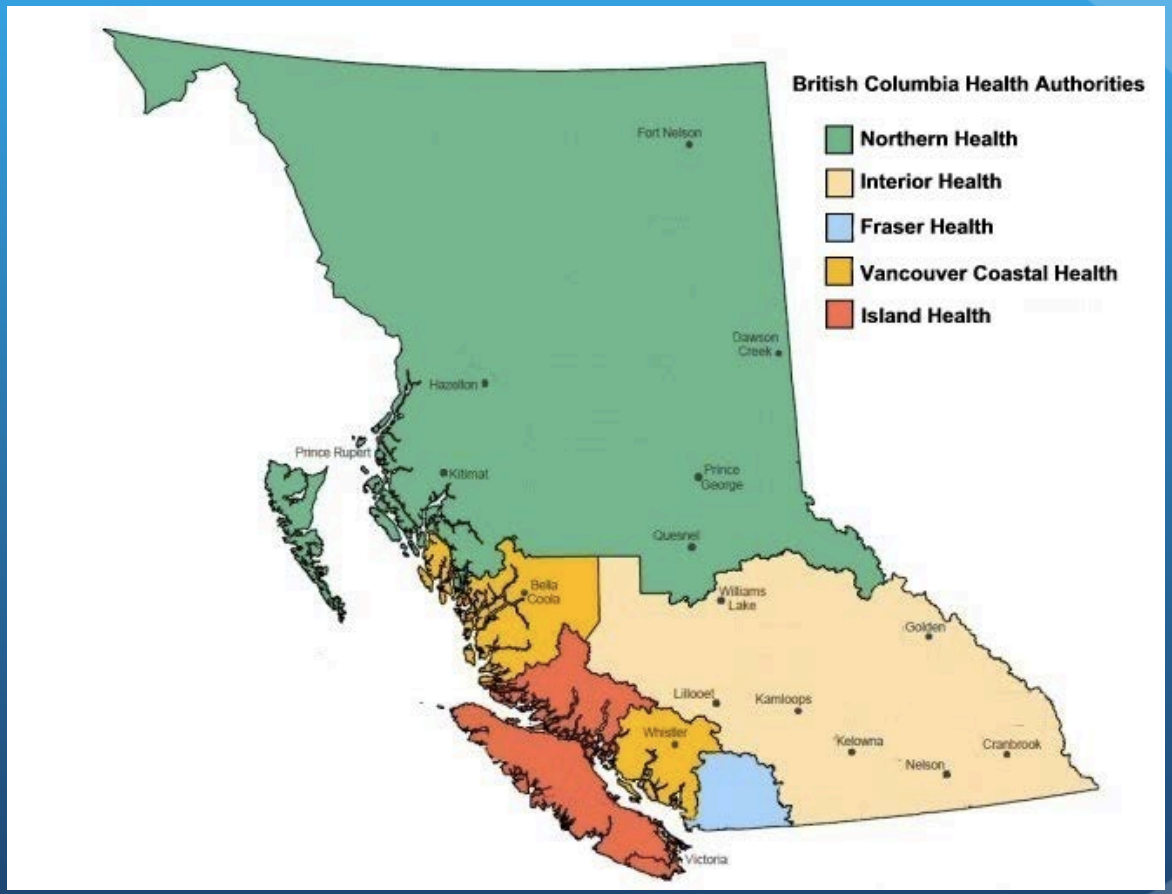
Colorectal Cancer

Dr. Sian Shuel

GPO

BCCA Abbotsford Centre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Disclosures

- Dr. Sian Shuel
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  - No disclosures
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  - Amgen, Bayer - honoraria

Learning Objectives

- Describe key patient care issues in the management of colorectal cancer
- Identify strategies to optimize outcomes for patients with colorectal cancer
- Identify and address the unique challenges in management of colorectal cancer.

Outline

- Risk factors for CRC
- CRC screening guidelines
- Approach to symptoms concerning for CRC
- Staging for colon cancer
- Adjuvant systemic therapy
- Follow up after adjuvant therapy
- Surgical resection of hepatic metastases
- Systemic therapy with palliative intent

Case

- ED, a 65 year old female booked an appointment with you today to discuss her risks for developing colon cancer. She is worried as she recently discovered his mother has a history of colon cancer.
- What would you like to know to help you identify her risk factors?

