

Alternative Cancer Therapies and Cancer Prevention

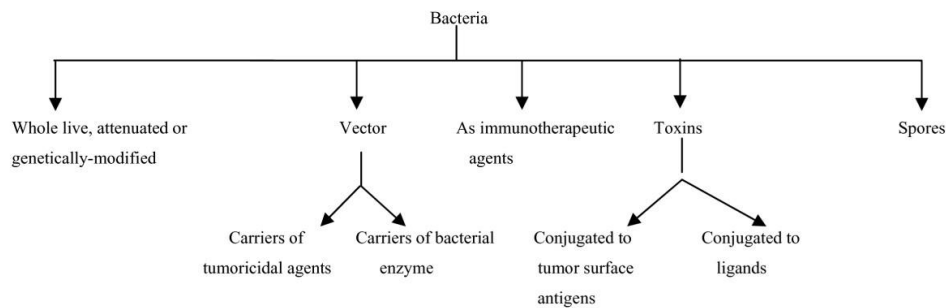
Cancer is a disease that is the result of cells multiplying and dividing abnormally. Usually, there are mechanisms that cells use when multiplying but some mutations can make cells not follow these checkpoints. Virus infections, pollution, chemicals, certain inherited genes can lead to random mutations that perturb the normal cell division process. This essay is a review of what we know about alternative cancer therapies. Certain foods and lifestyle changes can help one keep healthy and free of cancer. Cancer rates are lower in countries like Nigeria and India. Why? These are some of the questions I would like to explore.

Some cancers are triggered when a virus infects the host. For example, the Epstein-Barr virus which causes mononucleosis, is a risk factor for different kinds of cancer like Hodgkin's lymphoma, stomach cancer and nasopharyngeal carcinoma. Human papillomavirus is behind most cervical cancers. Peanuts infected with a fungus that releases a toxin called aflatoxin are a hepatocarcinogen raising greatly the risk of liver cancer. But as some viruses, fungi and bacteria can cause disease, some other could also help in finding a cure to cancer. Viruses have shown great potential as they have the ability to insert altered genes into cancer cells.

The use of bacteria as an anti-cancer agent was first observed by two German physicians almost one hundred years ago, who noticed that cancer patients with a bacterial skin infection (erysipelas) would get better. The American physician William Coley developed a vaccine using killed bacteria (*Streptococcus pyogenes*) and noticed many patients improving when they developed a fever. He continued injecting his patients and if he was able to maintain the fever in his patients, their cancer regressed [1]. This was probably the first anti-cancer vaccine. Unfortunately, at the time (more than 100 years ago), radiation therapy became more popular as it was more uniformly successful. A hundred years ago not much was known about the immune system and this type of therapy was halted as the science behind the results was not understood. Only recently did scientists understand better the immune system. For example, cytokines were isolated in the 70s and 80s and tumor-specific antigens were discovered in the 90s. Standard cancer treatment consists of surgery, radiation, and chemotherapy. In addition, if the patient is not doing well and cancer is spreading, other treatments, like bacterial based treatments, may give good results and are worth considering.

Bacterial treatments may work because bacteria can multiply selectively in tumors and inhibit their growth. Attenuated or modified non-pathogenic bacteria may prefer oxygen-poor tumor cells and when they encounter healthy oxygen-rich tissue, they die. That means they don't affect healthy cells which is great for the patient as the treatment is not toxic. The bacteria that can be used are in the *Clostridium* genus. The bacteria can not kill all the tumor cells and this treatment works in conjunction with other treatments like chemotherapy. This bacterial treatment works as a sensitizing agent for chemotherapy [2].

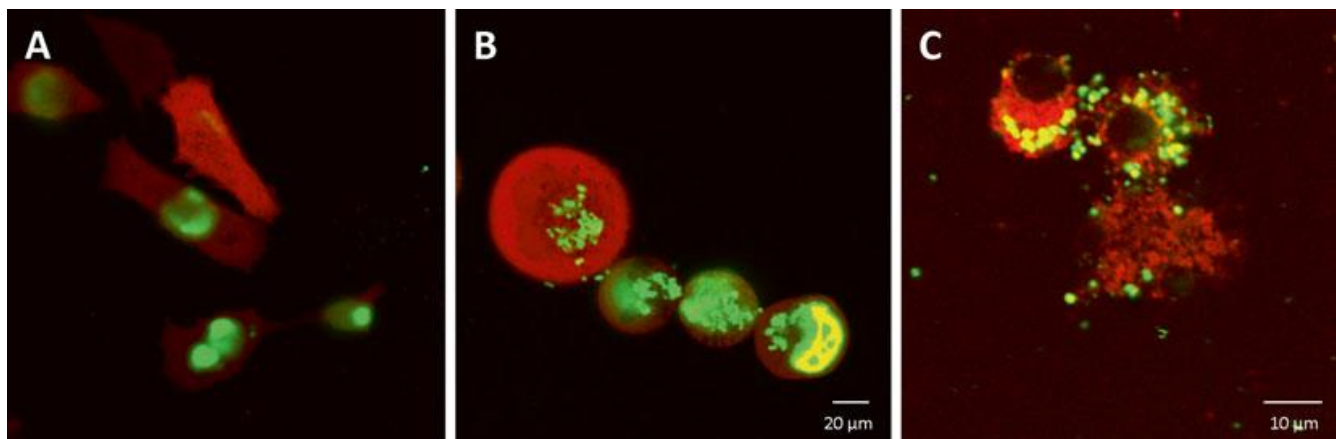
The ways bacteria can be used is summarized in the following diagram [2]:



