NEOPLASMS OF THE COLON AND RECTUM

2014/2015 FCDS Educational Webcast Series

February 19, 2015
Steven Peace, CTR

2015 Update; Background, Anatomy, Risk Factors, Screening Guidelines, MPH Rules Review
AJCC TNM 7thed, SS2000, CSv02.05 and SSFs
Plus…NCCN 2015 Tx Guidelines

1

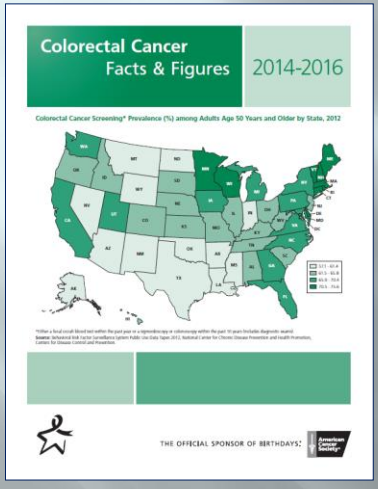
Presentation Outline

- Overview – Incidence/Mortality/Survival
- Risk Factors – Signs and Symptoms
- Anatomy of the Colon and Rectum
- Colorectal Cancer Screening
- Multiple Primary Rules
- Histology Coding Rules
- Molecular and Genetic Tumor Markers
- Staging – SS2000, AJCC TNM, CSv02.05
- NCCN Treatment Guidelines

http://safetyca.info

2

Overview



- 1 out of every 20 persons in the U.S. will develop colon or rectal cancer in their lifetime.
- Colorectal cancer is the #3 cause of cancer deaths in the U.S.
- Colorectal cancer often begins as a benign growth; a polyp.
- Adenomas are a type of polyp and are benign tumors of the tissue lining the colon or rectum.
- Most adenomas are benign.
- However, some adenomas have the potential to develop into cancer over the long term.
- When removed early, polyps are prevented from developing into malignant cancer.

American Cancer Society – Colorectal Cancer Facts & Figures 2014-2016

3

Overview

Leading Sites of New Cancer Cases and Deaths - 2015 Estimates

Estimated New Cases*		Estimated Deaths	
Male	**Female**	**Male**	**Female**
Prostate 220,800 (26%)	Breast 231,840 (29%)	Lung & bronchus 86,380 (28%)	Lung & bronchus 71,660 (26%)
Lung & bronchus 115,610 (14%)	Lung & bronchus 105,590 (13%)	Prostate 27,540 (9%)	Breast 40,290 (15%)
Colon & rectum 69,090 (8%)	Colon & rectum 63,610 (8%)	Colon & rectum 26,100 (8%)	Colon & rectum 23,600 (9%)
Urinary bladder 56,320 (7%)	Uterine corpus 54,870 (7%)	Pancreas 20,710 (7%)	Pancreas 19,850 (7%)
Melanoma of the skin 42,670 (5%)	Thyroid 47,230 (6%)	Liver & intrahepatic bile duct 17,030 (5%)	Ovary 14,180 (5%)
Non-Hodgkin lymphoma 39,850 (5%)	Non-Hodgkin lymphoma 32,000 (4%)	Leukemia 14,210 (5%)	Leukemia 10,240 (4%)
Kidney & renal pelvis 38,270 (5%)	Melanoma of the skin 31,200 (4%)	Esophagus 12,600 (4%)	Uterine corpus 10,170 (4%)
Oral cavity & pharynx 32,670 (4%)	Pancreas 24,120 (3%)	Urinary bladder 11,510 (4%)	Non-Hodgkin lymphoma 8,310 (3%)
Leukemia 30,900 (4%)	Leukemia 23,370 (3%)	Non-Hodgkin lymphoma 11,480 (4%)	Liver & intrahepatic bile duct 7,520 (3%)
Liver & intrahepatic bile duct 25,510 (3%)	Kidney & renal pelvis 23,290 (3%)	Kidney & renal pelvis 9,070 (3%)	Brain & other nervous system 6,380 (2%)
All sites 848,200 (100%)	All sites 810,170 (100%)	All sites 312,150 (100%)	All sites 277,280 (100%)

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

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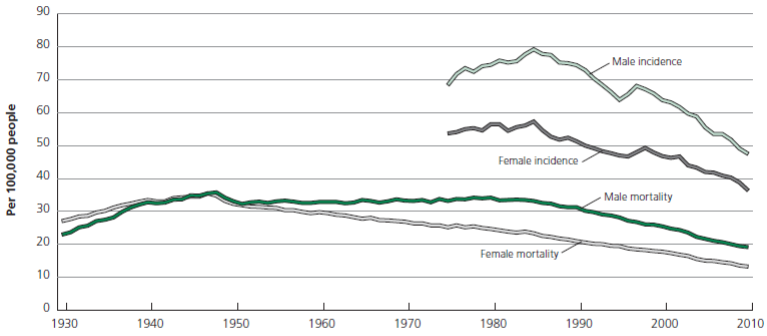
4

Incidence and Mortality

Figure 4. Trends in Colorectal Cancer Incidence and Death Rates by Sex, US, 1930-2010



Rates were age adjusted to the 2000 US standard population. Incidence rates were adjusted for delays in reporting. Due to changes in International Classification of Diseases (ICD) coding for mortality, numerator information has changed over time.

Source: Incidence - Surveillance, Epidemiology, and End Results (SEER) Program, SEER 9 registries, National Cancer Institute, 2013.
Mortality - US Mortality Volumes 1930 to 1959, US Mortality Data 1960-2010, National Center for Health Statistics, Centers for Disease Control and Prevention, 2013.

American Cancer Society, Surveillance Research, 2014

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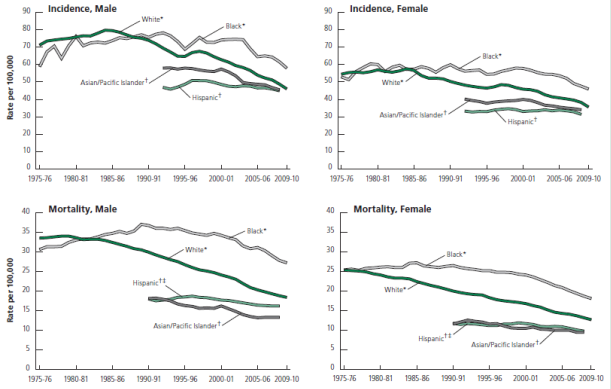
5

Incidence and Mortality

Figure 5. Trends in Colorectal Cancer Incidence and Mortality Rates by Race/Ethnicity and Sex, 1975-2010



Trends for American Indians/Alaska Natives are not included due to sparse data. Rates are per 100,000 and age adjusted to the 2000 US standard population. *Rates are two-year moving averages. †Rates are three-year moving averages. ‡Rates exclude deaths from Connecticut, District of Columbia, Louisiana, Maine, Maryland, Minnesota, Mississippi, New Hampshire, New York, North Dakota, Oklahoma, South Carolina, Vermont, and Virginia due to incomplete ethnicity data.

Source: Incidence - Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. Mortality - National Center for Health Statistics, Centers for Disease Control and Prevention, 2013.

American Cancer Society, Surveillance Research, 2014

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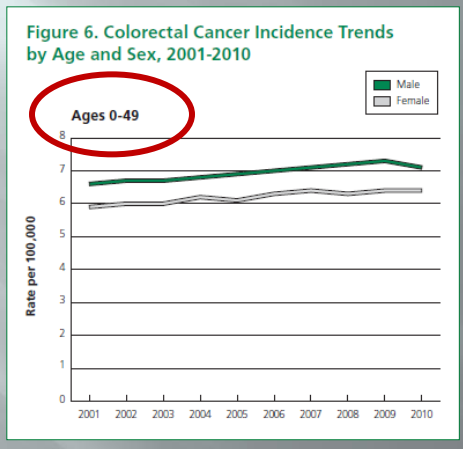
6

Incidence and Mortality



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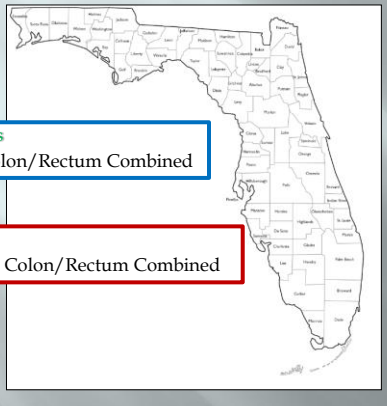
7

Incidence and Mortality

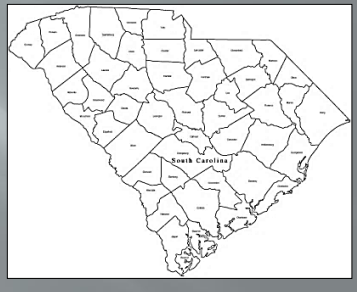
2015 New Cases and Deaths



New Cases
- 9,330 Colon/Rectum Combined

Deaths
- 3,520 Colon/Rectum Combined

New Cases
- 2,130 Colon/Rectum Combined



Deaths
- 840 Colon/Rectum Combined

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8

Trends in Five-year Relative Cancer Survival Rates (%), 1975-2010

Site	1975-1977	1987-1989	2004-2010
All sites	49	55	68
Breast (female)	75	84	91
Colon	51	60	65
Leukemia	34	43	60
Lung & bronchus	12	13	18
Melanoma of the skin	82	88	93
Non-Hodgkin lymphoma	47	51	71
Ovary	36	38	45
Pancreas	3	4	7
Prostate	68	83	100*
Rectum	48	58	68
Urinary bladder	72	79	79

5-year relative survival rates based on patients diagnosed in the SEER 9 areas from 1975-1977, 1987-1989, and 2004-2010, all followed through 2011.
*99.6%
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2014.

9

Survival

Five-year Relative Survival Rates* (%) by Stage at Diagnosis, 2002-2008

	All Stages	Local	Regional	Distant		All Stages	Local	Regional	Distant
Breast (female)	89	98	84	24	Ovary	44	92	72	27
Colon & rectum	64	90	70	12	Pancreas	6	23	9	2
Esophagus	17	38	20	3	Prostate	99	100	100	28
Kidney†	71	91	64	12	Stomach	27	62	28	4
Larynx	61	76	42	35	Testis	95	99	96	73
Liver‡	15	28	10	3	Thyroid	98	100	97	54
Lung & bronchus	16	52	25	4	Urinary bladder§	78	70	33	6
Melanoma of the skin	91	98	62	15	Uterine cervix	68	91	57	16
Oral cavity & pharynx	62	82	57	35	Uterine corpus	82	95	67	16

*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 18 areas from 2002-2008, followed through 2009.
†Includes renal pelvis. ‡Includes intrahepatic bile duct. §Rate for in situ cases is 96%.
Local: an invasive malignant cancer confined entirely to the organ of origin. **Regional:** a malignant cancer that 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes by way of lymphatic system; or 3) has both regional extension and involvement of regional lymph nodes. **Distant:** a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes.
Source: Howlader N, Noone AM, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2009*, National Cancer Institute, Bethesda, MD, www.seer.cancer.gov/csr/1975_2009/, 2012.

