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Cancer Causing Bacteria: A Review on Colorectal Cancer

Shrinu G. Ambade, Pratik B. Mandlik, Sanket A. Bhaik
Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India

Abstract: *An increasing number of cancer cases have been reported throughout the years. Many cancers are linked to an unhealthy lifestyle and heredity. However, many do not know, infections caused by germs such as bacteria, viruses, fungi and sometimes parasites, can also lead to the development of cancer. In this review, we discuss the links between types of bacteria and cancer. Many viruses associated with human cancer are classified as human carcinogens by the International Agency for Research on Cancer, IARC. The cancer-causing germs described are Helicobacter pylori (stomach cancer), Epstein-Barr virus (stomach cancer and lymphoma), Hepatitis B and C (liver cancer), Aspergillus spp. (liver cancer), Opisthorchis viverrine (bile duct cancer), Clonorchis sinensis (bile duct cancer), Fusobacterium nucleatum (colorectal cancer), Schistosoma haematobium (bladder cancer); Human Papillomavirus (cervical cancer), and Kaposi's Sarcoma Herpes Virus (Kaposi's sarcoma). We will also discuss the cancer of the colorectal Fusobacterium Nucleatum.[1]*

Keywords: Cancer, Bacteria, Carcinogens, Parasites

I. INTRODUCTION

Cancer is a disease in which cells break down uncontrollably and attack nearby tissues. This disease is a major cause of sickness and death. More than 100 types of cancer are being evaluated by 2020. Since the latest annual cancer report for 2020, the World Health Organization (WHO) estimates that more than 19.2 million new people are diagnosed and 9.9 million died of cancer. From a recent 2021 cancer report, the American Cancer Society estimates that more than 1.9 million new cases have been reported in the United States.[1] Carcinogenesis and the progression of cancer often do not appear on the outside; many cancers, such as pancreatic and colorectal cancers (CRC) are not detected until later in life. Carcinogenesis is manifested in cancer caused by infectious diseases, in which different agents are associated with different types of cancer. This review will define ten interacting agents whose roles have been confirmed in carcinogenesis.[5]

***Kaposi Sarcoma Herpesvirus*:** Kaposi sarcoma (KS) is **caused by a virus called Kaposi sarcoma - associated herpesvirus (KSHV), also known as human herpesvirus 8 (HHV8).** KSHV belongs to the same family as the Epstein-Barr virus (EBV), a virus that causes infectious mononucleosis (mono) and is linked to several types of cancer.[1]

***Hepatitis / Aspergillus spp*:** Hepatitis means **inflammation of the liver.** The liver is an important organ that utilizes nutrients, filters blood, and fights infections. When the liver becomes swollen or damaged, its function can be affected. Excessive use of alcohol, toxins, other drugs, and certain medical conditions can cause cirrhosis of the liver. It can cause live cancer. [12]

***Aspergillus spp*:** Aspergillus species are a **filamentous fungus commonly found in soil, decaying plants, and seeds and seeds, where they thrive as saprophytes.** Aspergillus strains can occasionally be dangerous to humans. It can also cause liver cancer. [1]

***Fusobacterium nucleatum*:** Fusobacterium nucleatum is **an oral bacterium, associated with the oral cavity, which plays a role in periodontal disease.** This organism is commonly found in a variety of monocultured microbial diseases as well as a mixture of humans and animals. It can cause Colorectal cancer. [14]