Risk Factors

- Age
  - After the age of 50, the risk of developing CRC increases [6]
  - 90% diagnosed after age 50

Probability of developing cancer in the next 10 years by age

	Lifetime prob. Developing CRC	Lifetime prob. Dying from CRC	30-39	40-49	50-59	60-69	70-79	80-89
Men	7.5	3.6	0.1	0.2	0.8	2.0	3.4	3.3
women	6.4	3.1	0.1	0.2	0.6	1.3	2.3	2.7

Source: GPAC 2013

Risk Factors [7]

- Family history
  - Any first degree relatives and age at diagnosis of CRC
  - Female relatives with endometrial cancer (Lynch Syndrome)
- History of inflammatory bowel disease (at least 8 years)
- Previous adenomatous polyps
- Previous colorectal cancer
- Lifestyle
  - Obesity, low physical activity, smoking, excessive alcohol, high fat and low fibre diets, red meat

System Review

System Review

- Rectal bleeding
- Diarrhea
- Weight loss
- Abdominal pain
- Loss of appetite
- Change in stooling frequency or caliber
- CRC screening in the past

Back to the case

- System review negative
  - For rectal bleeding, weight loss, loss of appetite, change in stooling frequency / caliber, diarrhea, abdo pain.

- Personal history negative for IBD, adenomatous polyps, CRC

- Healthy Lifestyle
  - Lifetime nonsmoker, Mediterranean diet, plays tennis twice a week, drinks 2 glasses wine per week, not overweight
- Mom was 64 at diagnosis
- No other 1st degree relatives with CRC
- Never had FIT or colonoscopy

- Does ED need to be screened for CRC?
- If so, how?

BC Colon Screening Program Who?

- Asymptomatic men and women ages 50 to 74

Screening: How?

- Fecal Immunochemical Test (FIT) for average risk colorectal cancer screening
  - 88% sensitivity
  - 90% specificity for detecting CRC

Screening: How?

- Screening colonoscopy for higher than average risk
  - One first degree relative diagnosed with colorectal cancer under the age of 60 (10 years prior to index case or age 40 – whichever is first)
  - Two or more first degree relatives diagnosed with colorectal cancer at any age
  - Personal history of adenomas

Screening: How Often?

- Average Risk
  - FIT every 2 years
  - Following a positive FIT and negative colonoscopy, FIT should resume in 10 years.

- Higher than average risk
  - Colonoscopy
    - Every 5 years if family history of colorectal cancer
    - In 5 years after diagnosed with low risk adenoma
    - In 3 years after diagnosed with high risk adenoma

FIT NOT Recommended If:

- Currently having symptoms
- Personal history of colon cancer
- Personal history of Crohn's or Ulcerative Colitis
- Normal flexible sigmoidoscopy or CT colonography within 5 years, normal colonoscopy within 10 years, normal FIT within 2 years
- Not medically fit to undergo colonoscopy

FIT Update (Nov 16/17)

- FIT temporarily suspended in BC Oct 3
  - Positives increased from 14% to over 20% from July to September (indicating too many false positives)
  - Believed to be a problem with the manufacturer reagent
  - Could take a number of months to resume

FIT Update (Nov 16/17)

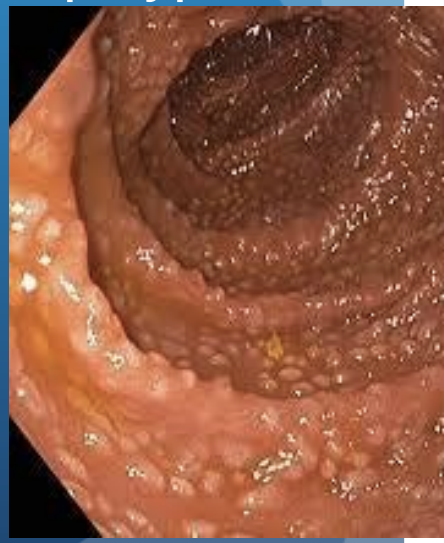
- Do not refer patients for FIT screening
- The Colon Screening Program will let physicians know once FIT is available
- No alternative test being recommended - complete the test when FIT becomes available