American Cancer Society, Surveillance Research 2013

SEER Cancer Statistics Review, 1975-2009

10

Survival by AJCC Stage

AJCC TNM Stage	5-year Relative Survival Rate
I	92%
IIA	87%
IIB	63%*
IIIA	89%*
IIIB	69%
IIIC	53%
IV	11%

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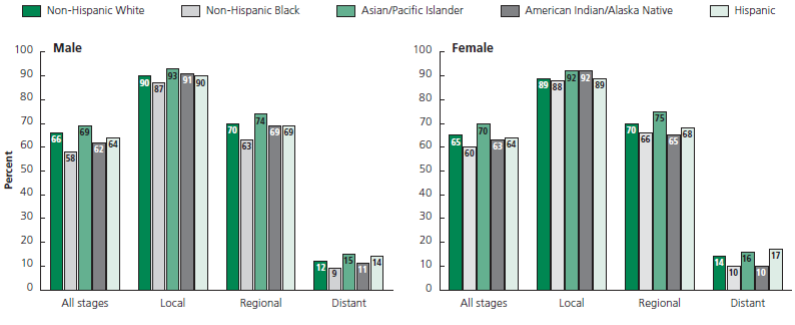
11

Survival

Figure 9. Five-year Colorectal Cancer-specific Survival* by Stage and Race/Ethnicity, 2003-2009



*The probability of not dying from colorectal cancer within 5 years of diagnosis. Patients were followed through 2010.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, SEER 18 registries, National Cancer Institute, 2013.
American Cancer Society, Surveillance Research, 2014

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12

Risk Factors

13

Risk Factors

- Family History
- Personal History
- Physical Inactivity
- Overweight
- Obesity
- Diet
- Alcohol
- Smoking
- Type 2 Diabetes

Table 2. Summary of Selected Risk Factors for Colorectal Cancer

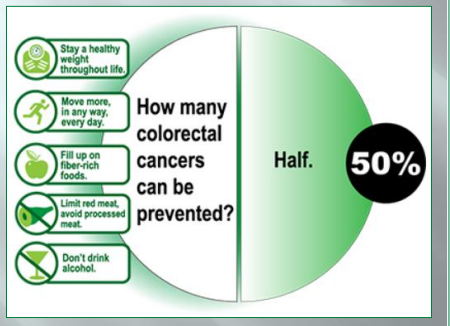
	Relative Risk*
Factors that increase risk:	
Heredity and Medical History	
Family history	
1 first-degree relative[43]	2.2
more than 1 relative[43]	4.0
relative with diagnosis before age 45[44]	3.9
Inflammatory bowel disease† [62]	
Crohn disease (colon)	2.6
Ulcerative colitis	
colon	2.8
rectum	1.9
Diabetes[42]	1.2
Behavioral factors[42]	
Alcohol consumption (heavy vs. nondrinkers)	1.6
Obesity	1.2
Red meat consumption	1.2
Processed meat consumption	1.2
Smoking (current vs. never)	1.2
Factors that decrease risk:	
Physical activity (colon)[73]	0.7
Dairy consumption[87]	0.8
Fruit consumption[85]	0.9
Vegetable consumption[85]	0.9
Total dietary fiber (10 g/day)[84]	0.9

*Relative risk compares the risk of disease among people with a particular "exposure" to the risk among people without that exposure. Relative risk for dietary factors compares the highest with the lowest consumption. If the relative risk is more than 1.0, then risk is higher among exposed than unexposed persons. Relative risks less than 1.0 indicate a protective effect.

†Several recent, small studies indicate that current risk may be lower due to improvements in treatment and the use of colonoscopy screening to detect precancerous lesions.

14

Prevention



Current Recommendations for the Prevention of Colorectal Cancer

1. Get screened regularly.
2. Maintain a healthy weight throughout life.
3. Adopt a physically active lifestyle.
4. Consume a healthy diet with an emphasis on plant sources; specifically:
   - Choose foods and beverages in amounts that help achieve and maintain a healthy weight.
   - Eat 5 or more servings of a variety of vegetables and fruits each day.
   - Choose whole grains in preference to processed (refined) grains.
   - Limit your consumption of processed and red meats.
5. If you drink alcoholic beverages, limit consumption.

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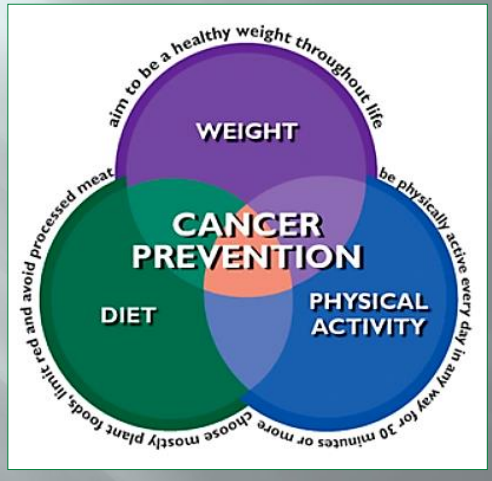
15

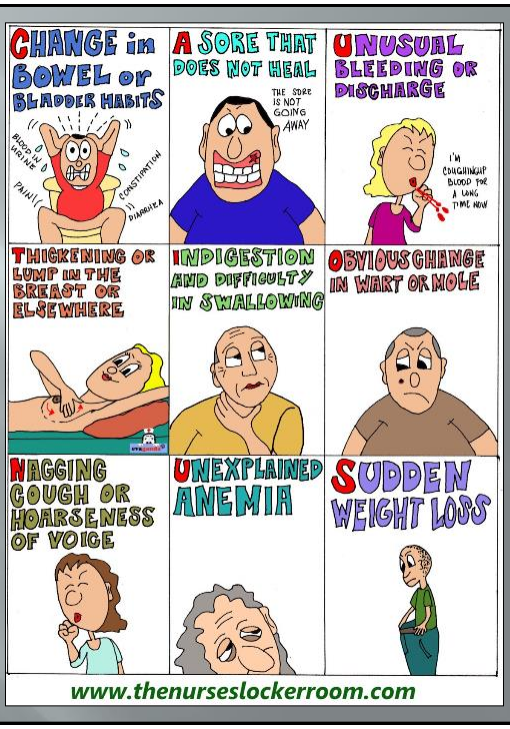
Prevention



Source: http://positivechoices.com

16

Signs and Symptoms



17

Screening

18

Colorectal Cancer Screening Guidelines*

Beginning at age 50, men and women should follow one of the following examination schedules:

Test	Time interval
Fecal occult blood test	Annual
Flexible sigmoidoscopy	5 yrs
Double contrast barium enema	5 yrs
Colonoscopy	10 yrs
CT Colonography	5 yrs

*For people at average risk; individuals at higher risk should talk with a doctor about a different testing schedule.

Recommendation Details

Structural Exams

Flexible Sigmoidoscopy			
• Fairly quick • Few complications • Minimal bowel preparation • Does not require sedation or a specialist	**Performance:** High for rectum & lower one-third of the colon **Complexity:** Intermediate	• Views only one-third of colon • Cannot remove large polyps • Small risk of infection or bowel tear • Slightly more effective when combined with annual fecal occult blood testing • Colonoscopy still needed if abnormalities are detected • Limited availability	5 years
Colonoscopy			
• Examines entire colon • Can biopsy and remove polyps • Can diagnose other diseases • Required for abnormal results from all other tests	**Performance:** Highest **Complexity:** Highest	• Full bowel preparation needed • Can be expensive • Sedation of some kind usually needed, necessitating a chaperone to return home • Patient may miss a day of work. • Highest risk of bowel tears or infections compared with other tests	10 years
Double-contrast Barium Enema			
• Can usually view entire colon • Few complications • No sedation needed	**Performance:** High (for large polyps) **Complexity:** High	• Full bowel preparation needed • Some false positive test results • Cannot remove polyps or perform biopsies • Exposure to low-dose radiation • Colonoscopy necessary if abnormalities are detected • Very limited availability	5 years
Computed Tomographic Colonography			
• Examines entire colon • Fairly quick • Few complications • No sedation needed • Noninvasive	**Performance:** High (for large polyps) **Complexity:** Intermediate	• Full bowel preparation needed • Cannot remove polyps or perform biopsies • Exposure to low-dose radiation • Colonoscopy necessary if abnormalities are detected • Not covered by all insurance plans	5 years

20

Recommendation Details

Stool Tests (Low-sensitivity stool tests, such as single-sample FOBT done in the doctor's office or toilet bowl tests, are not recommended)

High-Sensitivity Guaiac-based Fecal Occult Blood Test (FOBT)			
• No bowel preparation • Sampling is done at home • Low cost • Noninvasive	**Performance:** Intermediate for cancer **Complexity:** Low	• Requires multiple stool samples • Will miss most polyps • May produce false-positive test results • Pre-test dietary limitations • Slightly more effective when combined with a flexible sigmoidoscopy every five years • Colonoscopy necessary if abnormalities are detected	Annual
Fecal Immunochemical Test (FIT)			
• No bowel preparation • Sampling is done at home • Low cost • Noninvasive	**Performance:** Intermediate for cancer **Complexity:** Low	• Requires multiple stool samples • Will miss most polyps • May produce false-positive test results • Slightly more effective when combined with a flexible sigmoidoscopy every five years • Colonoscopy necessary if abnormalities are detected	Annual
Stool DNA Test			
• No bowel preparation • Sampling is done at home • Requires only a single stool sample • Noninvasive	**Performance:** Intermediate for cancer **Complexity:** Low	• Will miss most polyps • High cost compared to other stool tests • New technology with uncertain interval between testing • Colonoscopy necessary if abnormalities are detected	Uncertain

*Complexity involves patient preparation, inconvenience, facilities and equipment needed, and patient discomfort.

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21

Screening High Risk Populations

- Individuals at High Risk Include:
  - Family History – 1st degree relative
  - Family History – more than 1 relative
  - Family History – relative with dx < age 60
  - Personal History – Colon Cancer
  - Personal History – Colon Polyp(s)
  - Personal History – Inflammatory Bowel Disease/Syndrome
    - Crohn's Disease/Ulcerative Colitis
  - Personal History – Diabetes
  - High Risk Hereditary Syndromes
- Screening should begin before age 50
- Colonoscopy is recommended screening method
- Discuss your personal risk and routine screening schedule with your personal healthcare provider

22

Heredity and Colon Cancer

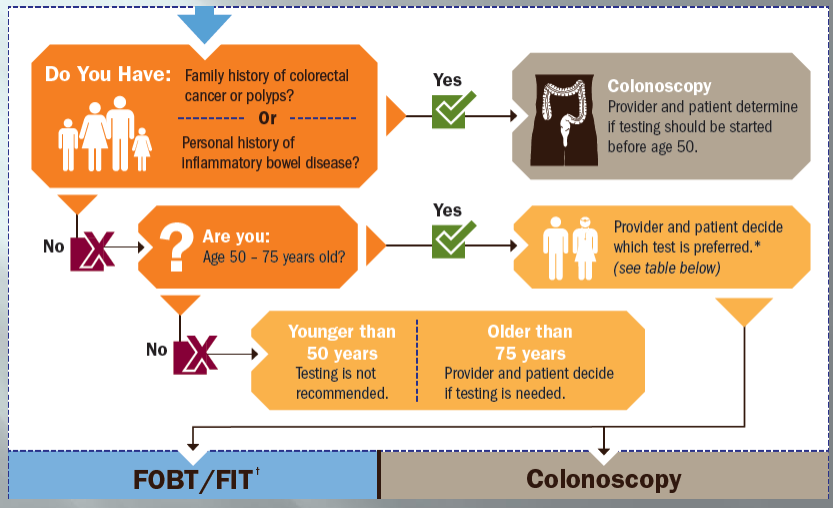
ESTIMATED RISK FOR COLON CANCER BY SYNDROME

Syndrome	Gene(s)	Risk
FAP (familial adenomatous polyposis)	*APC*	90% by age 45
Attenuated FAP	*APC*	69% by age 80
Lynch (HNPCC)	*MLH1, MSH2, MSH6 PMS2, EPCAM*	40% to 80% by age 75
MUTYH-associated polyposis	*MUTYH*	35% to 53%
Peutz-Jeghers	*STK11*	39% by age 70
Juvenile polyposis	*BMPR1A, SMAD4*	17% to 68% by age 60

http://www.ambrygen.com

23

Choosing the Right Test



SOURCE: Vital Signs 2013 and USPSTF
http://www.uspreventiveservicestaskforce.org/uspstf/uspscolo.htm

24

Choosing the Right Test

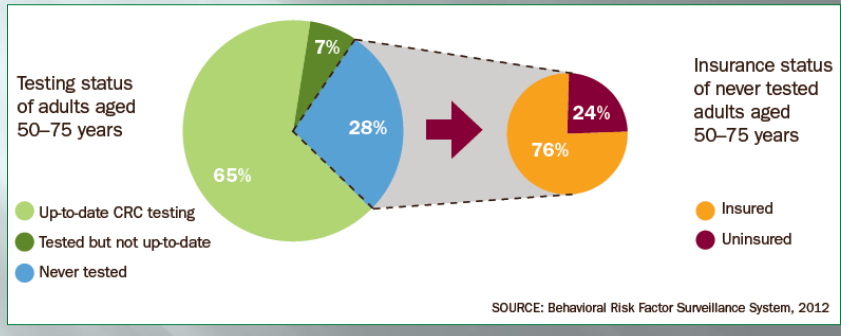
FOBT/FIT†	Colonoscopy
Key facts	**Key facts**
· Reduces death from colorectal cancer	· Reduces death from colorectal cancer
· Safe, available, and easy to complete	· Can prevent cancer by removing polyps (or abnormal growths in the colon) during test
· Done on your own at home and returned	· Examines entire colon
· Finds cancer early by finding blood in the stool	· Finds most cancers or polyps that are present at the time of the test
· Finds most cancers early when done every year	· Done every 10 years if no polyps are found
Things to consider	**Things to consider**
· May produce positive test results, even when no polyps or cancer are in the colon	· Stomach pain, gas or bloating is possible before, during or after test
· When the test is positive colonoscopy is required	· Must be performed at a hospital or clinic, usually with sedation or anesthesia, and someone must go with the person to take him or her home after the test
· Person testing themselves comes into brief close contact with stool samples on a test kit	· A clear liquid diet is required before test
	· Must take medication that will cause loose bowel movements to clean out the colon prior to test
	· Likely needs to take a day off work/activities
	· Small risk of serious complications (for example, bleeding or perforated colon)

