ALCOHOL

ALCOHOL AND CANCER

What in alcohol causes the cancers?

Ethanol in our bodies is converted to a chemical called **acetaldehyde** which is highly toxic and can promote carcinogenesis.

How?

Firstly, acetaldehyde can interfere with both DNA synthesis and repair. It in addition, can cause point mutations, inducing a base change in the DNA strand and thus altering the genome. In particular, acetaldehyde causes a mutation in a specific locus in human lymphocytes, causing chromosomal abnormalities during cellular division.

Moreover, acetaldehyde also binds to specific proteins, which impedes several vital functions needed to regulate cells. For instance, certain specific enzymes involved with DNA repair and DNA methylation may be structurally altered, making them unable to perform their roles in the body.

Acetaldehyde is also able to bind to DNA and form stable DNA adducts (a damaged DNA segment bound to a cancer promoting chemical). Furthermore, alcohol increases the production of certain molecules called reactive oxygen species (ROS) that can also produce DNA adducts. DNA adducts are therefore more prevalent in alcohol consumers than non-consumers. These DNA adducts are then regulated by several defense mechanisms including DNA repair systems and apoptosis. However, long-term ingestion of ethanol may affect and inhibit these defense mechanisms, allowing abnormal cells to thrive.

Ethanol also causes cancer by allowing liver cells to divide abnormally fast and regenerate cells that are more prone to gene alterations. Furthermore, alcohol can also increase the level of specific hormones like oestrogen. These hormones are messengers in the body and control certain cell divisions. However, elevated levels of these hormones could potentially lead to uncontrolled growth.

Which cancers does alcohol affect?

The American Cancer Society declared alcohol as a risk factor for mouth, pharynx, larynx, esophagus, liver, colorectal, breast, stomach, and pancreatic cancer.

Should I completely give up alcohol; I thought red wine was good for you?

Again, your changes in diet should be made in moderation. Red wines have been shown to be good for the heart and have probable anticancer properties so it isn't necessary for you to give up alcohol completely. However, there are consequences for extreme levels of alcohol consumption. Thus, it is best to limit yourself (especially college students!!)

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DIET

So should I stop eating red meat?

Note every change should be made in moderation. Red meat should not be given up completely; nutritionists do emphasize the good protein, iron, and vitamins that red meat provides. If possible, some of the daily protein and iron should also come from eggs, beans, or other sources and not only just from red meats. However, experts also suggest individuals to try to stay away from processed meats completely and to eat fresher options.

What is the point of telling me this if nothing is for certain? It's impossible to not have sugar in my diet.

The point is not to get you to cut sugar completely from your life. Rather, it is to make you more aware of the effects of sugar. High levels of sugar are known to be correlated with obesity, which is a risk factor for several different cancers. Despite this, lots of sugars are great for you. For example, fruits contain lots of fructose. However, this sugar is not "bad" for you; in fact, we need sugar as an energy source to live. In addition, fruit provides fiber, vitamins,

RED AND PROCESSED MEATS

Are they carcinogens?

In 2015, the World Health Organization declared processed meat as a carcinogen and red meat as a possible carcinogen. Processed meat includes hot dog meat, bacon, sausage, etc. and refers to meat that has been salted, cured, fermented, smoked, or undergone other processes to enhance flavor or preservation. Numerous studies have shown strong evidence of a positive correlation between red meat and processed meat consumption, and colorectal, pancreatic and prostate cancer. Furthermore, the International Agency for Research on Cancer (IARC) found that eating 50 grams of processed meat every day (which is equivalent to 4 strips of bacon) increases the risk of colorectal cancer by 18%.

How do they cause cancer?

There is still very much unknown about exactly what in red and processed meats causes the cancer. However, scientists do know that the chemicals found in meat are responsible. Firstly, both red meat and processed meats contain a chemical called haem iron that is broken down after being digested. It breaks down to form N-nitroso compounds (NOCs) which are known to damage the cells that line our colon. As a result, our colon needs to replicate these damaged cells to make up for the depletion. These extra replications increase the chances of mutations and alterations in certain DNA strands, potentially initiating the first steps of cancer.
In addition, curing and smoking can also form carcinogenic chemicals, one being NOC mentioned above. Another chemical that can be formed is polycyclic aromatic hydrocarbons (PAH). PAH can cause DNA damage, but still more needs to be researched to obtain a full understanding. Also note, cooking meats at high temperatures can produce heterocyclic aromatic amines (HAA) as well as PAH. HAA are genotoxic and thus are harmful to DNA as well.

