429 Biochemistry team

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Some facts about Colon Cancer:

- Incidence: 155,000 cases/year (colorectal)

- Deaths per Year: 60,000

- 2nd most common cause of cancer deaths in men (after prostate cancer)

- 3rd most common cause of death in women

- Overall 5 year survival: about 50%

- 90% of cases in those > 50 years of age

Colorectal Cancer (CRC):

- Colorectal cancer is cancer that occurs in the colon or rectum

- Colon is the large intestine or large bowel

- The rectum is the passageway that connects the colon to the anus
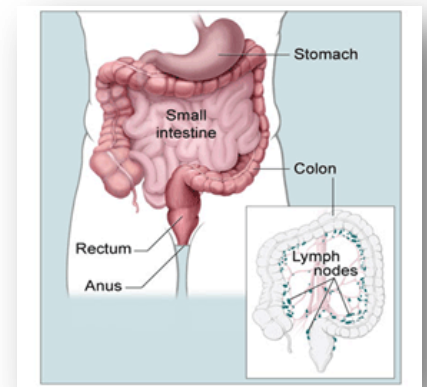
Colorectal Cancer: Distribution and Clinical Presentation:

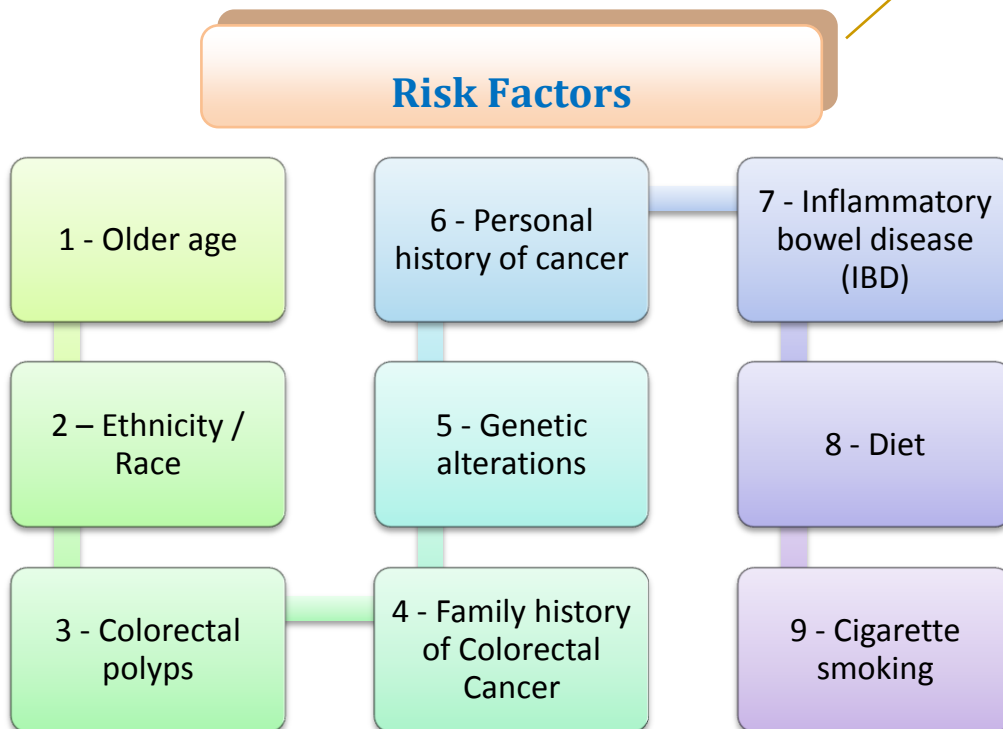depends on the site of the Colorectal Cancer .

most common: rectum &sigmoid colon
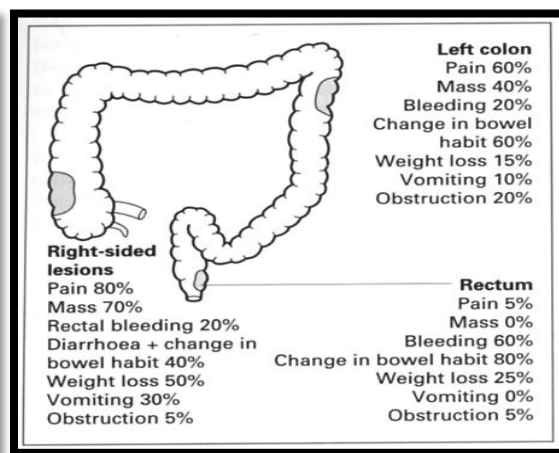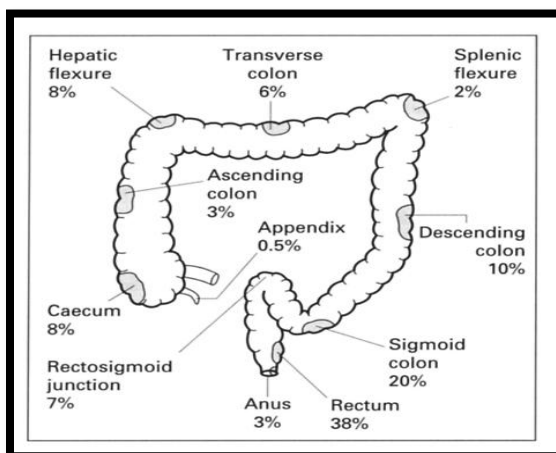
Symptoms Associated with CRC :