† *Guaiac Fecal Occult Blood Test (FOBT) or Fecal Immunochemical Test (FIT)*

**Flexible sigmoidoscopy may not be readily available and has largely been replaced by colonoscopy in the US.*

25

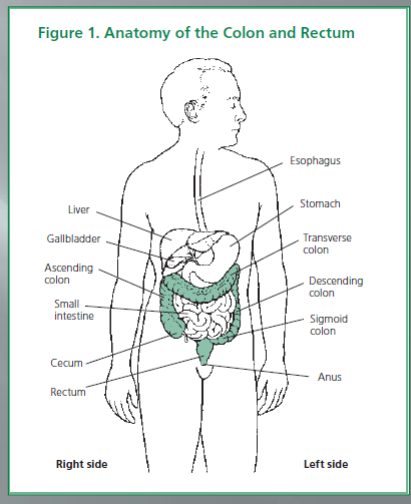
23 Million Adults Never Screened



SOURCE: Vital Signs 2013 and USPSTF
http://www.uspreventiveservicestaskforce.org/uspstf/uspscolo.htm

26

Anatomy



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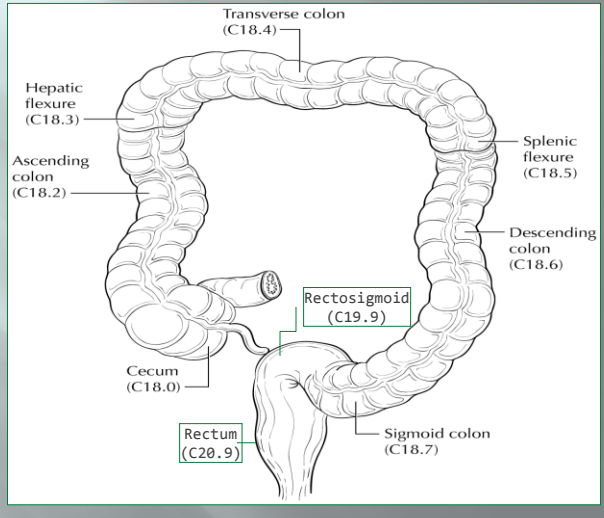
27

Colon and Rectum

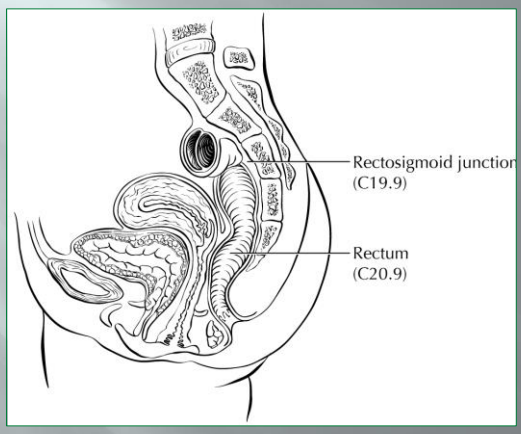
RIGHT COLON



LEFT COLON

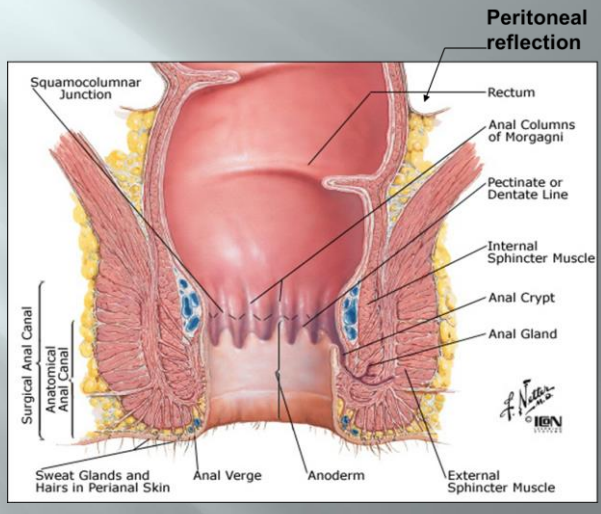
28

Rectosigmoid and Rectum



29

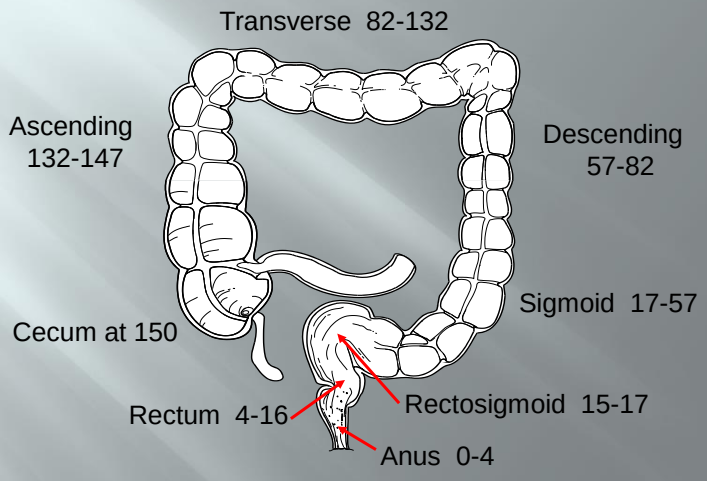
Rectum – Anorectum – Anus



Source: www.analcancerinfo.ucsf.edu

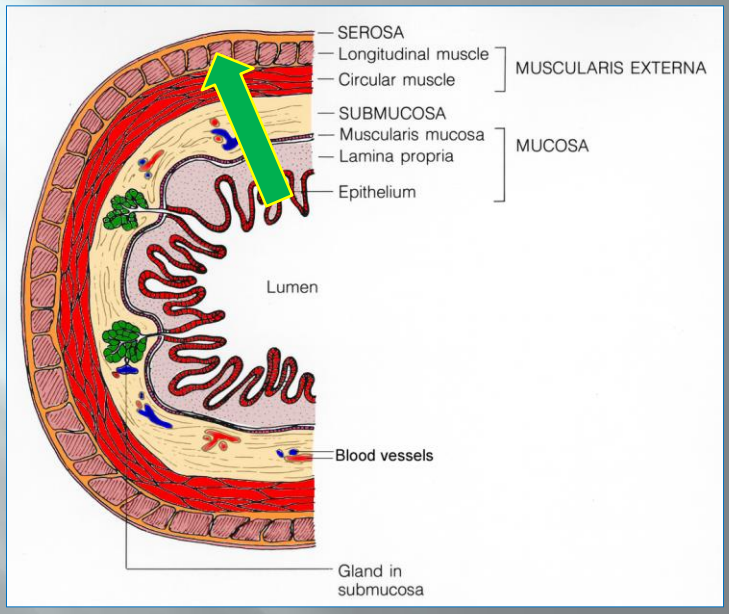
30

Colonoscopy Measurements



Distance from Anal Verge (approximations only)
Adapted from AJCC Cancer Staging Manual

31



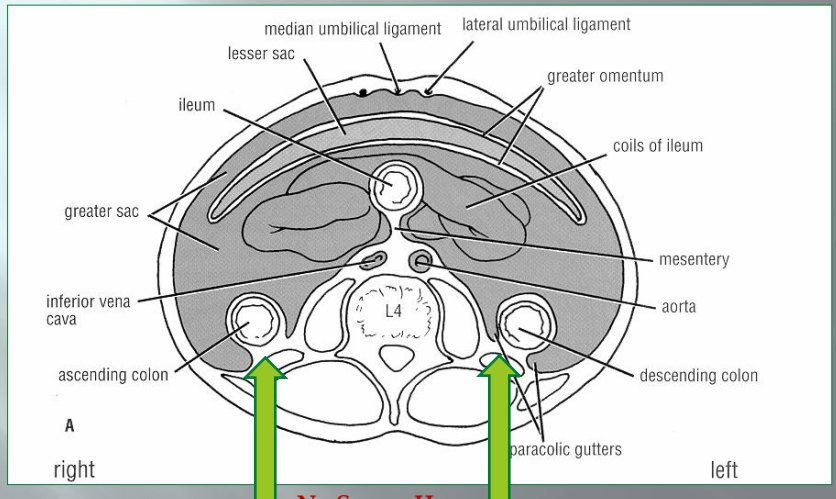
32

"Non-Peritonealized" Surface

- Some colon surfaces have no serosa at the exterior surface (around the hollow organ)
- The serosa acts as barrier for tumors that begin on inside surface of the colon and invade down into the mucosa and through the wall of the colon (the serosa).
- When there is no serosa – you lose a natural barrier that helps contain the colon cancer
- Non-Peritonealized Surfaces in Colon-Rectum:
  - Rectum – no serosa in rectum below peritoneal reflection
  - Descending Colon – no serosa covering posterior surfaces
  - Ascending Colon – no serosa covering posterior surfaces

33

"Non-Peritonealized" Surface



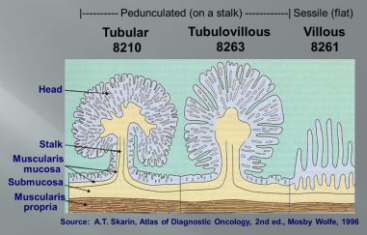
No Serosa Here

Source: *Clinical Anatomy for Medical Students, 5th Edition,* Richard S. Snell. Little, Brown and Company, 1995.

34

Polyps and Colon Cancer

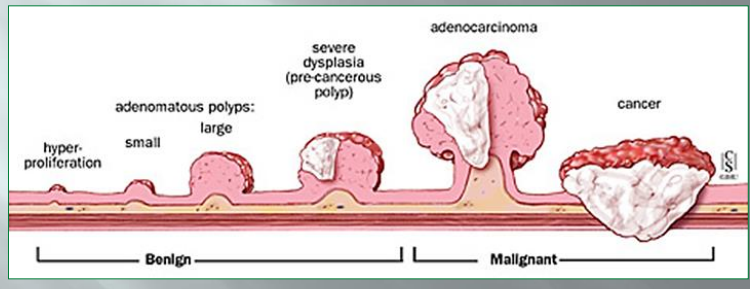
- 95-98% of colon cancers - adenocarcinoma
  - Most originate in polyps or adenomas
  - But, only 10% of adenomas develop into cancers
- Types of adenoma
  - Tubular
  - Villous
  - Tubulo-villous
- Process takes up to 10 years



- De Novo Cancers – mucinous, signet ring
  - >10% of all colon ca are mucinous (>50% mucin production)
  - <1% of all colon ca are signet ring cell (>50% signet rings)

35

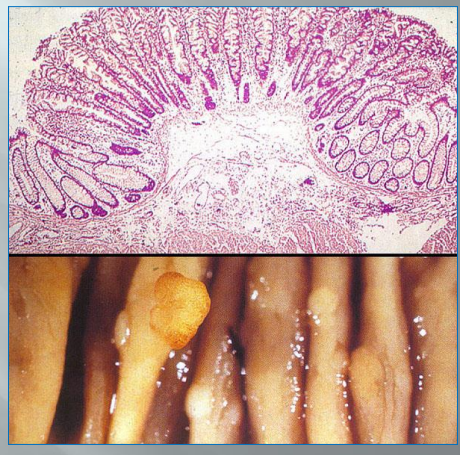
Polyps and Colon Cancer



http://hopkinscoloncancercenter.org

36

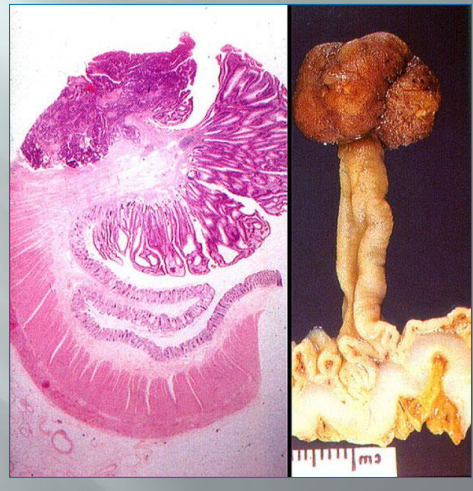
Polyps and Colon Cancer



http://www.pathology.pitt.edu/lectures/gi/colon-a/14.htm

37

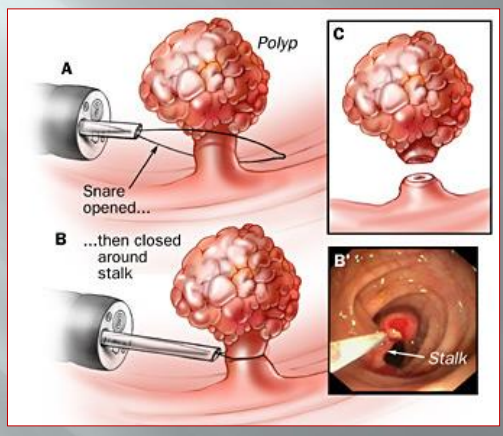
Polyps and Colon Cancer



http://www.pathology.pitt.edu/lectures/gi/colon-a/16.htm

38

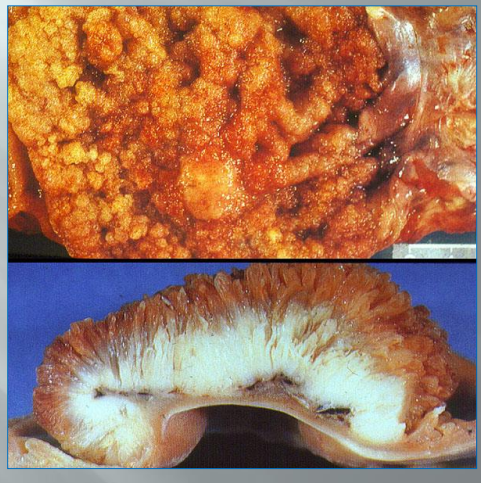
Polyps and Colon Cancer



http://hopkinscoloncancercenter.org

39

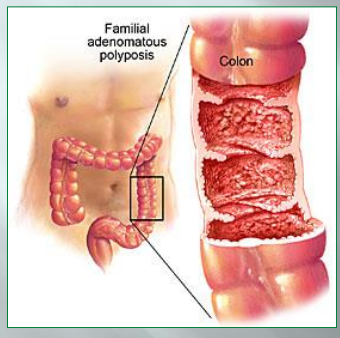
Polyps and Colon Cancer



http://www.pathology.pitt.edu/lectures/gi/colon-a/17.htm

40

Polyps and Colon Cancer

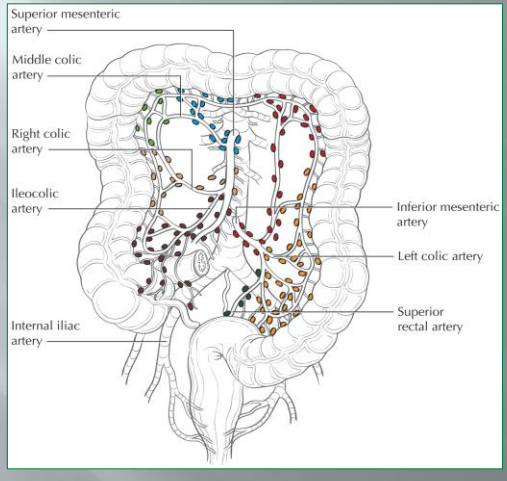


http://www.mayoclinic.org/images

http://www.mlibrary.med.utah.edu

41

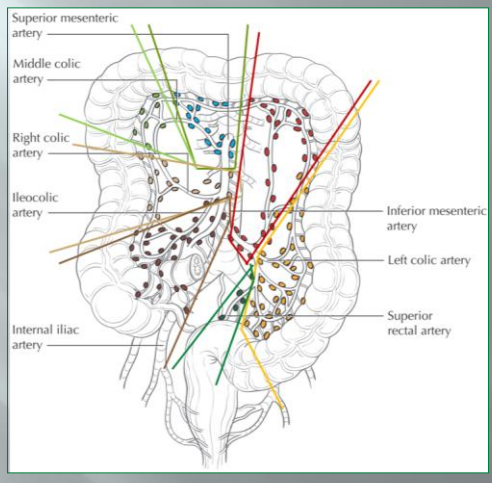
Lymphatics of Colon / Rectum



AJCC Image - The regional lymph nodes of the colon and rectum are colored by anatomic location.

42

Lymphatics of Colon / Rectum



Modified AJCC Image - The regional lymph nodes of the colon and rectum are colored by anatomic location.

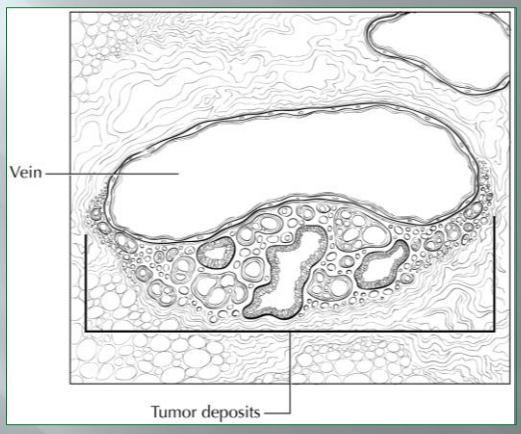
43

"Tumor Deposits"

- Definition
  - Separate tumor nodules or tumor deposits of malignant cells in perirectal or pericolic fat with no evidence of lymph node tissue
- Found in primary lymphatic drainage area
- Other names
  - Peri-tumoral deposits, satellite nodules, discontinuous extramural extension, or malignant tumor foci
- N1c = Specific TNM "N" Code for tumor nodule or deposit(s) in the subserosa, mesentery, or non-peritonealized pericolic or perirectal tissues without regional nodal metastasis.

44

"Tumor Deposits"



Discrete foci of tumor found in the pericolic or perirectal fat or in adjacent mesentery (mesocolic fat) away from the leading edge of the tumor and showing no evidence of residual lymph node tissue but within the lymph drainage area of the primary carcinoma are considered to be peritumoral deposits or satellite nodules, and their number should be recorded in the site-specific Prognostic Markers on the staging form as Tumor Deposits .

45

"Tumor Deposits"

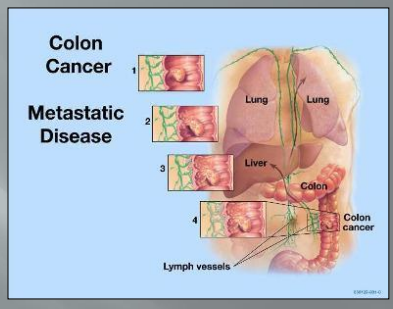
- Mesenteric
- Pericolonic
- Perirectal
- Subserosa
- All Regional Lymph Nodes Negative
- Deposits + LNs

- N1c = Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis.

46

Metastatic Sites

- Lung
- Liver
- Lymph Nodes
- Seeding in peritoneum
- Seeding of small intestine
- Seeding of other segments of colon



www.colorectal-surgeon.com

47

MPH RULES
TERMS AND DEFINITIONS

- 2017 MPH Rules Update
- New MPH Database
- Text Only Rules
- Stay Tuned

Colon Equivalent Terms, Definitions and Illustrations
C180-C189
(Excludes lymphoma and leukemia M9590-9989 and Kaposi sarcoma M9140)

Introduction

Note 1: Rectum and rectosigmoid are covered by The Other Sites rules.
Note 2: For the purpose of these rules, the words "exophytic" and "polypoid" are not synonymous with a polyp.

Use these rules only for cases with primary colon cancer.

Ninety-eight percent of colon cancers are adenocarcinoma. Ten to fifteen percent of these cases produce enough mucin to be categorized as mucinous/colloid.* Mixed histologies and specific types other than mucinous/colloid or signet ring cell are rare.

**ACS Clinical Oncology*

Equivalent or Equal Terms

Note: For the purpose of these rules, the words "exophytic" and "polypoid" are not synonymous with a polyp.

- Familial polyposis, familial adenomatous polyposis, (FAP)
- Intramucosal, lateral extension
- Invasion through colon wall, extension through colon wall, transmural
- Low grade neuroendocrine carcinoma, carcinoid
- Most invasive, most extensive
- Mucin producing, mucin secreting
- Mucinous, colloid
- Polyp, adenoma
- Serosa, visceral peritoneum
- Tumor, mass, lesion, neoplasm
- Type, subtype, predominantly, with features of, major, or with ____differentiation.

Definitions

Adenocarcinoid (8245/3): A specific histology commonly found in the appendix.

Adenocarcinoma with mixed subtypes (8255): Rarely used for colon primaries (see introduction).

Adenocarcinoma, intestinal type (8144) is a form of stomach cancer. Do not use this code when the tumor arises in the colon.

Adenoma: A **benign** lesion composed of tubular or villous structures showing **intraepithelial neoplasia** (See definition of **intraepithelial neoplasia**).

Colon Terms and Definitions

Colon Equivalent Terms, Definitions and Illustrations
C180-C189
(Excludes lymphoma and leukemia M9590-9989 and Kaposi sarcoma M9140)

Composite carcinoid (8244): One tumor which contains both carcinoid and adenocarcinoma.

Familial polyposis, familial adenomatous polyposis (FAP), adenocarcinoma in: a condition characterized by the development of many adenomatous polyps, often seen in several members of the same family.

Frank adenocarcinoma: Adenocarcinoma arising from the colon wall (no evidence of a polyp)

In Situ: Noninvasive; intraepithelial; (adeno)carcinoma in a polyp or adenoma, noninvasive.

Intestinal type adenocarcinoma (8144) is a gastric histology term and is not listed in the WHO Histological Classification of Tumors of the Colon and Rectum.

Intraepithelial neoplasia, high grade may be either severe dysplasia or carcinoma in situ. Report cases of carcinoma in situ only.

Intraepithelial neoplasia, low grade is not a reportable condition. A person with intraepithelial neoplasia is at risk for developing invasive cancer.

Intramucosal tumors may be noninvasive or invasive. The term intramucosal may refer to the surface epithelium, the basement membrane, or the lamina propria..

Invasive tumor: A tumor that penetrates the basement membrane and invades the lamina propria.

Most invasive: The tumor with the greatest continuous extension through the wall of the colon. The layers of the colon wall in order of least to greatest extension:

- Mucosa (surface epithelium, lamina propria, basement membrane)
- Submucosa
- Muscularis propria
- Subserosa (pericolic fat, subserosal fat)
- Retroperitoneal fat (pericolic fat)
- Mesenteric fat (pericolic fat)
- Serosa (visceral peritoneum).

MPH RULES
MULTIPLE PRIMARY RULES

- 2017 MPH Rules Update
- New MPH Database
- Text Only Rules
- Stay Tuned

Multiple Primary Rules

Unknown Number

- M1. Unknown whether single or multiple tumors = single

One Tumor

- M2. Single tumor = single

Multiple Tumors

- M3. Adenoca in adenomatous polyposis coli in one or multiple segments = single

Source: AFritz and Associates, LLC

52

Multiple Primary Rules

Multiple Tumors, continued

- M4. Different topography = multiple
- M5. Diagnosis dates > 1 year apart = multiple
- M6. Invasive after in situ > 60 days = multiple
- M7. Frank adenocarcinoma and malignant tumor in a polyp = single
- M8. Non-specific and specific histology = single
- M9. Multiple polyps (all malignant) = single
- M10. Histology different = multiple
- M11. All other scenarios = single

Source: AFritz and Associates, LLC

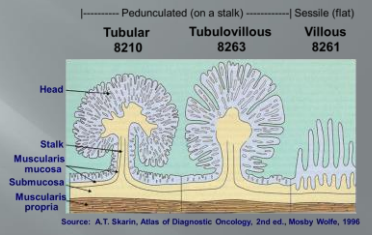
53

MPH RULES
HISTOLOGY CODING RULES

- 2017 MPH Rules Update
- New MPH Database
- Text Only Rules
- Stay Tuned

Histopathology Review

- 95-98% of colon cancers - adenocarcinoma
  - Most originate in polyps or adenomas
  - But, only 10% of adenomas develop into cancers
- Types of adenoma
  - Tubular
  - Villous
  - Tubulo-villous
- Process takes up to 10 years



- De Novo Cancers – mucinous, signet ring
  - >10% of all colon ca are mucinous (>50% mucin production)
  - <1% of all colon ca are signet ring cell (>50% signet rings)

55

New Histologic Terms and Code

- Glandular intraepithelial neoplasia, high grade
- Glandular intraepithelial neoplasia, grade III
- Flat intraepithelial neoplasia, high grade

- 8148/2 – Use Code for GI Tract in 2016 (?)