Lynch Syndrome (Hereditary nonpolyposis CRC)

- Due to germline mutation in mismatch repair gene
- Autosomal dominant inheritance
- Lifetime risk of CRC is 40-90%
- Earlier presentation of CRC
- Increased risk of other malignancies
- Screening program of yearly colonoscopy beginning at 20-25 years old

Familial adenomatous polyposis

- Due to mutations of adenomatous polyposis coli gene
- Autosomal dominant inheritance
- Develop between 100-1000 adenomatous colonic polyps by age 30
- 90% risk of developing colorectal cancer
- Mutation carriers should have yearly flexible sigmoidoscopy starting at puberty
- Once polyposis identified, colectomy indicated



Back to our case…

- ED presents to your office 4 years later with abdominal pain, occasional diarrhea, and occasional maroon stools.
- What else do you want to know?
  - Amount
  - Systemic symptoms
  - Change in frequency or caliber of stool

- Physical exam
  - Fullness and tenderness to right lower quadrant

- Labs
  - CBC and ferritin (reasonable if over 40 or other risks for colon cancer)

  - microcytic anemia (hemoglobin 117, MCV 72)

How do you proceed?

How do you proceed?

- Colonoscopy

Results

- Colonoscopy
  - “a circumferential constricting mass with a lumen too narrow to pass the endoscope through to reach the cecum. We took multiple biopsies.”

- Pathology
  - “invasive moderately differentiated adenocarcinoma”

What investigations are now recommended?

What investigations are now recommended?

- CT chest abdomen pelvis
- CEA
  - Guides subsequent follow up

- CT chest abdo pelvis
  - Thickening of the cecal wall
  - No evidence of metastatic disease
- CEA
  - Elevated at 9.7

Next Step?

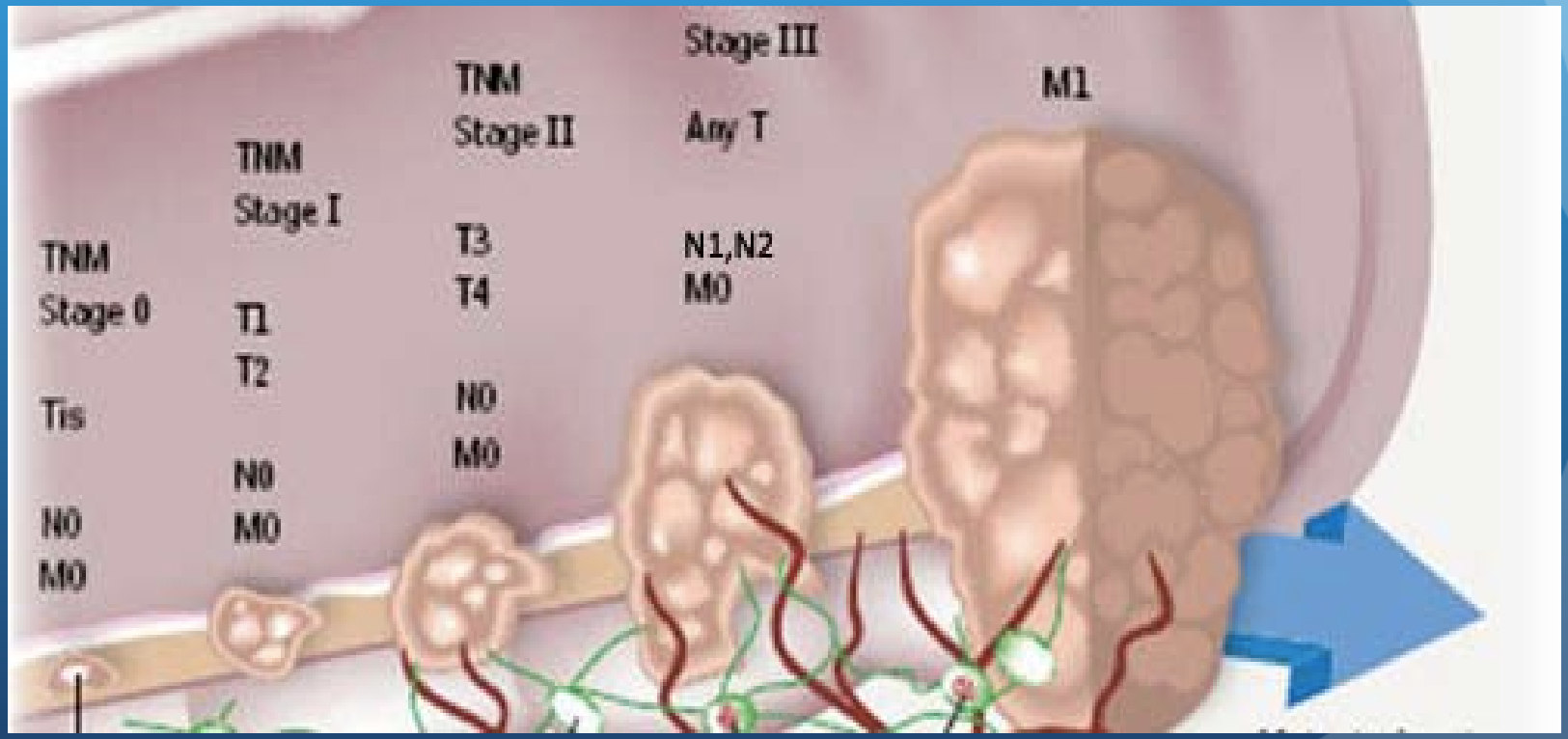
Next step?

