INTRODUCTION

What is the connection between cancer incidence and the environment? What is the relative role of nature versus nurture, or genetic inheritance or environmental milieu, in cancer incidence? While both factors play an important, often perversely synergistic role in the development of cancer, approximately two-thirds of all cancer occurrences are related to environmental factors. The percentage of cancer cases attributed to environmental factors would be even higher were modifiable lifestyle choices included. What are the two major environmental culprits? Tobacco smoking and food consumption. More than half of all cancers are linked to a history of smoking tobacco or obesity (from a combination of food consumption and a sedentary lifestyle). Other environmental exposures, for example, to metals and industrial chemicals in the environment, also can cause certain types of cancer.

Humans suffer from more than 100 types of cancer. Cancers first emerge inside a human cell. When the body is functioning properly, it occasionally needs to produce more cells. It does so by allowing old cells to die and younger cells to divide and form new cells. When cancer emerges, the cell regulatory mechanism goes awry and cells continue to divide incessantly, ultimately leading to a tumescent mass. A difficulty in preventing and diagnosing cancers is that it may take many years for a tumor to grow sufficiently for detection. Lung cancer patients, for example, do not develop detectable cancer until 20, 30 or more years after smoking. While there remains much to learn about environmental causes of cancer, clear patterns have emerged.

CANCER PATTERNS

The annual rate of newly reported cancer cases increased during the 1970s and 1980s yet have been slowly decreasing since the mid-1990s (graph 1). However, this general pattern conceals diverse trends among diverse types of cancers: Cancers of the digestive system, from the mouth and throat to the stomach and colon, have decreased while lung (particularly for women), bladder, prostate, kidney, liver, brain, lymphomas, and melanomas have increased.
ENVIRONMENTAL CAUSES

Because of the complex interaction with endogenous factors it remains impossible to predict whether exposure to a certain environmental toxin will cause a given person to develop cancer. We can identify genetic and environmental characteristics that increase cancer risk. Over 100,000 chemicals are employed commonly in Americans households in the form of cleaners, food additives, solvents, pesticides, and a host of other products. Each year, approximately 1,000 more are added to the list. Complicating the matter further, as single substances they may have myriad affects on cancer pathways; when multiplied ensemble, the potential concatenations of cancer causing etiologies is nearly limitless. Additionally, numerous natural products can promote cancer. While *in vitro* studies describe
potential carcinogens in humans, epidemiological designs following subjects over time to observe potential cause and effect patterns are the most reliable way to research cancer processes.

Further complicating cancer epidemiology, cancers emerge over many months, and often years, and arise from a complex interaction of endogenous, or genetic, and exogenous, or environmental, factors. While there may be little we can do to control endogenous sources themselves, given that the majority of cancers are related to environmental factors, limiting exposure to these sources can greatly decrease morbidity and mortality to a large range of cancers. In addition to smoking and poor diets, exposure to cancer-inducing viruses and bacteria, drugs, hormones, radiation, and food, air, or water-borne chemicals all increase the risk of developing cancer.

How do we know what portion of cancer cases, and under what circumstances, we can attribute to environmental factors? Although research remains limited, there is a lot we do know. A notable effect of smoking having decreased in the US in recent decades is the concomitant decline in rates of cancers of the lung, bladder, mouth, colon, kidney, throat, voice box, esophagus, lip, stomach, cervix, liver, and pancreas. Another way scientists can identify carcinogenic sources is by observing how groups who switch from one diet to another have markedly different cancer rates. People who have migrated from Asia to the US, for example, experienced low rates of several cancers, most notably prostate and breast cancer in their native countries. Following migration to the United States, prostate and breast cancer soared among these migrant populations to ultimately match levels observed in the general US population. Conversely, stomach cancer rates among these groups have declined. In both cases, environmental pathways explain the differential patterns. To the extent that fat and sugar-rich, fiber and nutrient-poor diets in the US replace traditional Asian diets, thus increasing obesity, breast and prostate cancer rates also increase. Stomach cancer, however, declines in such an instance as Helicobacter pylori bacterial infections, which are linked to higher colorectal cancer rates, are less common in the US.