- All low grade intraepithelial neoplasia = /0
- All grade I or grade II intraepithelial neoplasia = /0

56

Mucinous and Signet Ring Cell

- Mucinous adenocarcinoma (8480)
  Code when
  - Final diagnosis is mucinous OR
  - Documentation says > 50% mucinous
    - May use microscopic section of path report
- Signet ring cell carcinoma (8490)
  Code when
  - Final diagnosis is signet ring cell OR
  - Documentation says > 50% signet ring cell
    - May use microscopic section of path report
  - "…with signet ring cells" ≠ signet ring cell CA

57

Colorectal NETs and GISTs

- **NET – Neuroendocrine Tumor**
  - Carcinoid Tumor – 2015 ALL are reportable/malignant
  - Neuroendocrine Carcinoma
  - Mitotic Count Matters
  - Serum Chromogranin A (CgA)
  - Urinary 5-Hydroxyindoleacetic Acid (5-HIAA)
- **GIST – Gastrointestinal Stromal Tumor**
  - Tumor Size Matters
  - Mitotic Count Matters
  - KIT (CD117) Mutation
  - PDGFRA (CD140A) Mutation

58

Histology Coding Rules

Single tumor

- H1. If no tissue, code physician's statement
- H2. If no primary tissue, code metastasis
- H3. Adenocarcinoma, NOS vs. intestinal type adenocarcinoma
- H4. 8210, 8261, or 8263 - carcinoma in a polyp
- H5. Mucinous or signet ring cell > 50% of tumor
- H6. Adenocarcinoma, NOS when mucinous or signet ring cell < 50% of tumor
- H7. 8255 combined mucinous and signet ring

Source: AFritz and Associates, LLC

59

Histology Coding Rules

Single tumor, continued

- H8. 8240 carcinoid when combined neuroendocrine and carcinoid
- H9. 8244 composite carcinoid when combined adenoca and carcinoid
- H10. 8245 adenocarcinoid when diagnosis is exactly "adenocarcinoid"
- H11. Single histology
- H12. Invasive if both invasive and in situ
- H13. Most specific term
- H14. Higher code

Source: AFritz and Associates, LLC

60

Histology Coding Rules

Multiple tumors abstracted as a single primary

- H15. If no tissue, code physician's statement
- H16. If no primary tissue, code metastasis
- H17. 8220 Familial polyposis
- H18. 8263 - carcinoma is tubulo-villous adenoma
- H19. 8221 when < 100 polyps
- H20. Most invasive tumor
- H21. 8210, 8261, or 8263 - carcinoma in a polyp
- H22. Single histology
- H23. Most specific term
- H24. Higher code

Source: AFritz and Associates, LLC

61

Prognostic and Predictive Biochemical and Molecular Tumor Marker Testing, Genetic Testing, & Required SSFs

62

College of American Pathologists

Colon and Rectum • Biomarkers
ColonBiomarkers [1.0.0.0]

cap

Template for Reporting Results of Biomarker Testing of Specimens From Patients With Carcinoma of the Colon and Rectum

For the Members of the Cancer Biomarkers Reporting Workgroup, College of American Pathologists

College of American Pathologists

Immunohistochemistry Testing (IHC) for Mismatch Repair Proteins (select all that apply) (Note A)

___ MLH1
- ___ Intact nuclear expression
- ___ Loss of nuclear expression
- ___ Cannot be determined (explain): _____

___ MSH2
- ___ Intact nuclear expression
- ___ Loss of nuclear expression
- ___ Cannot be determined (explain): _____

___ MSH6
- ___ Intact nuclear expression
- ___ Loss of nuclear expression
- ___ Cannot be determined (explain): _____

___ PMS2
- ___ Intact nuclear expression
- ___ Loss of nuclear expression
- ___ Cannot be determined (explain): _____

___ Background nonneoplastic tissue/internal control with intact nuclear expression

Microsatellite Instability (MSI) (Note A)

___ MSI–Stable (MSS)
___ MSI–Low (MSI-L)
- ___ 1%-29% of the markers exhibit instability
- ___ 1 of the 5 NCI or mononucleotide markers exhibit instability
- ___ Other (specify): _____

___ MSI–High (MSI-H)
- ___ ≥30% of the markers exhibit instability
- ___ 2 or more of the 5 NCI or mononucleotide markers exhibit instability
- ___ Other (specify): _____

___ MSI-Indeterminate

Microsatellite Instability - MSI

- What is MSI?
  - Genetic Test using PCR (polymerase chain reaction) looking for DNA Repair errors and HNPCC features
- What does positive result indicate?
  - MSI predicts response to chemotherapy
  - MSI may indicate patient's overall prognosis
  - MSI-H (highly positive MSI Test) may be related to development of HNPCC or Lynch Syndrome
- Who should get tested?
  - Patient under age 50 with colon cancer
  - Patient under age 50 with rectal cancer
  - Patient with other HNPCC-associated tumors
  - Patient with family history of colon/rectal cancer

65

Genetic Mutations in Colon Cancer

ESTIMATED RISK FOR COLON CANCER BY SYNDROME

Syndrome	Gene(s)	Risk
FAP (familial adenomatous polyposis)	*APC*	90% by age 45
Attenuated FAP	*APC*	69% by age 80
Lynch (HNPCC)	*MLH1, MSH2, MSH6 PMS2, EPCAM*	40% to 80% by age 75
MUTYH-associated polyposis	*MUTYH*	35% to 53%
Peutz-Jeghers	*STK11*	39% by age 70
Juvenile polyposis	*BMPR1A, SMAD4*	17% to 68% by age 60

http://www.ambrygen.com

66

KRAS Mutation

- What is KRAS wild-type?
- What is KRAS mutation?
- When is KRAS testing done?
- What does positive result mean?
- What about BRAF V600E Mutation?

67

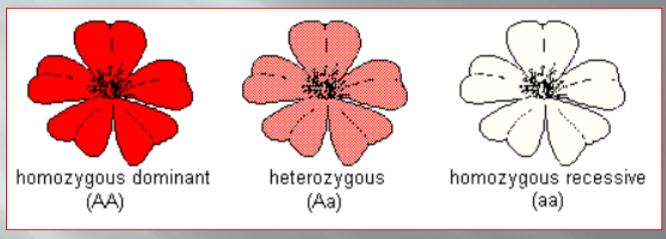
Other Genetic Mutation Tests

- APC Mutation
- PIK3CA Mutation
- PTEN Mutation
- TFAP2E – fluorouracil resistance

- Multi-parameter Gene Expression Testing
- Protein Expression Assay
- DNA Microarrays

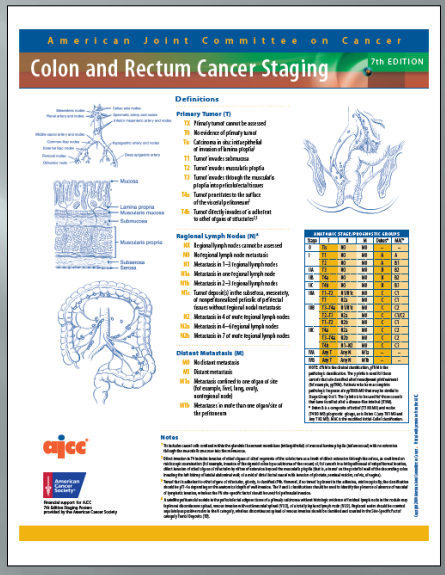
68

18q Loss of Heterozygosity



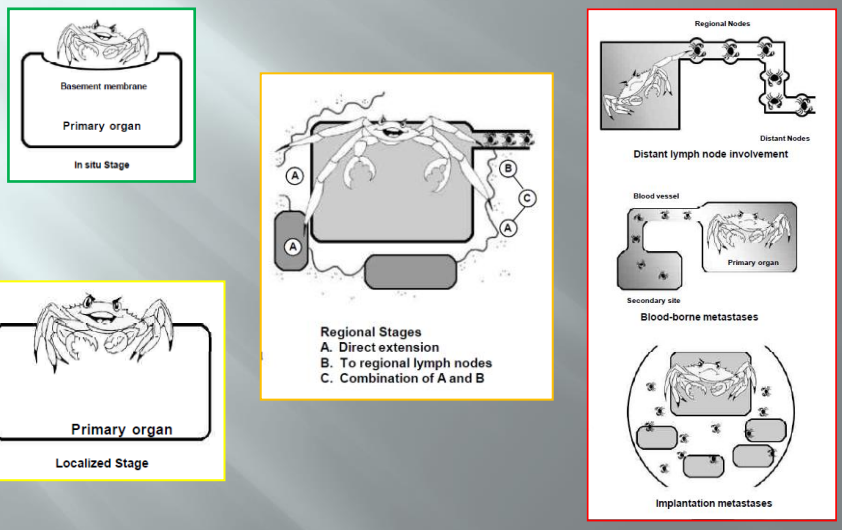
69

Cancer Staging



70

SEER Summary Stage



Source: SEER Summary Staging Manual 2000

71

SEER Summary Stage

COLON
C18.0-C18.9
C18.0 Cecum
C18.1 Appendix
C18.2 Ascending (right) colon
C18.3 Hepatic flexure of colon
C18.4 Transverse colon
C18.5 Splenic flexure of colon
C18.6 Descending (left) colon
C18.7 Sigmoid colon
C18.8 Overlapping lesion of colon
C18.9 Colon, NOS

SUMMARY STAGE

0 In situ: Noninvasive; intraepithe
(Adeno)carcinoma in a

1 Localized only
Invasive tumor confined to:
Intramucosa, NOS
Lamina propria
Mucosa, NOS
Muscularis mucosae
Muscularis propria
Perimuscular tissue inva
Polyp, NOS:
Head of polyp
Stalk of polyp
Submucosa (superficial
Subserosal tissue/(sub)s
Transmural, NOS
Wall, NOS

Confined to colon, NOS
Extension through wall, NOS
Invasion through muscularis

Localized, NOS

Note: Ignore intraluminal extension to adjac

2 Regional by direct extension only
Extension to:
All colon sites:
Invasion of/through serosa (mesothe
Extension into/through:
Abdominal wall###
Adjacent tissue(s), NOS
Connective tissue
Fat, NOS
Greater omentum
Mesenteric fat
Mesentery
Mesocolon
Pericolic fat
Retroperitoneum (excluding fat)
Small intestine

Ascending colon:
Kidney, right###
Liver, right lobe
Retroperitoneal fat###
Ureter, right###

Transverse colon and flexures:
Bile ducts###
Gallbladder###
Gastrocolic ligament
Kidney
Liver
Pancreas
Spleen
Stomach###

Descending colon:
Kidney, left###
Pelvic wall###
Retroperitoneal fat###
Spleen
Ureter, left

Sigmoid colon:
Pelvic wall###

3 Regional lymph node(s) involved only
REGIONAL Lymph Nodes

All colon subsites:
Colic, NOS
Epicolic (adjacent to bowel wall)
Mesenteric, NOS
Paracolic/pericolic

Nodule(s) in pericolic fat

Cecum and Appendix:
Cecal, NOS
Anterior (prececal)
Posterior (retrocecal)
Ileocolic
Right colic

Ascending colon:
Ileocolic
Middle colic
Right colic

Transverse colon and flexures:
Inferior mesenteric **for splenic flexur**
Left colic **for splenic flexure only**
Middle colic£
Right colic **for hepatic flexure only**

Descending colon:
Inferior mesenteric
Left colic
Sigmoid###

Sigmoid:
Inferior mesenteric
Sigmoidal (sigmoid mesenteric)
Superior hemorrhoidal###
Superior rectal###

Regional lymph node(s), NOS

4 Distant site(s)/node(s) involved
All colon sites unless included in code 2
Distant lymph node(s):
Para-aortic
Retroperitoneal
Superior mesenteric§
Other distant lymph node(s)
Extension to:
Adrenal (suprarenal) gland
Bladder
Diaphragm
Fallopian tube£
Fistula to skin
Gallbladder
Other segment(s) of colon via seros
Ovary£
Uterus£

Cecum and appendix:
Distant lymph node(s):
Inferior mesenteric
Other distant lymph node(s)
Extension to:
Kidney, right
Liver###
Ureter, right

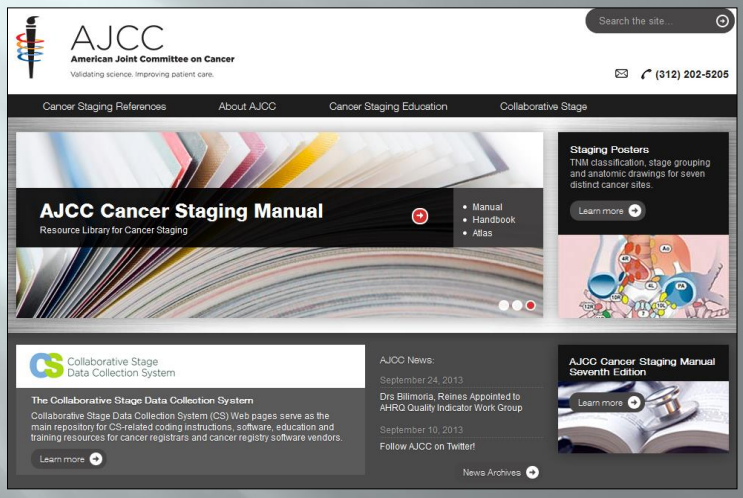
Ascending colon:
Distant lymph node(s):
Inferior mesenteric
Other distant lymph node(s)