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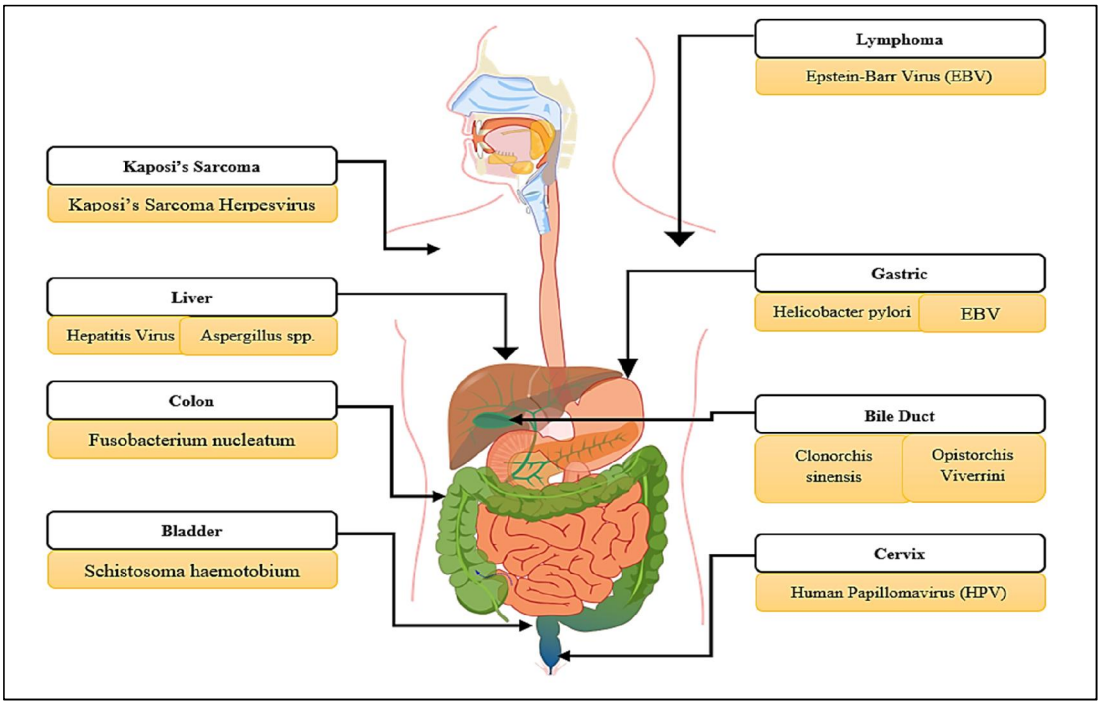
Schistosoma haematobium: Schistosoma haematobium (urinary blood fluke) is a type of digenetic trematode, which is part of a group (type) of blood flukes (Schistosoma). It can cause bladder cancer. [5]

***Epstein-Barr virus* (EBV):** *Epstein-Barr virus* **(EBV)**, also known as human herpesvirus 4, **is a member of the herpes virus family**. It is one of the most common human infections. EBV is found all over the world. Many people get EBV at some point in their lives. EBV is highly contagious through body fluids, especially saliva. It can cause lymphoma and stomach cancer. [10]

Figure 1: Tropism of Pathogens Associated with the Development of Human Cancer Described in this Review



***Helicobacter pylori*:** *Helicobacter pylori* (H. pylori) infection **occurs when the H bacteria. pylori infect your stomach**. This often happens in childhood. The most common cause of stomach ulcers (peptic ulcers), H infection. pylori may be present in more than half of the world's population. It can cause stomach cancer. [9]

Clonorchis sinensis / Opisthorchis viverrini: Trematode Clonorchis sinensis **(Chinese or oriental liver fluke)** is a food-borne virus that causes liver disease in Asia. This appears to be the only species involved in human infection. It can cause cancer in the Bile Duct. [5]

***Opisthorchis viverrini: Opisthorchis viverrini*,** a common name for the Southeast Asian liver fluke, a food-borne trematode parasite from the Opisthorchiidae family that infects the gallbladder and can cause cancer. [5]

***Human papillomavirus* (HPV): Human papillomavirus (HPV)** is **a highly contagious disease that is transmitted to humans through skin-to-skin contact.** There are more than 100 types of HPV, more than 40 of which are sexually transmitted and can affect your genitals, mouth, or throat and can also cause cervical cancer. [5]

Colorectal cancer that can be caused by Fusobacterium nucleatum is a very common and dangerous cancer.

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II. HOW COMMON IS COLORECTAL CANCER IS?

Apart from skin cancer, skin cancer is the third most commonly found in the United States. The American Cancer Society estimates for the number of colorectal cancer cases in the United States by 2022 are:

- 106,180 new cases of bowel cancer.
- 44,850 new cases of breast cancer.