**CARCINOGENS**

**Tobacco**

Approximately one-third of all United States’ cancer deaths yearly are caused by direct and indirect environmental exposure to tobacco smoke. Tobacco exposure increases the risk of a wide range of cancers: lung, mouth, bladder, colon, kidney, throat, nasal cavity, voice box, esophagus, lip, stomach, cervix, liver, and pancreas, as well as leukemia. Cigarette smoke releases over 100 carcinogens into the environment. A synergistic effect is observed whereby mouth, voice box, and esophagus cancer incidence is exacerbated among smokers who also consume at least two drinks/day; similar synergies are documented for smoking and radiation exposure in exacerbating lung cancer incidence.

**Diet/Weight/Physical Inactivity**

Numerous studies have corroborated that high consumption of red and processed meats increase colorectal and stomach cancer incidence. Conversely, higher and more diverse consumption of fruits and vegetables decreases a host of cancers, particularly esophageal, stomach, and colorectal cancers. Obesity is highly correlated with cancers of the breast, kidney, esophagus, colon. Independent of obesity, sedentary lifestyles increases colon and breast cancer risk. Ensemble, inactivity and obesity are linked to over one quarter or more of breast and colon cancers.
Alcohol consumption

The consumption of more than two drinks daily is linked to an increased risk of cancer, particularly among smokers. Cancers particularly connected to heavy drinking are mouth, throat, voice box, liver, and esophageal. However, emerging evidence suggests that the type of alcohol matters. Some studies, for example, have shown a notably higher risk of certain lymphomas among high drinkers of spirits than among red wine drinkers. Naturally occurring compounds present at relatively high levels in red wine, such as quercetin and resveratrol, may be responsible for the relatively lower cancer incidence rate among red wine drinkers.

Viruses, bacteria, and fungi

Viruses and bacteria promote the emergence of several cancers. Among the clearest links researched is the sexually transmitted virus, human papillomavirus (HPV), as the main cause of cervical and anal cancer. Other known virus-cancer links are Hepatitis B (HBV) and hepatitis C (HCV) as major determinants of liver cancer. A virus for which most US adults are carriers, Epstein-Barr virus (EBV), known commonly as mononucleosis, is linked to certain types of lymphoma, including a several-fold increased incidence of Hodgkin’s lymphoma within several years of suffering EBV symptoms. Similarly, Kaposi’s sarcoma-associated herpesvirus (KSHV), or human herpesvirus 8 (HHV-8), is linked to Kaposi’s sarcoma. Lastly, Helicobacter pylori bacteria infection, the primary cause of gastritis and peptic ulcers, is a precursor to stomach cancer.

Some species of fungi foment aflatoxin growth on food, which can lead to liver cancer. Grains and peanuts house aflatoxin-producing fungi. Meat and dairy products can also be contaminated through aflatoxin-contaminated feed given to livestock and dairy animals. Agricultural laborers, particularly in the developing world where screening is lax, are particularly at risk through inhaled airborne dust particles.

Prescription drugs

Research is increasingly encountering links between prescription drugs and cancer, including, perversely, drugs used to treat cancers. Some research suggests an increased risk of breast and endometrial cancers among users of estrogen, and synthetic estrogen-like substances, consumed to treat post-menopausal conditions. When used as a contraceptive, synthetic estrogen-like products have also been implicated in cervical and vaginal cancers. However, estrogen use is also associated with a reduced incidence of colon cancer. It is therefore unsurprising that Tamoxifen, a synthetic hormone that blocks estrogen, is used to treat breast cancer recurrence or as a preventative measure for women with high risk for contracting breast cancer.