Transverse colon and flexures:
Distant lymph node(s):
Inferior mesenteric **for hepatic fle**
Other distant lymph node(s)
Extension to:
Ureter

Sigmoid colon:
Extension to:
Cul de sac (rectouterine pouch)
Ureter

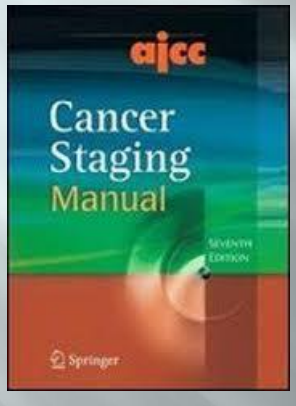
72

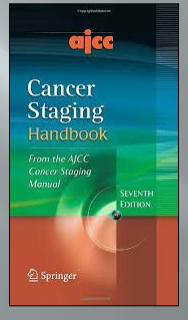
AJCC Cancer Staging - TNM

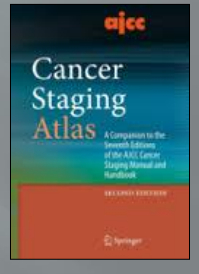


73

AJCC Cancer Staging - TNM





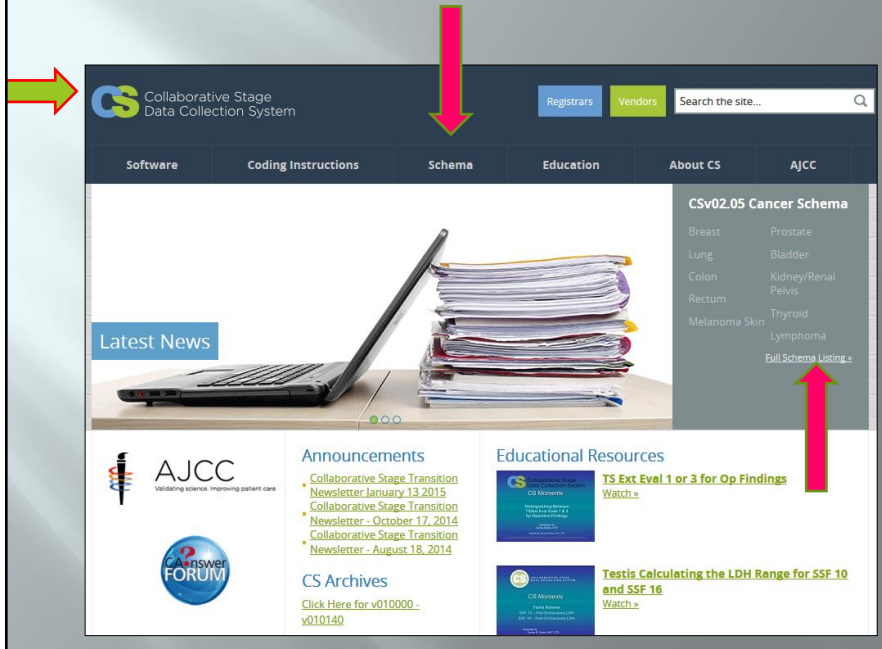


74

Pathologic Staging Parameters

- Primary Tumor Grade
- Depth of Invasion ("T" and CS Extension)
- Number of Lymph Nodes Examined
- Number of Lymph Nodes Positive
- Extranodal Tumor Deposits
- Status of Resection Margins – proximal, distal and radial or not a full evaluation of margins
- Lymph-vascular Invasion (LVI)
- Perineural Invasion (PNI)
- Response to Neoadjuvant Treatment as applicable

75



76

CS Extension

In situ

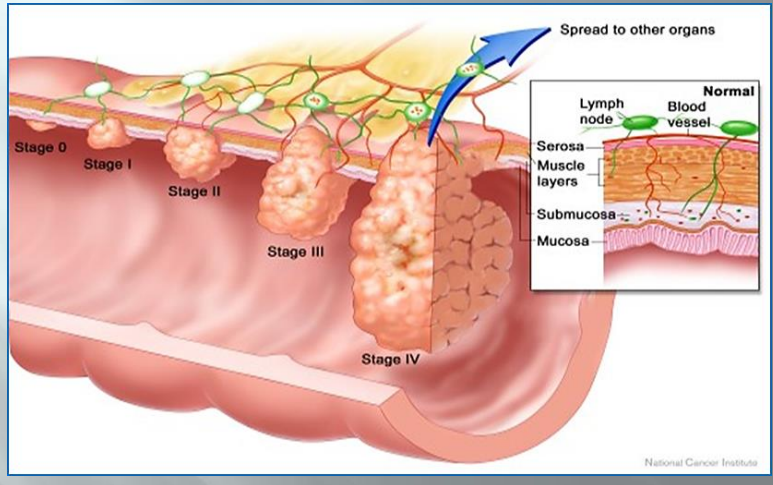
In situ

Invasive

Code	Description	TNM 7 Map	TNM 6 Map	SS77 Map	SS2000 Map
000	In situ, intraepithelial, noninvasive	Tis	Tis	IS	IS
050	(Adeno)carcinoma, noninvasive, in a polyp or adenoma	Tis	Tis	IS	IS
100	Invasive tumor confined to mucosa, NOS, including intramucosal, NOS	Tis	Tis	L	L
110	Invades lamina propria, including lamina propria in the stalk of a polyp	Tis	Tis	L	L
120	Confined to and not through the muscularis mucosae, including muscularis mucosae in the stalk of a polyp.	Tis	Tis	L	L
130	Confined to head of polyp, NOS	T1	T1	L	L
140	Confined to stalk of polyp, NOS	T1	T1	L	L
150	Invasive tumor in polyp, NOS	T1	T1	L	L
160	Invades submucosa (superficial invasion), including submucosa in the head or stalk of a polyp	T1	T1	L	L
170	Stated as T1 with no other information on extension	T1	T1	L	L

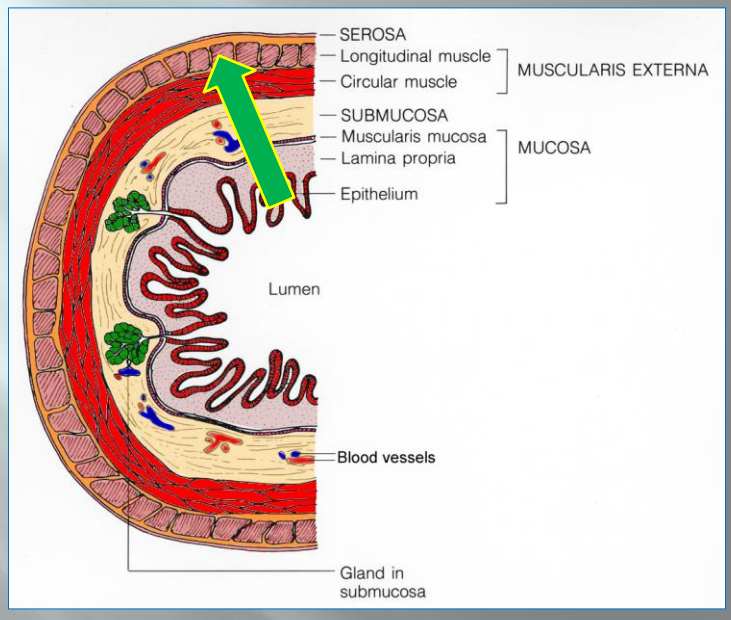
intramucosal

77



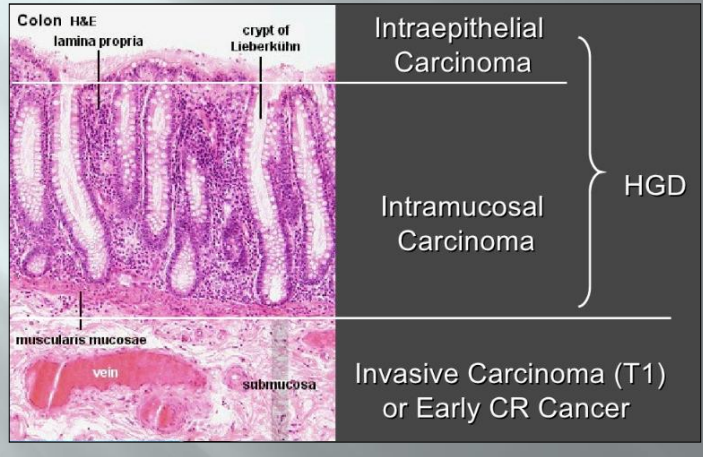
Source: National Cancer Institute

78



79

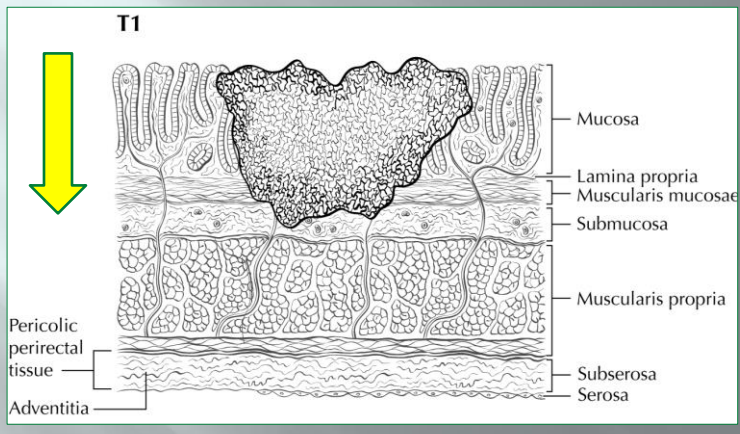
Intramucosal Colon Cancer



Source: http://www.slideshare.net/giaffa/petruzziello

80

CS Extension



Tumor invades submucosa

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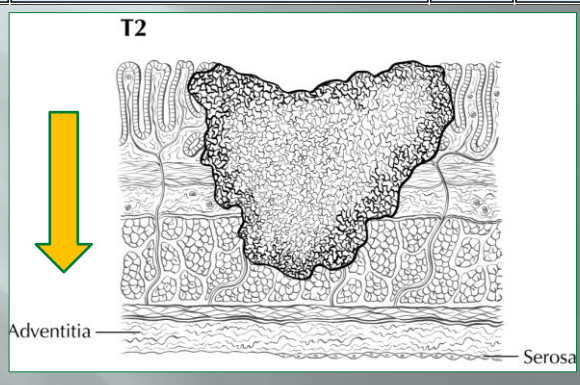
81

CS Extension

200	Muscularis propria invaded Stated as T2 with no other information on extension	T2	T2	L	L



Tumor invades muscularis propria

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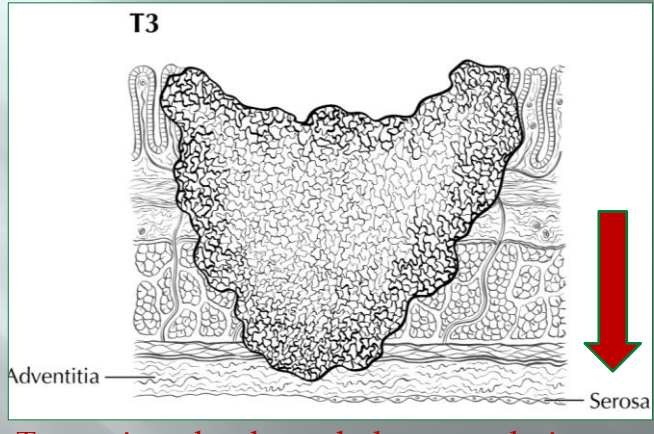
82

CS Extension

400	Extension through wall, NOS Invasion through muscularis propria or muscularis, NOS Non-peritonealized pericolic tissues invaded Perimuscular tissue invaded Subserosal tissue/(sub)serosal fat invaded Transmural, NOS Wall, NOS	T3	T3	L	L
450	Extension to: All colon sites: Adjacent tissue(s), NOS Connective tissue Mesenteric fat Mesentery Mesocolon Pericolic fat Ascending and descending colon Retroperitoneal fat Transverse colon and flexures Gastrocolic ligament Greater omentum	T3	T3	RE	RE