According to the diagram, bacteria can be used as a vector for gene therapy. In cancer gene therapy, one of the problems is targeting the tumor for treatment. Bacteria can be genetically engineered to express a therapeutic gene that produces a protein as an adjuvant to other cancer treatments. Bacteria can serve as vectors for preferentially delivering anticancer agents, cytotoxic peptides, therapeutic proteins or pro-drug converting enzymes to solid tumors. One such bacteria is *Salmonella typhimurium* which was engineered to express interleukin-2 for the treatment of liver cancer. This bacteria naturally colonizes in the liver and it is believed that it can be used to deliver cytokines to the liver[2].

Multiphoton tomography was used in a study to show *Salmonella Typhimurium* kills different cancer cells. It uses different mechanisms – apoptosis and necrosis in the human PC-3 prostate cancer cell line and cell bursting in the human LNCaP and DU-145 prostate cancer cell lines [4].

Following is an example of prostate cancer cells bursting when infected with *S. Typhimurium*.



Dual-color DU-145 human prostate cancer cell death induced by *S. typhimurium* A1-R. (**A**) Untreated dual-color DU-145 human prostate cancer cells (0 time point); (**B**) *S. typhimurium* A1-R- GFP invasion and proliferation in the DU-145 cells (2-h time point); (**C**) DU-145 cell death caused by bursting after extensive intracellular bacterial proliferation (24-h time point) (Fluoview FV1000 confocal fluorescence microscopy) [4]. Similar results were shown for Lewis lung carcinoma. *S. Typhimurium* is able to infect and kill cancer cells in live mice [4].

Salmonella Typhimurium can also be used as an immunotherapeutic agent. Bacteria are immunogenic, meaning they stimulate the immune system. Attenuated *S. Typhimurium* can infect malignant cells both *in vitro* and *in vivo*, thereby triggering an immune response. The bacteria invades the cancer cells and then the immune system attacks the bacteria that are lodged in cancer cells [2].

Tumor antigen DNA sequences have been introduced into Salmonella and Listeria, helping the immune system keeping tumors in check[2]. Clostridium novyi was able to induce massive leukocytosis and inflammation. Inflammation is known as having antitumor effects [2]. Bifidobacterium adolescentis has been used as a delivery system for the antiangiogenic protein endostatin. All these results show that bacteria can be an important tool in finding a cure for cancer.

If detected early, cancer treatment has a high rate of success. Cancer screening tests help doing that. The Pap smear test is used to find cancerous or pre-cancerous cells on the cervix. It was the first cancer screening test. Other widely used cancer screening tests are the colonoscopy test and stool blood test for colon cancer screening and mammography for breast cancer screening.

When comparing cancer rates from different countries, Korea, Mongolia, and Japan have the highest incidence of stomach cancers. One of the known risks factors of stomach cancer is infection with Helicobacter pylori. According to the World Cancer Research Fund, other known risks factors are alcohol consumption, tobacco use, greater body fat, processed meats and foods preserved by salting [8]. In Korea and Japan, salt is widely used for food preservation (for example kimchi in Korea). While fermented kimchi pickled vegetables contain many microorganisms that may be beneficial, the very high salt content could be the reason of higher stomach cancer rates. Another factor for stomach cancer may be using nitrates for curing and flavoring meat dishes [9]. Nitrates are also used in preserving deli meats, so consuming less ham, salami and other deli meats, that are widely used in our western diet, may be a good prevention measure against cancer. Another reason for stomach cancer may be smoking foods. Smoking is a way of preserving foods, especially meats, used widely before refrigeration but it is still used as many consider these foods more flavorful.

Cooking meat at high temperatures elevates the risk for cancer. Heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs) are chemicals formed when meat is cooked at high temperatures like pan frying or grilling directly over an open fire [6]. HCAs and PAHs are mutagenic causing DNA changes that elevate the risk of cancer. HCAs are formed when amino acids, sugars and creatine (found in muscle) react at high temperatures. PAHs are formed when fat from meat grilled over an open fire drips into the fire, causing flames that contain PAHs that adhere to the surface of the meat. PAHs are also found in smoked meats, in charred foods, in cigarette smoke and car exhaust fumes [6].