- Segmental colectomy (right hemicolectomy)
  - At least 5cm of grossly normal looking tissue from distal and proximal margins
  - En bloc regional lymphadenectomy (12 or more lymph nodes removed)
  - Primary anastomosis

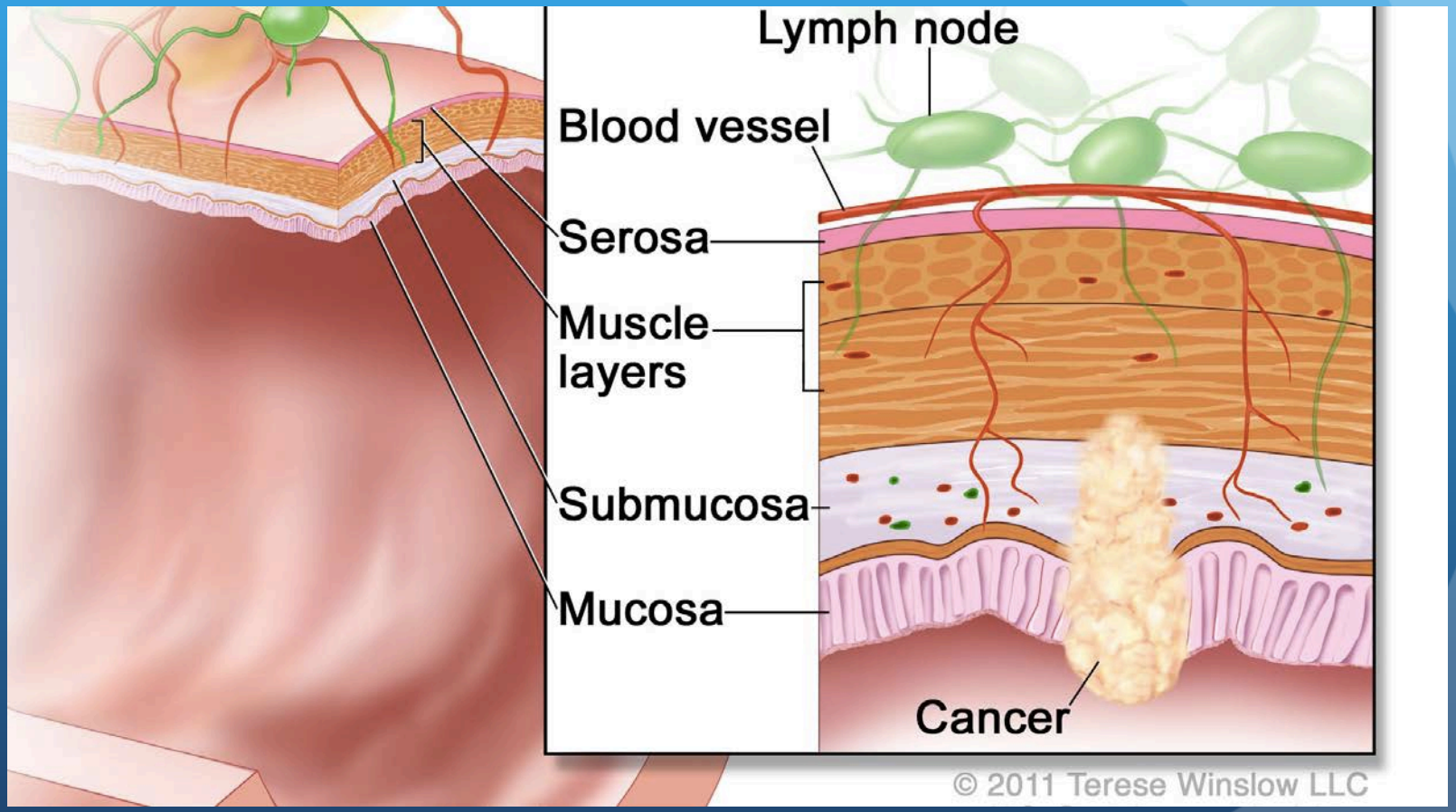
Pathology report

- Cecal moderately differentiated adenocarcinoma invading into the pericolic fat.
- No perforation
- Lymphovascular invasion present
- Perineural invasion present
- 7/15 lymph nodes positive
- What stage cancer does our patient have?

TNM Staging


TNM
Stage 0
Tis
N0
M0
TNM
Stage I
T1
T2
N0
M0
TNM
Stage II
T3
T4
N0
M0
Stage III
Any T
N1,N2
M0
M1

TNM Staging


Lymph node
Blood vessel
Serosa
Muscle layers
Submucosa
Mucosa
Cancer
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Our case:

- pT3 pN2b Mx right sided colon cancer
- Stage 3 (any T, N1-2, M0)

Treatment Options [4]

- Stage 0 (cancer limited to mucosa; no invasion of lamina propria)
  - Endoscopic polypectomy with margins clear
  - Segmental colectomy if lesions not amenable to local excision
- Stage 1 (T1-T2, N0, M0)
  - Segmental colectomy
  - No role for adjuvant chemotherapy

Treatment Options – stage 2

- Stage 2 (T3-T4, N0, M0)
  - Controversial
  - High risk features:
    - Inadequate lymph node sampling (<12 nodes)
    - T4
    - Complete obstruction
    - Perforation
