent DJ, JCO 2010

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Question 7

In the previously mentioned 45yo from Q5 with Stage II…

When would you repeat the 1st surveillance colonoscopy?

1. 3 months
2. 6 months
3. 12 months
4. 18 months
5. Never-Why would u want to torture her?

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Question 8

In the same patient……

When would you scan her?

1. 3 months
2. 6 months
3. 12 months
4. 18 months

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NCCN

- **HnP:** 3-6 months X 2yrs; 6months X 3yrs
- **CEA:** 3-6 months X 2yrs; 6months X 3yrs
- **CT:** CAP 6-12 months X 5 years
- **Colonoscopy:** Initially at 12 months

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Questions?

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Bonus 1

A 58-year-old man undergoes routine colonoscopy revealing a fungating mass in the ascending colon.

- **Biopsy:** adenocarcinoma
- **Imaging:** no evidence of metastatic disease
- **Right hemi:** pT3 pN1

Which of the following is the most appropriate management at this time?

1. Leucovorin, 5-fluorouracil, and oxaliplatin (FOLFOX)
2. Radiation therapy
3. ChemoRadiation followed by capecitabine plus oxaliplatin (CAPOX)
4. Observation
5. CAPOX

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Bonus 2

A 58-year-old man undergoes follow-up evaluation for bleeding PR.

- **Colonoscopy:** mass 6 cm from the anal verge
- **Biopsy:** adenocarcinoma
- **MRI Pelvis:** multiple perirectal LN's
- **CT:** CA - no other evidence of metastatic disease

Which of the following is the most appropriate management at this time?

1. Leucovorin, 5-fluorouracil, and oxaliplatin (FOLFOX)
2. Radiation therapy
3. Radiation with concurrent capecitabine
4. Observation
5. Surgery

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