BPA

Bisphenol A (BPA) is a chemical found in several different grocery packaging, such as food cans and certain plastics. Though there is still much to be studied about BPA, there have been numerous animal studies, as well as some human studies, that link high BPA exposure and specific cancers. Thus, it may be safe to stay away from canned foods whenever possible and consider using other products instead of plastic to store food and water.

In 2012, there was a study conducted that found that BPA can promote human breast cancer cell growth. It does so by influencing the stimulatory action through the G protein-coupled receptor, an estrogen receptor, in breast cancer cells.

In another study, scientists found that BPA is a xenoestrogen, which mimics the role of estrogen. The xenoestrogen participates in several different pathways that all promote carcinogenesis of various types of cancer.
Furthermore, the study also found that BPA interacts with certain steroid receptors by inducing alterations in the DNA methylation patterns. By

antioxidants. and several other nutrients. Thus, you should not be cutting fruits from your diet by any means.

On the other hand. you should consider cutting refined sugars from your diet. These sugars have very little nutrients for you and often times cause you to exceed the recommended sugar amount per day, potentially leading you up the road to becoming overweight. So next time you're at a restaurant, consider getting water instead of the root beer or coke you always get. Remember, make these changes in moderation for sugar is still very important in our diet.

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doing so, BPA could be promoting the growth of prostate cancer cells as well.

Lastly, some other studies have found evidence that fetal BPA exposure alters the gene expression that help regulate the cell cycle, and increase the production of free radicals (chemicals that damage the DNA).

As you can see, researchers are studying a broad spectrum of the mechanisms of BPA and there is still much to be learned. Though there have been many consistent studies linking BPA exposure and higher risks of certain cancers, such as ovarian, breast, and prostate, it is important to note that the International Agency for Research on Cancer (IARC) did not classify BPA as a carcinogen, unlike tobacco and UVR. However, it is still important to remain cautious of containers and cans with BPA-- there still is evidence linking them with potential carcinogenesis. Better be safe than sorry!

SUGAR

Sugar consumption has been on a rise over the past decades in the US. And don't get me wrong; I'm not saying that sugar causes cancer by any means. However, excess sugar consumption indirectly increases your risks of cancer by increasing your chances of obesity. Obesity (BMI> 30kg/m^2) has been shown in several studies to increase the risk of hepatocellular carcinoma (HCC), as well as breast, prostate, colorectal, and pancreatic cancer. More details will be discussed in the obesity section later on.

In addition, high sugar consumption is associated with insulin resistance and increases the chances of type 2 diabetes and liver disease. These metabolic alterations are recognized to also be linked to the development of HCC. Moreover, cancer cells are known to depend on anaerobic glycolysis for energy. Several studies have suggested that dietary fructose may be able to promote cancer growth by uncoupling glycolysis from mitochondrial respiration, thereby feeding cancer cells and allowing them to thrive.

In addition, there was an experiment carried out with rats where researchers fed the rats with either a high-fat diet or a high-fructose diet. They then allowed to the rats to be exposed to hepatocarcinogen, DEN, in their drinking water. The study ultimately found that the group fed the high-fructose diet had much higher incidences of precancerous lesions of HCC than the group fed a high-fat diet. There have also been several other mice studies linking high sugar levels and cancer growth.

* Note, still limited information is known about the exact effects of fructose. Nevertheless, there are consistent associations seen in several studies. *

OBESITY

DEFINITION

What is the definition of obesity?

Quantitatively speaking, obesity is defined as when one's body mass index (BMI calculated by weight (kg) /height^2 (m^2)) is greater than 30 kg/m^2. Overweight is when one's BMI is between 25-29.9 kg/m^2.

So what are should I do if I am overweight or obese?

Caloric restrictions may help with some of the issues discussed above. By lowering your calorie intake, you are not only lowering your body's levels of free fatty acids and fat cells in general, but you are also lowering your inflammation levels.

In addition, exercise is key. Try to get yourself to exercise at least 30 minutes a day whether it be a walk, a run, a hike, a swim, a bike ride, etc. Regardless, you should always try to do some form of physical exercise.