The number of people diagnosed with bowel cancer or breast cancer each year has dropped dramatically since the mid-1980's, largely because many people are being tested and changing risk factors related to their lifestyle. From 2013 to 2017, incidence rates decreased by about 1% each year. But this decline tends to occur more frequently in older adults and the rising masks in younger adults from at least the mid-1990s. From 2012 to 2016, it increased annually by 2% for people under 50 and 1% for people aged 50 to 64.[2]

III. LIFELONG RISK OF COLORECTAL CANCER

Overall, the lifelong risk of colorectal cancer is: about one in 23 (4.3%) in men and one in 25 (4.0%) in women. Many other factors (described in Colorectal Cancer Risk Factors) may also affect your risk of colon cancer.[4]

V. COLORECTAL CANCER MORTALITY

In the United States, cervical cancer is the third leading cause of cancer-related deaths in both men and women, and the second most common cause of cancer in men and women. It is expected to cause 52,580 deaths in 2022.[20]

The mortality rate (100,000 deaths per year) due to colorectal cancer has dropped in both men and women for a few decades. There are many possible reasons for this. One of the reasons is that colorectal polyps are now more likely to be diagnosed and removed before they become cancerous, or that cancer is diagnosed early when it is easier to treat. In addition, treatment for colorectal cancer has improved over the past few decades. As a result, there are now more than 1.5 million colorectal cancer survivors in the United States. Although the overall mortality rate has continued to decline, the number of deaths from colorectal cancer among people under the age of 55 increased by 1% per year from 2008 to 2017.[25]

5.1 Colorectal Cancer

A. What Is Colorectal Cancer?

Colorectal cancer begins in the colon or rectum. These cancers can also be called colon cancer or rectal cancer, depending on where they start. Colon cancer and rectal cancer are often combined because they have many similarities.

Cancer begins when cells in the body begin to grow out of control.

Colon and rectum: To understand colorectal cancer, it is helpful to know the general structure and function of the colon and rectum.[27]

The colon and rectum form a large intestine, which is part of the digestive system, also called the gastrointestinal system (GI).

Most large intestines are colonized, a muscle tube about 1.5 feet long. Parts of the colon are called how food travels in them. The first part is called the ascending colon. It starts with a sac called the cecum, where undigested food enters from the small intestine. It continues up to the right side of the abdomen (belly).

- The second part is called the cross colony. It runs across the body from right to left.
- The third part is called the descending colon because it descends (goes down) to the left.
- The fourth part is called the sigmoid colon because of its “S” shape. The sigmoid colon joins the rectum, which also connects to the anus.
- The ascending and descending parts of the joint are called the proximal colon. The descending colon and sigmoid are called the distal colon.[26]

B. How does Colorectal Cancer Start?

- **Polyps in the colon or rectum:** Most colorectal cancers start as a growth on the inner lining of the colon or rectum. These growths are called polyps. Some types of polyps can turn into cancer over time (usually for many years), but not all polyps become cancerous. The probability that a polyp turns into cancer depends on the type

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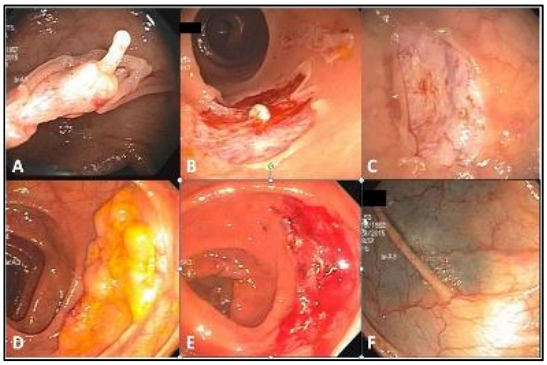
of polyp it is. There are different types of polyps.[23]

- **Adenomatous polyps (adenomas):** These polyps sometimes turn into cancer. Because of this, adenomas are called pre-cancerous conditions. The 3 types of adenomas are tubular, villous, and tubulovillous
- **Hyperplastic polyps and inflammatory polyps:** These polyps are very common, but usually do not have pre-cancerous cancer. Some people with large polyps (over 1cm) may need colorectal cancer screening with repeated colonoscopy.[13]
- **Sessile serrated polyps (SSP) and traditional serrated adenomas (TSA):** These polyps are often treated as adenomas because they have a higher risk of colorectal cancer.[28]

Other factors that can make a polyp more likely to develop cancer or increase a person's risk of developing colorectal cancer include:

- If a polyp more than 1 cm is found.
- If more than 3 polyps are found.
- If dysplasia appears in the polyp after discharge. Dysplasia is another dangerous condition. It means that there is a place in the polyp or colonic membrane or rectum where the cells look abnormal, but do not cause cancer.[17]

Fig 2: Polyp



C. How is Colorectal Cancer Spread?

If the cancer develops in the polyp, it can grow into a wall of the colon or rectum over time. The wall of the colon and rectum are made up of many layers. Skin cancer starts in the inner lining (mucous membranes) and can grow out of some or all of the layers. If the cancer cells are on the wall, they can grow into blood vessels or lymph nodes (small ducts that carry waste and fluids). From there, they can travel to nearby lymph nodes or distant parts of the body. The stage (spread rate) of colorectal cancer depends on how deep the wall grows and whether it spreads beyond the colon or rectum.[19]