    - Poor differentiation
    - Lymphovascular invasion
    - Perineural invasion
    - Positive margins

Treatment Options – stage 2

- Tumor microsatellite instability [5]
  - High levels (MSI-H) associated with favourable prognosis (and lack of benefit of 5-FU chemotherapy)

Treatment Options – stage 2

- stage 2A (T3N0) with high risk features may be offered adjuvant capecitabine for 6 months

- stage 2B (T4aN0) and stage 2C (T4bN0)
  - may be offered adjuvant capecitabine
  - modified FOLFOX6 (GIAJFFOX) may be considered if more high risk features in very motivated patients

- Early referral to medical oncology for stage 2 advised
  - Adjuvant chemotherapy should start 4 weeks after surgery if possible

Treatment Options – stage 3

- Stage 3 (any T, N1-N2, M0)
  - Segmental colectomy
  - Adjuvant chemotherapy to start about 4 weeks post op
  - Options include FOLFOX or CAPOX for 6 months
  - Capecitabine or 5FU for less fit or less interested patients

  - For patients with low risk disease (T1-3, N1) 3 months of oxaliplatin-based chemo is being looked at but results are still preliminary and initial evidence not overwhelming

Back to our case:

- Adjuvant CAPOX, switched to FOLFOX due to side effects
- Completed 6 months of therapy
- Completion CT scan negative
- CEA 1

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