Physical activity is considered one of the best cancer prevention measures available that protects against colorectal cancer, breast cancer, and endometrial cancer [7]. Being overweight or obese increases the risk for esophagus, pancreas, kidney, endometrium, breast, bladder and stomach cardia cancers [7]. Staying out of the sun prevents skin cancer.

Consuming more vegetables and fruits and less meat are a possible explanation for a much lower incidence of colorectal cancer in India and Nigeria as opposed to developed countries. Another hypothesis is that people have a more diverse gut bacteria in these populous countries that may confer some protection against certain cancers. Many vegetables have compounds that have anti-cancer properties. Tomatoes contain lycopene. Mushrooms (which are fungi) have anti-cancer compounds like lentinan, krestin, hispolon, lectin, calcaelin, illudin etc [11]. Berries and in particular blueberries have anti-cancer compounds like anthocyanins, catechins, quercetin, kaempferol and other flavonoids, ellagitannins and ellagic acid, pterostilbene and resveratrol [12]. Garlic contains saponins which are studied for their anti-tumor activity. Beans and peas contain saponins, lignans, resistant starch which is not digested in the small colon, but used by healthful bacteria in the colon to produce short-chain fatty acids, which seem to protect colon cells [12]. Other foods that fight cancer are apples, broccoli and cruciferous vegetables, carrots, cherries, cranberries, dark leafy vegetables, flaxseed, grapefruit, grapes, soy, squash, tea, coffee, walnuts and whole grains.

Certain professions are considered more hazardous to health. Here is a list [10]

Cancers associated with various occupations or occupational exposures

Cancer	Examples of substances or processes	Examples of occupations
Bladder	Benzidine, beta-naphthylamine, 4-aminobiphenyl, arsenic	Rubber, leather, paving, roofing, printing and textile industries; paint/dyeing products; chimney sweeping; machinists; hairdressers and barbers; truck drivers
Kidney	Cadmium, trichloroethylene, herbicides, wood dust	Painting; metalworking; petroleum, plastics, and textile industries
Larynx	Asbestos, wood dust, paint fumes	Metal working; petroleum, rubber, plastics, and textile industries
Leukemias	Formaldehyde, benzene, ethylene oxide, pesticides	Rubber manufacturing; oil refining; shoemaking
Liver	Arsenic, vinyl chloride, aflatoxins	Plastic manufacturing
Lung	Radon, secondhand smoke, asbestos, arsenic, cadmium, chromium compounds, diesel exhaust, sulfur mustard	Rubber manufacturing, paving, roofing, painting, chimney sweeping, iron and steel foundry work, welding
Lymphomas	Benzene, 1, 3-butadiene, ethylene oxide, herbicides, insecticides	Rubber manufacturing, painting, hairdresser or barber
Mesothelioma	Asbestos	Mining, railroad, automotive, plumbing, painting and construction industries; factory workers
Nasal cavity and sinuses	Mustard gas, nickel dust, chromium dust, leather dust, wood dust, radium	Textile and baking industry, flour milling, nickel refining, furniture and cabinet builders, shoemaking
Skin	Arsenic, coal tars, paraffin, certain oils, sunlight	Chimney sweeping; outside jobs that involve a lot of sun exposure

From this list it can be inferred that many chemicals are hazardous. Dust can be a hazard, for example asbestos, nickel and chromium dust, leather and wood dust. Coal tars are a hazard for chimney sweepers. Another occupational health hazard not included in this list is bitumin which is considered a cancer risk for road workers laying out asphalt.

Alternative cancer therapies show promise and used together with a standard cancer treatment can be effective with a higher rate of success. Knowing your family history and with a bit of luck, one may be able to avoid getting cancer by exercising regularly, eating foods that have anti-cancer properties, avoiding stress which can lower the immune system, and avoiding staying too much in the sun or using sunscreen to protect against harmful UV rays.

Work Cited

1. <https://www.cancerresearch.org/news-publications/our-blog/april-2015/whatever-happened-to-coleys-toxins>
2. <https://jbiomedsci.biomedcentral.com/articles/10.1186/1423-0127-17-21>
3. <http://www.medicalnewstoday.com/info/cancer-oncology/treatments-for-cancer.php>
4. Bacterial Therapy of Cancer: Methods and Protocols (Methods in Molecular Biology) 1st ed. 2016 Edition, by Robert Hoffman (Editor), book
5. <https://www.cancer.org/latest-news/cancer-research-progress-challenges-and-opportunities.html>
6. <https://www.cancer.gov/about-cancer/causes-prevention/risk/diet/cooked-meats-fact-sheet>
7. <http://www.wcrf.org/int/link-between-lifestyle-cancer-risk>
8. <http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/stomach-cancer-statistics>
9. <http://www.livestrong.com/article/361804-japanese-diet-stomach-cancer/>
10. <https://www.cancer.org/content/dam/cancer-org/cancer-control/en/booklets-flyers/occupation-and-cancer-fact-sheet.pdf>
11. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3339609/>
12. <http://www.aicr.org/foods-that-fight-cancer/blueberries.html>