5.2 Types of Cancers in the Colon and Rectum

The most common colorectal cancer is adenocarcinomas. These cancers begin in the mucous membranes to cover the inside of the colon and rectum. When doctors talk about colorectal cancer, they are probably always talking about this type. Some subtypes of adenocarcinoma, such as the signature ring and mucinous, may have a worse predictor (vision) than other subtypes of adenocarcinoma. Also, very rare forms of abscesses can also start in the colon and rectum. These include:

- Carcinoid growth: These start in specialized cells that produce hormones in the gut.
- Gastrointestinal stromal tumours (GISTs) originate from special cells in the colon wall called Castal interstitial cells. Some are healthy (not cancer). This Growth can be found anywhere in the digestive tract, but they are rarely colonized.
- Lymphomas are cancer cells of the immune system. It mainly begins in the lymph nodes, but can also begin in the colon, rectum, or other organs. Information on lymphomas of the digestive system can be found in Non-Hodgkin Lymphoma. Sarcoma can start in blood vessels, muscle groups, or other tissues connected to the colon wall and rectum. Sarcoma of the colon or rectum is rare.[8]

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5.3 Reducing the Risk of Colorectal Cancer

Many studies have focused on identifying the causes of colorectal cancer. Hopefully this can lead to new ways to help stop it. Other studies are looking at whether certain foods, supplements, or medications can reduce the risk of colorectal cancer. For example, many studies have shown that aspirin and painkillers like these can help reduce the risk of skin cancer, but these drugs can have serious side effects.

Researchers are now trying to determine if the benefits outweigh the risks to certain groups of people who are thought to be at greater risk for colorectal cancer.[23]

- **Early detection:** Doctors are looking for better ways to detect colorectal cancer early by studying new types of tests (such as blood tests) and developing those that are already used.
- **Diagnosis:** Researchers are trying to explain the lower forms of colorectal cancer. This means combining colorectal cancer based on factors such as genetic mutations in cancer cells, the way cells look and behave, how quickly cells divide, and the characteristics of the tumour itself. As it has been found in other types of cancer, this can lead to a better understanding of disease progression and its consequences, as well as more clearly defined treatment strategies.[6]
- **Genetic testing to help plan treatment:** As physicians continue to learn more about genetic mutations in colorectal cancer cells, specific genetic tests have been developed to help predict which patients are at greater risk of recurrent colorectal cancer (cancer that comes after treatment).
- **Liquid biopsy to help plan treatment:** Researchers are researching liquid biopsies to diagnose and treat cancer. A liquid biopsy is usually a blood sample taken for cancer screening. It is much easier to get a blood sample than to get a tumour sample with a needle.
- **Treatment:** Researchers are constantly looking for better ways to treat colorectal cancer.
- **Surgery:** Surgeons continue to develop surgery for colorectal cancer. Rectal cancer surgery with an anus, without cutting the skin, is also being studied.
- **Organ maintenance** - keeping your body functioning is another purpose of research. For example, doctors look for the right time for surgery after chemo has been used to reduce a tumour and how they know they are getting the best response from each patient.
- **Chemotherapy:** Chemotherapy is an important part of treatment for many people with colorectal cancer, and doctors always try to make it effective and safe. There are various methods tested in clinical trials, including:
  - Testing for new chemo drugs or drugs already used for other cancers. Looking for new ways to combine drugs that are already known to work against colorectal cancer to see if they work better.
  - Study the best methods to combine chemotherapy with radiation, targeted therapies, and / or immunotherapy.
- **Targeted treatment:** Targeted therapies work differently from conventional chemotherapy drugs. They affect certain parts of the cancer cells that make them different from normal cells. Several targeted therapies are already being used to treat rectal cancer. Researchers are learning the best way to administer these drugs and are looking for new targeted therapies.[6]

VI. CONCLUSION

Infection with certain pathogens may trigger carcinogenesis pathways that lead to cancer in infected individuals. Identifying viruses can work as human beings carcinogens, understanding how exposure to these bacteria occurs, and the sequential carcinogenic mechanisms that cause them will be important. Information in these areas will provide useful clues for the effective management of pathogen-associated cancer, and finally, prevention.

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