- Rectal bleeding
- Change in bowel habits
- Obstruction & vomiting
- Abdominal pain & mass
- Weight loss
- Iron-deficiency anemia (due to bleeding)

Colorectal Cancer: Types

- Sporadic (95%) {{ occurring in individuals without a family history of cancer}}

- Familial (5%) {{ that occurs in families and often occur at an early age }} (more severe)

A risk factor is something that may increase the chance of developing a disease.

Risk Factors

1 - Older age	6 - Personal history of cancer	7 - Inflammatory bowel disease (IBD)
2 – Ethnicity / Race	5 - Genetic alterations	8 - Diet
3 - Colorectal polyps	4 - Family history of Colorectal Cancer	9 - Cigarette smoking

- About **90 percent** of people diagnosed with colon cancer **are older than 50**
- Colon cancer can occur in younger people, but it occurs much less frequently.

1 - Older age

- African-Americans have a greater risk of colon cancer than do people of other races
- Jews of Eastern European descent (Ashkenazi Jews) have one of the highest colorectal cancer risks of any ethnic group in the world **(b/c they married from the same family)**

2 – Ethnicity / Race

- Polyps are growths on the inner wall of the colon or rectum
- They are common in people **over age 50**
- Most polyps are benign (not cancer), but some polyps (adenomas) can become cancer

3 - Colorectal polyps

- - Close relatives (parents, brothers, sisters, or children) of a person with a history of colorectal cancer are somewhat **more likely** to develop this disease themselves
- - If many close relatives have a history of colorectal cancer, **the risk is even greater**

4 - Family history of Colorectal Cancer

- Changes in certain genes increase the risk of colorectal cancer.
- **like:**
  1- Hereditary nonpolyposis colon cancer (HNPCC)
  2- Familial adenomatous polyposis (FAP)

5 - Genetic alterations

- - A person who has already had colorectal cancer may develop colorectal cancer a second time even it treat it
- - Also, women with a history of cancer of the ovary, uterus (endometrium), or breast are at a somewhat **higher risk** of developing colorectal cancer

6- Personal history of cancer

- IBD includes *ulcerative colitis* and *Crohn's disease*
- It is a condition in which the colon is inflamed over a long period of time
- People who have had IBD for many years **often develop dysplasia**
- **Dysplasia** is a term used to describe cells in the lining of the colon or rectum that look abnormal **(but not like true cancer cells)** when viewed under a microscope. These cells can change into cancer over time.

7 - Inflammatory bowel disease (IBD)
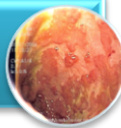
- Studies suggest that diets high in fat (especially animal fat) and low in calcium, folate, and fiber may **increase the risk** of colorectal cancer
- Also, some studies suggest that people who eat a diet very low in fruits and vegetables.. **(Also caffeine)** may have a higher risk of colorectal cancer

8 - Diet

- A person who smokes cigarettes may be at **increased risk** of developing polyps and colorectal cancer
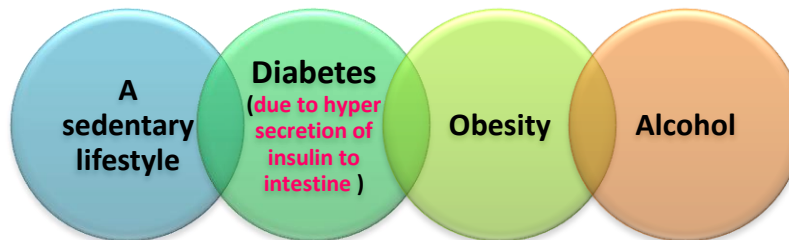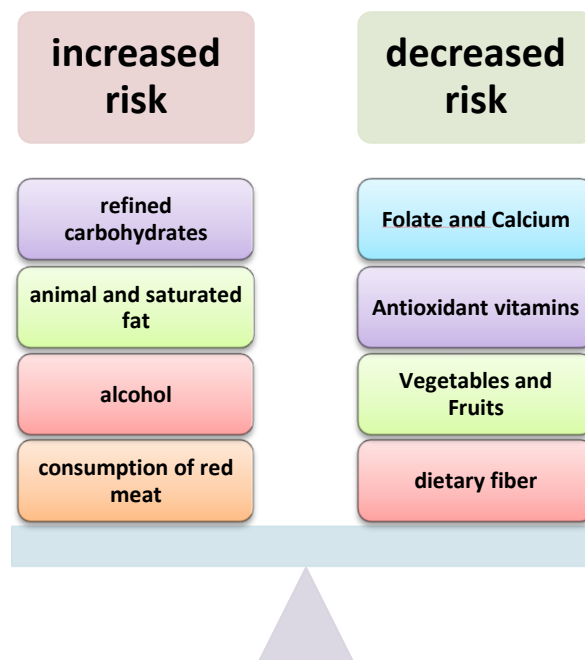
9 - Cigarette smoking

Genetic alterations	Hereditary nonpolyposis colon cancer (HNPCC)	Familial adenomatous polyposis (FAP)
Definition	the most common type of inherited (genetic) colorectal cancer	It is a rare, inherited condition in which hundreds of polyps form in the colon and rectum
The cause	mutations of mismatch repair (MMR) genes	mutations in a specific gene called adenomatosis polyposis coli (APC)
The age	The average age at diagnosis of colon cancer is 44	Unless FAP is treated, it usually leads to colorectal cancer by age 40

Poyposis: means multiple polyps.

Other Risk Factors

A sedentary lifestyle

Diabetes (due to hyper secretion of insulin to intestine)

Obesity

Alcohol

Dietary factors implicated in colorectal carcinogenesis

increased risk

- refined carbohydrates
- animal and saturated fat
- alcohol
- consumption of red meat

decreased risk

- Folate and Calcium
- Antioxidant vitamins
- Vegetables and Fruits
- dietary fiber

What are Tumor Markers?

- Biological substances synthesized and released by cancer cells or produced by the host in response to the presence of tumor

- Detected in:

  - a solid tumor,
  - circulating tumor cells
  - lymph nodes
  - bone marrow
  - peripheral blood
  - or in other body fluids (urine, pleural, peritoneal, …)

Potential Uses of Tumor Markers:

- Population Screening (Some, e.g., PSA (prostate specific antigen) for men > 50 years)

- Diagnosis (as a part of work up for patients)

- Prognosis (The most valuable clinical use):

  - ✓ Post-operative evaluation
  - ✓ Monitor treatment response
  - ✓ Surveillance for recurrence

  > So if treatment useful → ↓ marker
  >
  > And the opposite is true

- Tumor Specific Proteins
- Expressed only in tumor cells

- Non-Specific Proteins or Markers Related to Malignant Cells
- Oncofetal proteins : expressed by cells as they de-differentiate and take on embryonic characteristics
  - α-FP : Hepatocellular carcinoma, testicular
  - CEA : GI tumors

- Cell Specific Proteins Overexpressed in Malignant Cells
- Proteins expressed normally by differentiated cells, but are expressed at higher rates in the corresponding tumor cells
  - PSA : prostate cancer

Carcinoembryonic Antigen:

- Carcinoembryonic antigen (CEA)

  - **fetal glycoprotein** found on cell surfaces, produced by fetal GI tract, liver, and pancreas (not precent at birth)

  - Normal serum and tissue fluid value：**<3.0** ng/ml

  - Circulating half-life：**weeks**

  - Detect early relapse of colorectal cancer and prognostic indicator

    - **Normal pretherapy CEA:** lower metastasis incidence

    - **High initial CEA:** higher metastasis incidence (Reach the lymph node > to circulation > other tissue)

  - **In 2/3** of patients an elevated CEA may be the **1ˢᵗ indication of relapse**

CEA:

- Found also in **30~50%** of breast cancer, small cell lung cancer, ovarian and cervical cancer

- Elevation **(<10** ng/ml) in smokers, COPD, inflammatory or peptic bowel disease, liver inflammation or cirrhosis, renal failure, fibrocystic breast disease

Marker	Associated non-malignant conditions
AFP	Viral hepatitis, liver injury, inflammatory bowel disease, pregnancy
BHCG	Testicular failure, marijuana smokers, pregnancy
CEA	Smokers, inflammatory bowel disease, hepatitis, cirrhosis, pancreatitis, gastritis
CA 125	Peritoneal irritation, endometriosis, pelvic inflammatory disease, hepatitis, pregnancy

Early Detection of Recurrence:

- **CEA**

  - ✓ **Useful even** for those with normal level at first resection

  - ✓ **Cost-effective, Safe**

- **Patients with prior colorectal cancer 1.5 – 3 times more likely than general population to develop a second colorectal cancer**

- **Should continue serial screening colonoscopy every 3-5 years**