83

CS Extension



Tumor invades through the muscularis propria (muscle layer) into peri-colorectal tissues

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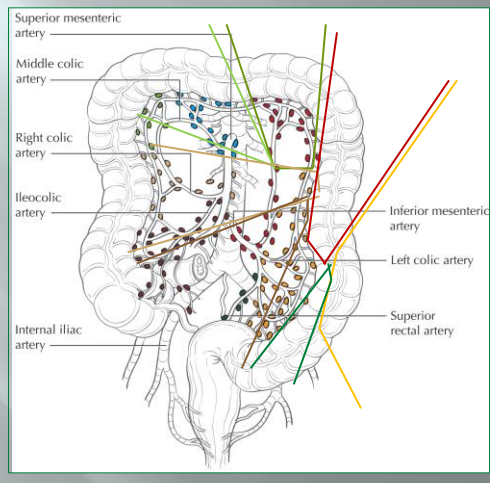
84

CS Extension

500	Invasion of/through serosa (mesothelium) (visceral peritoneum) Tumor penetrates to surface of visceral peritoneum	T4a	T4	RE	RE
550	500 + (450 or 458)	T4a	T4	RE	RE
560	Stated as T4a with no other information on extension	T4a	T4	RE	RE
565	Adherent to other organs or structures clinically with no microscopic examination Tumor found in adhesion(s) if microscopic examination performed	T4b	T4	RE	RE
570	Adherent to other organs or structures, NOS	T4b	T4	RE	RE
600	All colon sites: Small intestine Cecum: Greater omentum Ascending colon: Greater omentum Liver, right lobe Transverse colon and flexures: Gallbladder/bile ducts Kidney Liver Pancreas Spleen	T4b	T4	RE	RE

85

Lymphatics of Colon / Rectum

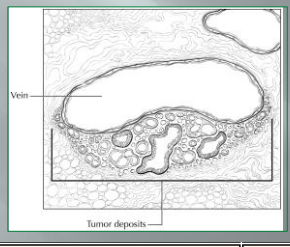


Modified AJCC Image - The regional lymph nodes of the colon and rectum are colored by anatomic location.

86

CS Lymph Nodes

050	TD in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues WITHOUT regional nodal metastasis Stated as N1c with no other information on regional lymph nodes	N1c	N1	RN	RN



110	Regional lymph nodes for all colon sites: Colic, NOS Epicolic (adjacent to bowel wall) Mesocolic, NOS Paracolic/pericolic	^	*	RN	RN

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87

CS Lymph Nodes

210	Regional lymph nodes, for specific colon sites: Cecum: Cecal: Anterior (prececal), Posterior (retrocecal); NOS Ileocolic Right colic Ascending colon: Ileocolic Middle colic Right colic Transverse colon and flexures: Inferior mesenteric for splenic flexure only Left colic for splenic flexure only Middle colic Right colic for hepatic flexure only Descending colon: Inferior mesenteric Left colic Sigmoid colon: Inferior mesenteric Sigmoidal (sigmoid mesenteric) Superior hemorrhoidal Superior rectal	^	*	RN	RN
220	Regional lymph nodes for descending colon: Sigmoid	^	*	D	RN
300	Regional lymph nodes for all colon sites: Mesenteric, NOS Regional lymph node(s), NOS	^	*	RN	RN

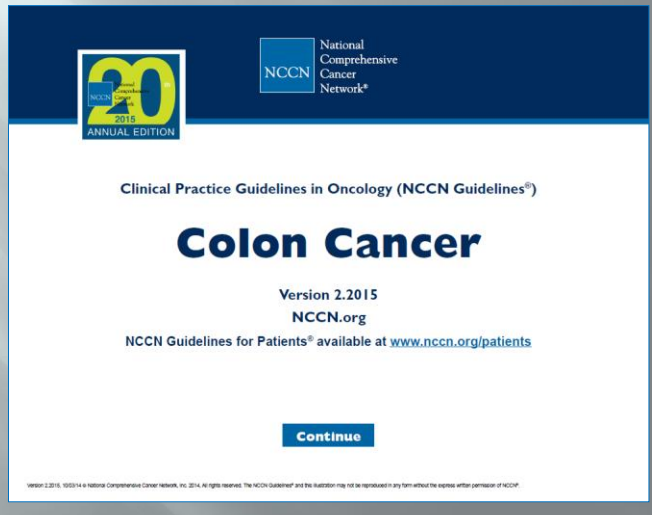
88

CS Lymph Nodes

400	OBSOLETE DATA CONVERTED V0203 See code 430 Stated as N1 pathologic	ERROR	ERROR	ERROR	ERROR
410	Stated as pathologic N1a with no other pathologic information on regional lymph nodes	N1a	N1	RN	RN
420	Stated as pathologic N1b with no other pathologic information on regional lymph nodes	N1b	N1	RN	RN
430	Stated as pathologic N1 [NOS] with no other pathologic information on regional lymph nodes	N1NOS	N1	RN	RN
450	OBSOLETE DATA CONVERTED V0203 See code 480 Stated as N2 pathologic	ERROR	ERROR	ERROR	ERROR
460	Stated as pathologic N2a with no other pathologic information on regional lymph nodes	N2a	N2	RN	RN
470	Stated as pathologic N2b with no other pathologic information on regional lymph nodes	N2b	N2	RN	RN
480	Stated as pathologic N2 [NOS] with no other pathologic information on regional lymph nodes	N2NOS	N2	RN	RN

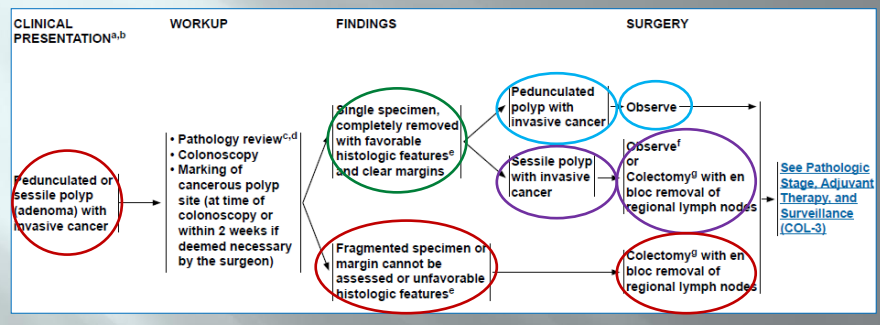
89

Treatment



90

Polyp Removal – Any Type



- Favorable histologic features: grade 1 or 2, no angiolymphatic invasion, and negative margin of resection. There is no consensus as to the definition of what constitutes a positive margin of resection. A positive margin has been defined as 1) tumor <1 mm from the transected margin, 2) tumor <2 mm from the transected margin, and 3) tumor cells present within the diathermy of the transected margin.[1-4]
- Unfavorable histologic features: grade 3 or 4, angiolymphatic invasion, or a "positive margin." See the positive margin definition above.

There is controversy as to whether malignant colorectal polyps with a sessile configuration can be successfully treated by endoscopic removal. The literature seems to indicate that endoscopically removed sessile malignant polyps have a significantly greater incidence of adverse outcomes (residual disease, recurrent disease, mortality, and hematogenous metastasis, but not lymph node metastasis) than do polypoid malignant polyps. However, when one closely looks at the data, configuration by itself is not a significant variable for adverse outcome, and endoscopically removed malignant sessile polyps with grade I or II histology, negative margins, and no lymphovascular invasion can be successfully treated with endoscopic polypectomy.[3-7]

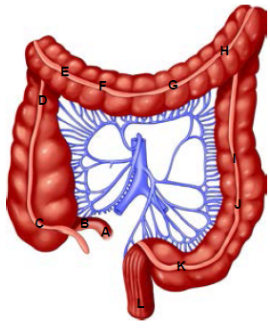
91

Surgical Resection

DEFINITIONS OF COMMON COLORECTAL RESECTIONS

The extent of colorectal resection depends on the location of the tumor, any underlying condition (eg, inflammatory bowel disease, hereditary syndrome), and the vascular supply to the colorectum.

Definitions of common colorectal resections are as follows:[1]



A through C	Ileocecectomy
A through D	Ascending colectomy
A through F	Right hemicolectomy
A through G	Extended right hemicolectomy
E through H	Transverse colectomy
G through I	Left hemicolectomy
F through I	Extended left hemicolectomy
J through K	Sigmoid colectomy
A through J	Subtotal colectomy
A through K	Total colectomy
K through L	Low anterior resection with sphincter preservation
K through L	Abdominoperineal resection without sphincter preservation

[1]Adapted and reprinted with permission from Bullard KM and Rothenberger DA. (2005). Colon, Rectum, and Anus. In Brunicardi C (Ed.) Schwartz's Principles of Surgery, 8th Edition, page 1069. McGraw Hill: New York, NY.

NCCN Guidelines – Colorectal Cancer Screening

92

Neoadjuvant (Pre-Surgical) Treatment

- Advanced Stage at Diagnosis
  - Pre-Surgical Treatment with:
    - FOLFIRI or
    - mFOLFOX6 or
    - CapeOx plus
    - Any of Above may also add bevacizumab
    - If KRAS/NRAS Wild Type may also add
      - Panitumumab or Cetuximab
  - Unresectable or Post-Surgical Treatment with:
    - Same as Above or
    - Capecitabine
    - FOLFOXIRI
    - Irinotecan
    - IROX
    - Regorafenib

93

Adjuvant (Post-Surgical) Treatment

- Chemotherapy alone, or in combination with radiation, is given before and/or after surgery when cancer has deeply penetrated the bowel wall or spread to lymph nodes.
- FOLFOX/CapeOx regimens superior to 5-FU/leucovorin
- Bevacizumab, cetuximab, panitumumab, or irinotecan should NOT be used as adjuvant therapy for Stage II/III
- Adjuvant chemotherapy for colon cancer in otherwise healthy patients 70 years of age and older is equally effective as in younger patients.
- Toxicity in older patients can be limited if certain drugs (e.g., irinotecan, oxaliplatin) are avoided.

94

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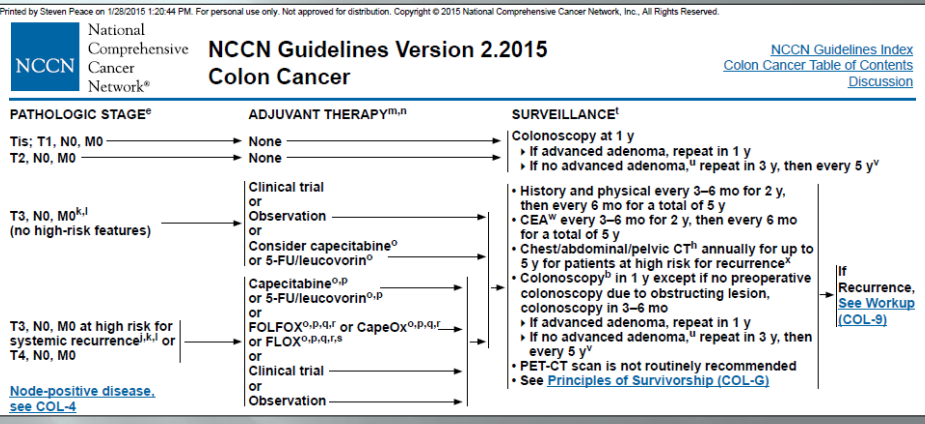
NCCN Guidelines Index
Colon Cancer Table of Contents
Discussion



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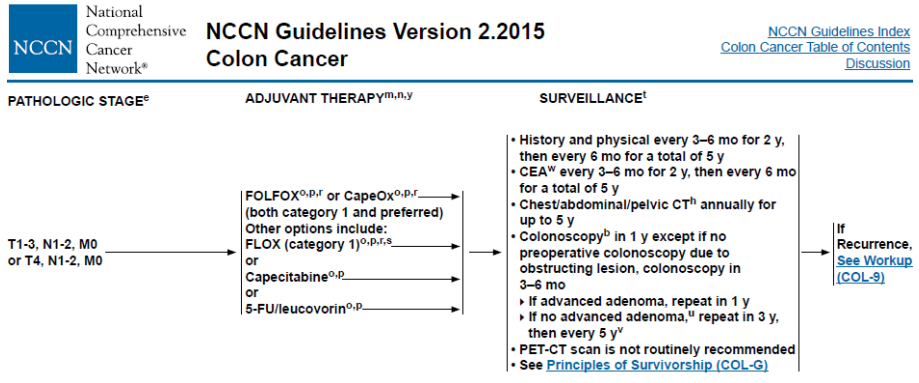
NCCN Guidelines Index
Colon Cancer Table of Contents
Discussion