A host of drugs employed in the front line against cancer increase the risk of second cancers. Synergistic effects leading to multiplicative increased risks for secondary neoplasms are observed with certain combinations of chemotherapy and radiotherapy. Drugs used as immunosuppressants, such as cyclosporin and azathioprine for patients having organ transplants, are related to increased cancer incidence, especially lymphomas. Conversely, some over the counter medicines have been associated with reduced risk of certain cancers, such as aspirin and colon cancer.

Radiation

Atmospheric, invisible, and odorless, radiation is constantly damaging our DNA. Most of these damaging effects are repaired by complex intracellular mechanisms. When
they are not, cancers sometimes result. Ultraviolet (UV) radiation from the sun causes premature skin aging and DNA damage that can lead to melanoma and other skin cancers. Skin cancer incidence is increasing quickly. However, recent research suggests that the overall incidence of cancer may be lower among people with regular exposure to solar radiation than among those with very low exposure. The latter is associated with low levels of vitamin D, which is increasingly linked to higher rates of a host of cancers. Research on links between vitamin D deficiency and breast cancer incidence is particularly convincing and has led to promising results with vitamin D supplementation in clinical trials.

While we are all exposed to small amounts of cosmic radiation (which may account for up to 1 percent of our total cancer risk), radioactive gas from soil sources such as radon (resulting from uranium decomposition) naturally emits ionizing radiation. Radon gas enters homes through underlying soil and bedrock through cracks and fissures in the home’s foundation. Approximately 5% all US homes are exposed to measurable levels of radon. Approximately 20,000 lung cancer deaths yearly are linked to radon exposure. Another source of radiation is from radioactive substances released by medical procedures, nuclear weapons or energy sources, leading to a wide range of cancers, including breast, thyroid, lung, and stomach. While few people today are exposed to most of these sources, irradiative medical treatment is becoming more common. Since radiation effects are multiplicative over time, people treated for acne, ringworm, or cancer with radiation as children suffer particularly high rates of diverse cancers as older adults.

**Industrial chemicals**

Benzidine was among the first chemicals found to cause cancer in humans. Higher bladder cancer rates were observed in the first half of the 19th century among textile and paper dye production workers. Dyes metabolize to benzidine *in vivo* but are hazards primarily in close proximity to dye and pigment plants, particularly where waste is discharged.

A handful of solvents used as paint thinners, grease removers, and in industrial dry cleaning industry have been associated with animal cancers. One of them, benzene, causes leukemia in people. Used widely as solvent and component of gas, it was banned in 1997 for use in pesticides. However, the chemical remains ubiquitous in a host of industrial products where people are principally exposed through inhalation. Present in high quantities around gas stations and in cigarette smoke (half of all benzene exposure in the US is estimated to be through cigarette smoke), about half the US population is exposed to benzene in industrial solvents and virtually all of us are exposed through gasoline. Diesel exhaust particles are also likely carcinogens; elevated lung cancer rates are found among people exposed to unusually high levels of diesel exhaust, such as train attendants, miners, mechanics, bus drivers and truckers.

Exposure to certain fibers and dust is omnipresent in industrial settings and are linked to elevated cancer risk. Elevated rates of mesothelioma, a rare lung and abdominal cancer, has been definitively linked to asbestos exposure, which accounts for the largest portion of occupation-related cancers. Further, ceramic fibers used as insulation materials used in lieu of asbestos also cause lung cancer in animals. Wood and silica dust, are linked to sinus and lung cancers of the nasal cavities and sinuses, is a known carcinogen for unprotected workers who are exposed regularly from sanding operations and furniture manufacturing.