OBESITY AND CANCER

There have been numerous studies showing the extremely high correlation between obesity and multiple different cancers, including postmenopausal breast, endometrial, esophageal, gastric, liver, and kidney cancer.

How do fat cells affect cancer growth?

Many studies have shown that the excess of caloric intake may lead to the proliferation of cancer cells. This is due to the fact that eating fatty foods, in addition to having excess body fat (especially in the abdomen area) increases the body's free fatty acid levels. As a result, body cells start to become more resistant to insulin; *in other words, your body has a harder time using insulin effectively and thus builds up glucose in your blood.* As compensation, the body signals the pancreas to release more and more insulin which commonly results in hyperinsulinemia. These elevated levels of insulin promote the development of colorectal, liver, pancreatic, endometrial, liver, etc. cancer cells. Moreover, high insulin levels affect the amount growth factors (aid in cell division) available to cells, thus allowing cancerous cells to become more aggressive and proliferate much faster.

In addition, as fat cells accumulate in your body, dead fat cells also become more prevalent. Macrophages are used to clear out these dead fat cells and release a chemical called cytokines. Cytokines signal other cells to help secrete these dead fat cells, but meanwhile also activate pro-inflammatory pathways. As a result, obesity may lead to chronic inflammation because dead fat cells are always in excess and are always needed to be secreted. Inflammation aids in the growth as well as the initiation of several cancers. In addition, chronic inflammation potentially results in other diseases such as pancreatitis, which can also increase an individual's risks of cancers.

Lastly, in pre-menopausal women, oestrogen is mainly produced by the ovaries. However, in postmenopausal women, fat cells are the main source of oestrogen production. Oestrogen makes breast, womb, and other cells in the body. High fat cell levels lead to high levels of oestrogen and these elevated levels of oestrogen may cause uncontrolled growth of certain cells. And thus, because of this positive correlation, obesity tends to have a high association with breast and womb cancers.

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SMOKING

STATISTICS

- The American Cancer Society predicts that in 2017, approximately 32% of all cancer deaths will caused by cigarette smoking (190,500 deaths out of 600,920).
- 80% percent of all US lung cancer deaths is attributed to smoking
- Smoking increases your risks of cancer 20 fold!
- Second hand smoking even causes 42,000 deaths every year! So if you think you're only harming yourself, think again!

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HOW EXACTLY DOES TOBACCO WORK?

Yes, we all should know by now that it is extremely bad for your health. But how does it exactly affect your body?

Though exactly how smoking contributes to carcinoma growth is still not fully known. We do know that tobacco contains at least 50 carcinogens. When one smokes a cigarette, the chemicals from the cigarette start injuring and harming the lung. For example, cigarette smoke contains acrolein, a chemical that is extremely harmful to the ciliated lining of lungs. In addition, the smoke produced also contains free radicals, which are reactive chemicals that harm cells by essentially damaging the DNA. All this damage could cause strong inflammation (biological response to harmful stimuli for tissue repair). As a result, the harm tends to trigger the body's defense mechanisms. Alveolar macrophages, which are basically cells that eat foreign particles harmful to the body, and white blood cells start to remove the pathogens and chemicals from the smoke in order to protect the lung from further damage. However, these defense cells soon start to deteriorate due to these toxic chemicals, and the bronchoalveolar (part of the lung) stem cells must replace these damaged cells. As one continues to smoke more and more, the stem cells must continue to proliferate in order to compensate for the loss of cells. During the proliferation, however, there are higher chances for mutations to occur (due to elevated levels of free radicals), potentially causing these cells to become malignant and ultimately leading up to cancer.

Cigarettes also contain toxic chemicals such as chromium that make poisons that bind to DNA, potentially altering or damaging the sequence. There are also other chemicals that interfere with several regulatory pathways such as the DNA repair pathway.

What about people who develop lung cancer who don't smoke? Is there a difference?

Smokers tend to have several types of mutations that are different from the mutations in the lung cancer of never-smokers, suggesting that cigarette smoking may very well induce several specific mutations. For example, one study claimed a particular mutation, the deletion of a chromosome 19p, caused the inactivation of protein LKB1/STK11, a protein that helps suppress tumors. This mutation, in addition to several others, is ***significantly*** more frequent in lung cancers of smokers than that of non-smokers. So, yes. There is a difference.

UVR

TIPS

- Check the weather forecast every day and pay particular attention to the UV strength.
- Try to wear sunscreen if you know you will be spending a lot of time outside in the sun.
- Try to always carry a small bottle of sunscreen around with you
- If you wear makeup, try finding a foundation or moisturizer that has SPF in it.
- For the best protection, try wearing long-sleeves and pants (I know this is not the best during the summer time).
- Wearing hats can protect your face.

BACKGROUND ON SKIN CANCER

Skin cancer is the most common type of cancer diagnosed in the US. Skin cancer can be divided into two large categories: melanoma skin cancer (MSC) and keratinocyte carcinoma (KC), difference being that KCs are usually more benign. KCs also splits off into 2 more subtypes: basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), with the latter being much more aggressive. BCCs account for the majority of the keratinocyte cancers, but has a much lower mortality rate. On the other hand, SCCs often times spread to other parts of the body, thus causes more frequent deaths. However, despite all this, our primary concern is with melanoma skin cancers for it is much most aggressive and deadly. Although invasive melanoma accounts for only 1% of skin cancers, it accounts for the majority of the mortalities from skin cancer

And though more and more awareness is being spread about this issue, the rate of skin cancer occurrences is still proliferating at a startling rate

Okay, so skin cancer is scary. But what is the point of telling me all this...I can't control my genes?

Genes do contribute to your risks of developing of skin cancer. However, studies have also linked Ultraviolet radiation (UVR) to all forms of these skin cancers as well.

UVR

What even is it?

UVR is a type of radiation that the sun produces. You probably have heard of UVA before. UVA is a subcategory of UVR, which is a huge threat to our bodies and is considered both a mutagen and a damaging agent. *In other words, UVR causes mutations and damages our DNA, ultimately promoting tumor growth.* UVR can divided into Ultraviolet A, B, and C. UVA is the most prevalent because the ozone layer does not filter out much of it. It has longest wavelengths and penetrates deep into the skin. UVB has higher energy, penetrates through the upper layers of the skin and causes sunburns and tans. It, in addition, is the most carcinogenic UVR out of the three. Lastly, UVC is the most dangerous and strongest. However, it doesn't reach the earth for the ozone layer filters it out.

What Does UVR do?

UV-mediated Mutagenesis:

One way UVR causes cancer is by mutating our p53 tumor suppressor genes. p53 are genes that act like a guard or judge in order to make sure

the DNA is correct before cell duplication. They help with damaged DNA repair and signal cells to undergo apoptosis (cell death) if the damage is too great. Thus, if there is a mutation in p53, there is a lack of regulation, allowing mutated cells that could become malignant to proliferate.

UV-mediated DNA Damage

In addition, as mentioned before, UVR also directly damages the DNA. The UV rays may chemically alter DNA nucleotide bases, break bonds, and may even form new irregular bonds within and between the nucleotides. These alterations can block replication, impair transcriptions (impair production of essential proteins), and result in abnormal base pairing. As a result, these changes can lead to inflammatory responses as well as development of malignant cells. The body responds by trying to repair the DNA (why a sunburn hurts so badly).

WHO IS MOST SUSCEPTIBLE?

Our skin has a substance called melanin, which determines our skin color. Melanin can be subdivided into 2 forms, eumelanin and pheomelanin. Eumelanin is a dark colored pigment in the skin, whereas pheomelanin is a light colored pigment. Eumelanin is much better at blocking UV photons and thus decreases the penetration of the UV rays. Because of the higher levels of eumelanin, darker individuals are much less prone to developing skin cancer. On the other hand, fair skinned individuals, especially gingers, have very little eumelanin in their skin and are much more sensitive UV rays.

In addition, the melanocortin 1 receptor (MC1R) is a huge determinant of skin cancer risk. High levels of exposure to UVRs signal to MC1R to increase the production of eumelanin pigments in order to help block the UV photons from penetrating into the skin. It is also the reason why you become tanner because you have a higher levels of eumelanin pigments. MC1R also plays a large role in damaged DNA repair. Studies have shown that there is ***a loss*** of signaling MC1R polymorphisms in lighter and fairer skinned individuals, putting them at a higher risk. In 2016, American Cancer Society found that melanoma was most diagnosed in non-Hispanic whites. Moreover, the incident rate of melanoma rate was 26:1, non-Hispanic whites to blacks.

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