ORAL CHEMOTHERAPY

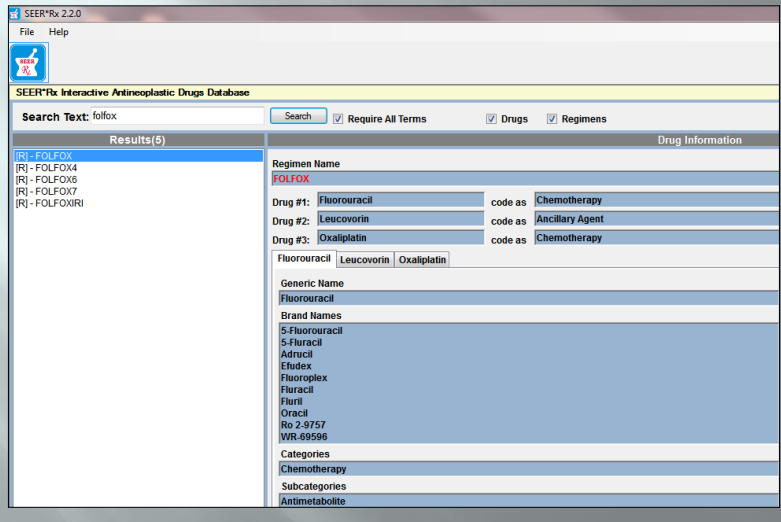
Capecitabine

Brand Name: Xeloda®

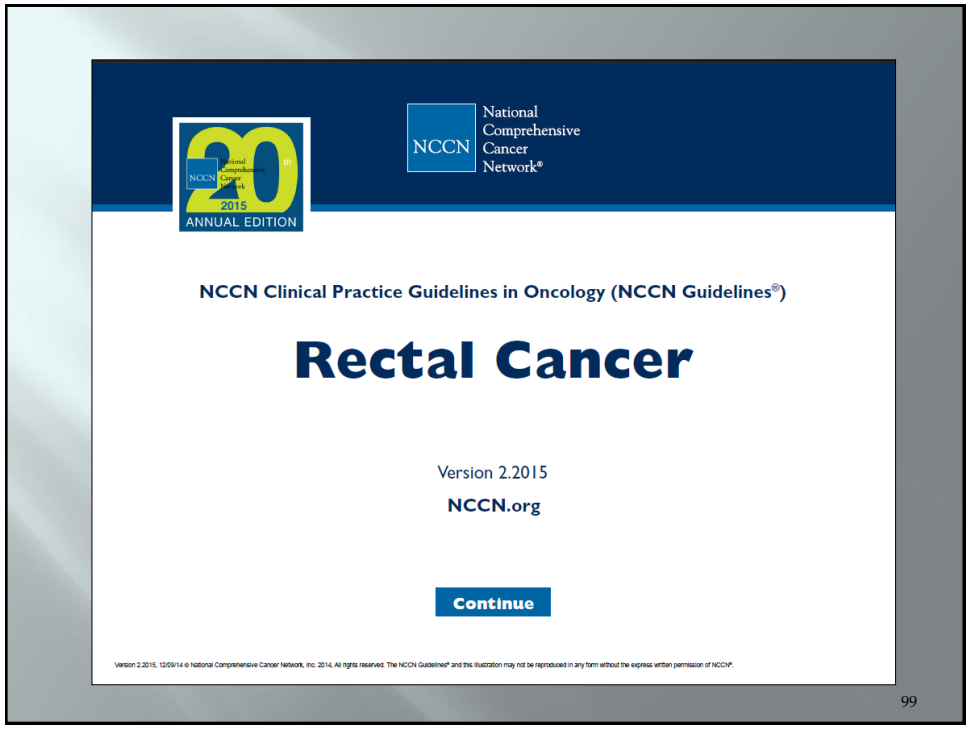
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3066368

97

Use SEER*Rx to Code Agents



98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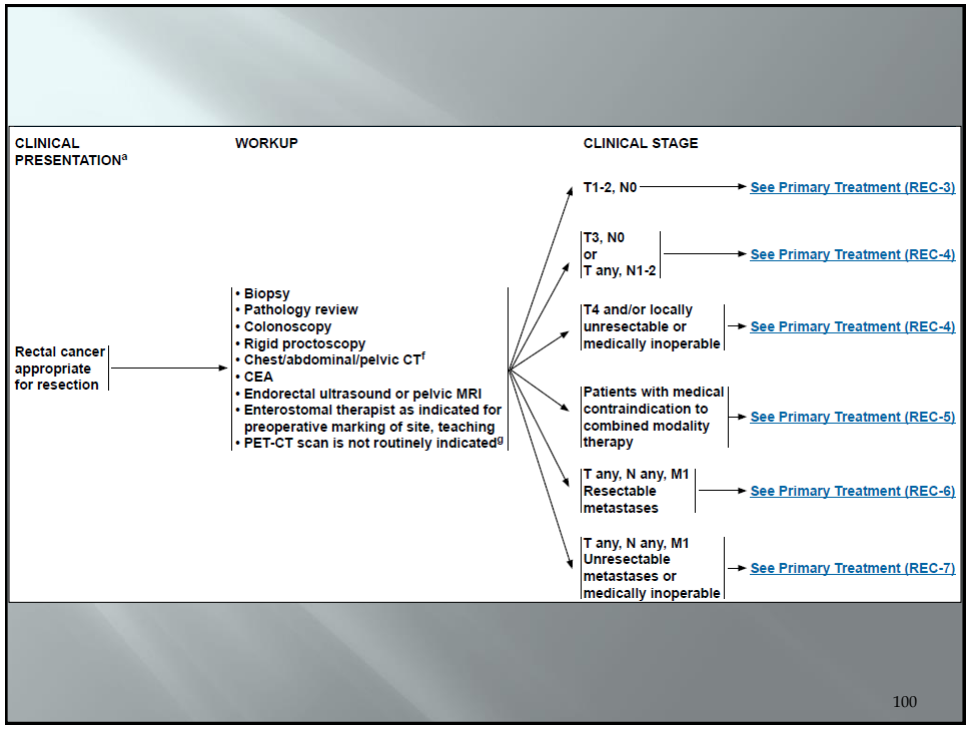
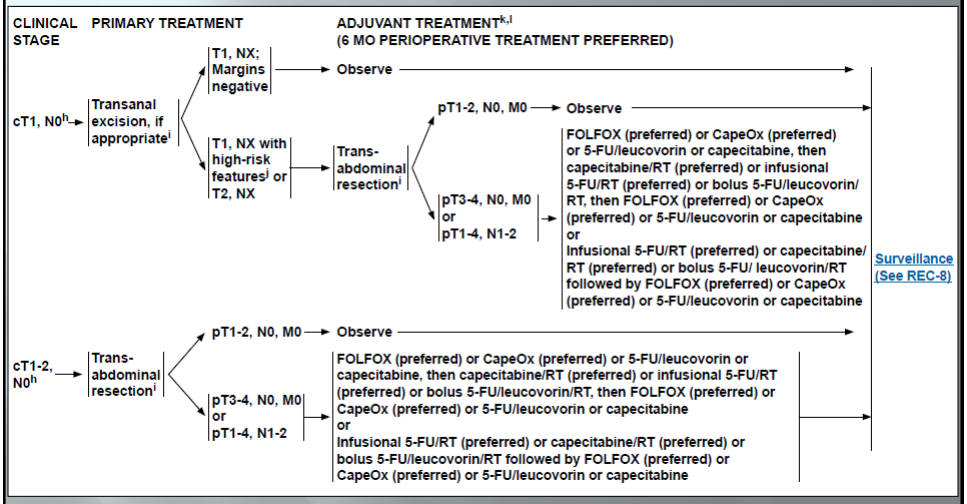
99


CLINICAL PRESENTATION[a]
WORKUP
CLINICAL STAGE
Rectal cancer appropriate for resection
• Biopsy
• Pathology review
• Colonoscopy
• Rigid proctoscopy
• Chest/abdominal/pelvic CT[f]
• CEA
• Endorectal ultrasound or pelvic MRI
• Enterostomal therapist as indicated for preoperative marking of site, teaching
• PET-CT scan is not routinely indicated[g]
T1-2, N0 → See Primary Treatment (REC-3)
T3, N0 or T any, N1-2 → See Primary Treatment (REC-4)
T4 and/or locally unresectable or medically inoperable → See Primary Treatment (REC-4)
Patients with medical contraindication to combined modality therapy → See Primary Treatment (REC-5)
T any, N any, M1 Resectable metastases → See Primary Treatment (REC-6)
T any, N any, M1 Unresectable metastases or medically inoperable → See Primary Treatment (REC-7)

100

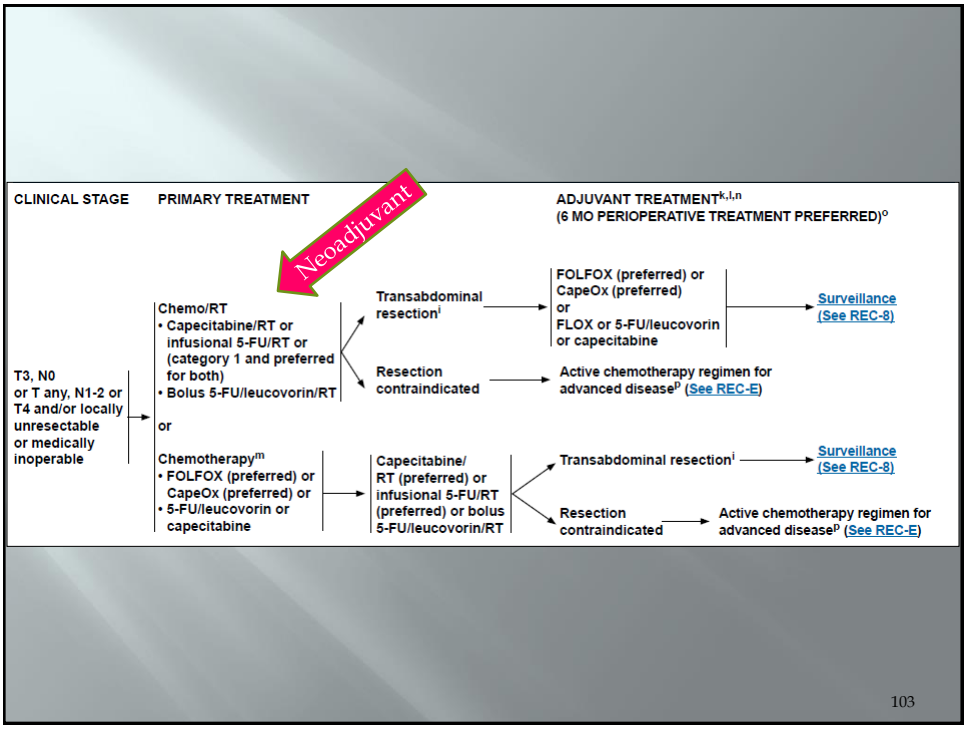


101

Neoadjuvant (Pre-Surgical) Treatment

- Colon – seldom used except for locally advanced tumors to shrink size of primary tumor mass or to reduce size of metastasis deemed resectable.
- Rectum – used for all stages > T2
- Chemo plus or minus XRT to primary tumor
- Not neoadjuvant unless surgery is performed after treatment – if no response may not resect.

102



103

What's New – Colorectal Cancer

- Next Generation Genetic Testing
  - Prognostic, predictive and response to treatments
  - Oncotype Dx/Colon Cancer Assay/ColoPrint/ColDx
- Chemoprevention – statins/vitamin D/calcium
- Earlier Detection and High Risk Group Screening
- Newer Surgical Techniques
  - Laparoscopic Resection
  - Robotic Surgery
- Targeted Therapies
  - Bevacizumab (Avastin)
  - Cetuximab (Erbitux)
  - Panitumumab (Vectibix)
- Immunotherapy – clinical trials for vaccine tx

104

What's New – Colorectal Cancer

- Next Generation Targeted Therapies
  - EGFR Inhibitors – epidermal growth factor receptor (EGFR) inhibitors work by slowing or stopping or otherwise interrupting cancer cell growth and/or proliferation of cancer cells in primary tumor and metastatic tumor(s).
    - Cetuximab
    - Panitumumab
  - VEGF Inhibitors – vascular endothelial growth factor (VEGF) inhibitors work by preventing the formation of new blood vessels necessary for tumor growth.
    - Bevacizumab
    - Aflibercept or Ziv-Aflibercept
    - Regorafenib
    - Ramucirumab

105

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  - Colon Cancer – 2015
  - Rectal Cancer - 2015

106

Questions