Dioxins emerge in the environment as unintended byproducts of chemical processes in paper and pulp bleaching. They are also present in some insecticides, herbicides, and wood preservatives. Dioxins accumulate in human fat tissue. Increased cancer-related death
rates are observed in people working in related industries. Similarly, lung, skin, and urinary cancers are higher in people exposed to polycyclic aromatic hydrocarbons (PAHs). PAHs are used in the plastics industry to produce containers, film wrapping, sundry housing products, and credit cards. PAHs are produced by burning wood and fuel in homes, and are also present in gasoline and diesel exhaust cigarette smoke, and charcoal-broiled foods. Vinyl chloride is a colorless gas related to liver, brain, lung cancers, and angiosarcomas (tumors of the blood vessels). While proximity to a plastics plant increases air-borne exposure, risk to people as end-users of the product appear low to absent.

Metals

Arsenic, found in various levels in drinking water, is related to skin, lung, bladder, kidney, and liver cancers; cancers are particularly linked to higher levels of exposure, such as found in mining and copper smelting, and herbicide production. Beryllium compounds, used in a wide range of industries, including fiber optics and cellular networks, aerospace and defense industries, as an ingredient in glass and plastics, dental applications, and sports equipment, causes lung cancer as observed in significantly higher morbidity among workers in beryllium production industries. People outside beryllium-related industries are exposed mainly through coal and fuel oil combustion and by inhaling or consuming trace beryllium residues in air and food. Another cancer-causing metal is cadmium, used as a coating to prevent corrosion, in batteries, and in fungicides. While food remains the primary source of human exposure to cadmium. Smoking, likely vis a vis contaminated topsoil represents the primary non-occupational exposure to cadmium. Other cancer-causing metals include chromium compounds, used to prevent corrosion in steel and popular in stainless steel products; lead acetates and phosphates used in coating metals; inks, paints, hair dyes; and in treat poison ivy treatments; and nickel, related to cancers of the nasal cavity, and lung, and ubiquitous in the air, water, and soil due to its wide use in steel, dental additives, magnets, and batteries.

Pesticides

While only a tiny fraction (approximately 20 of the nearly 1000 tested) of the ingredients used in pesticides within the US are proven to cause cancer in animals, many remained untested. As a result of pesticide links to cancer, many pesticides have been outlawed or highly regulated in the US but remain legal in much of the world. Where particularly noxious pesticides are unregulated and farmers have frequent contact with them, skin cancers and cancer of the lip, stomach, lung, brain, and prostate are notably elevated.

GREEN PREVENTION

With so many natural and human-made carcinogens in our environment, it seems a daunting task to prevent exposure. Living a green lifestyle, however, can go a long way to preventing the majority of cancers. Since at least two-thirds of cancer cases are exogenous, i.e. environmental, there is much we can do. Behavioral modification can drastically reduce the higher cancer rates associated with smoking, obesity, and excessive alcohol consumption. Most cancers can be prevented through behavioral change limiting risk through these three avenues. To live green, reduce environmental cancer risk, and increase longevity and vitality, a handful of simple rules conclude this entry:

- Don’t smoke and avoid second-hand smoke
• Exercise regularly
• Shun calorie and fat-dense and processed food in favor of the rainbow spectrum of naturally colored fruits, nuts, and vegetables.
• Drink alcohol moderately (e.g., one or two alcoholic drinks a day.)
• Avoid sunlight at midday and sun burns in favor of more consistent and mild exposure in the morning and evening, and a healthy skin color.
• Avoid viral and bacterial infections by engaging in safe sex, avoiding injection drugs, and acquiring vaccinations when appropriate, such as to HPV and Hepatitis B.
• Check your home for radon levels.
• Avoid contact contact with pesticides, solvents, and industrial chemicals.

REFERENCES
American Cancer Society’s nutrition and diet guidelines:
http://www.cancer.org/eprise/main/docroot/PED/ped_3_1x_ACs_Guidelines?sitearea=PED

Doll R. Epidemiological evidence of the effects of behavior and the environment on the risk of human cancer. Recent Results in Cancer Research 1998;154:3-21


http://www.cdc.gov/nchs/gis.htm

http://www3.cancer.gov/atlasplus

http://cancer.gov/cancer_information/cancer_literature


World Health Organization’s “Diet, nutrition and the prevention of chronic diseases”: