REVIEW OF INCREASED CANCER RISK BY HIGH INTAKE OF RED MEAT, PROCESSED MEAT AND GRILLED MEAT

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ABSTRACT
Cancer one of the leading disease causing death globally, several reports suggested that the some aspect of lifestyle factor or diet influences the incidence of cancer in people especially in the western countries. Now a days intake of grilled or barbecued meat is popular which leads to the occurrence of cancer due to the carcinogen like HCA, HAA and PAH. HCA, HAA and PAH are found to be potent chemical carcinogens especially in case of colon, breast cancers. Due to exposure of high temperature during grilling or barbecuing meat enzymatic reaction takes place leads to formation of carcinogens. This can also be overcome either by limiting the intake of such diets or reduce the temperature by pre cooking in microwave oven or removing the charred portion.

KEYWORDS: Grilled meat, HCA, HAA, PAH.

INTRODUCTION
Cancer a major health problem worldwide begins when genetic changes cause the uncontrolled growth and division of cells.[1] These cells may form a mass called a tumor. It is characterized by an abnormal and unregulated growth of cells and this growth may destroyed by surrounding body tissue and it spreads to other parts of the body called metastasis.[2]

According to IARC report from WHO, it is expected that cancer incidence will be increases to 55% by 2035 and mortality rates are also increases by 65% at that period. Hence cancerincidence and mortality rates are increasing rapidly worldwide despite of several treatments.[3] The cause of this are complex but aging, lifestyle, diet shows a major contribution. Dietary factors have been thought to account for about 30% of cancers in
Western countries. Among the diet several reports shown that red meat and processed meat leads to carcinogenic effect in human especially stomach and colorectal cancer.\cite{4} From IARC report, nearly 34,000 cancer deaths occurred due to diets high in processed meat around the world yearly. Having red or processed meat more than four times a week causes to 15-25\% higher risk of cancer.\cite{5}

Suggested hypothesis for the relationship between meat consumption and cancer incidence is due to the presence of high fat or high protein which initiate carcinogenesis; or formation of carcinogens i.e., heterocyclic amine or polycyclic aromatic hydrocarbon while processing meat at high temperature; or presence of heme iron in meat leads to cell proliferation.\cite{6,7} Several studies have been undertaken to understand the effect of meat in different cancers and found it as a probable carcinogen and considered as group 2A.\cite{8}

**Processed red meat**

Red meat (beef, veal, pork, lamb and mutton) consumption contributes several important nutrients to the diet, for example essential amino acids, vitamins (including B12) and minerals (including iron and zinc). Processed red meat (ham, sausages, bacon, frankfurters, salami, etc.) undergoes treatment (curing, smoking, salting or the use of chemical preservatives and additives) to improve its shelf life and/or taste. During recent decades, consumption of red meat has been increasing globally, especially in developing countries. At the same time, there has been growing evidence that high consumption of red meat, especially of processed meat, may be associated with an increased risk of several major chronic diseases such as diabetes, coronary heart disease, heart failure, stroke and cancer at several sites, and mortality.\cite{9}

**Formation of heterocyclic amines and polycyclic aromatic hydrocarbons from cooked meats**

Heterocyclic amine (HCAs) and polycyclic aromatic hydrocarbons (PAHs) are chemicals formed when muscle meat, including beef, pork, fish, or poultry, is cooked using high-temperature methods, such as pan frying or grilling directly over an open flame. In laboratory experiments, HCAs and PAHs have been found to be mutagenic—that is, they cause changes in DNA that may increase the risk of cancer.

HCAs are formed when amino acids (the building blocks of proteins), sugars, and creatine or creatinine (substances found in muscle) react at high temperatures. PAHs are
formed when fat and juices from meat grilled directly over a heated surface or open fire drip onto the surface or fire, causing flames and smoke. The smoke contains PAHs that then adhere to the surface of the meat. PAHs can also be formed during other food preparation processes, such as smoking of meats.\textsuperscript{[10]}

HCAs are not found in significant amounts in foods other than meat cooked at high temperatures. PAHs can be found in other smoked foods, as well as in cigarette smoke and car exhaust fumes.

**Mechanism of meats in cancer progression**
Factors influence the formation of HCA and PAH in cooked meats

The formation of HCAs and PAHs varies by meat type, cooking method, and “doneness” level (rare, medium, or well done). Whatever the type of meat, however, meats cooked at high temperatures, especially above 300 °F (as in grilling or pan frying), or that are cooked for a long time tend to form more HCAs. For example, well-done, grilled, or barbecued chicken and steak all have high concentrations of HCAs. Cooking methods that expose meat to smoke contribute to PAH formation.[11]

HCAs and PAHs become capable of damaging DNA only after they are metabolized by specific enzymes in the body, a process called “bioactivation.” Studies have found that the activity of these enzymes, which can differ among people, may be relevant to the cancer risks associated with exposure to these compounds.[12–18]

HCAs and PAHs in cooked meats - increase cancer risk

Studies have shown that exposure to HCAs and PAHs can cause cancer in animal models (19). In many experiments, rodents fed a diet supplemented with HCAs developed tumors of the breast, colon, liver, skin, lung, prostate, and other organs.[20–25] Rodents fed PAHs also developed cancers, including leukemia and tumors of the gastrointestinal tract and lungs.[26]

However, the doses of HCAs and PAHs used in these studies were very high—equivalent to thousands of times the doses that a person would consume in a normal diet.

Population studies have not established a definitive link between HCA and PAH exposure from cooked meats and cancer in humans. One difficulty with conducting such studies is that it can be difficult to determine the exact level of HCA and/or PAH exposure a person gets from cooked meats. Although dietary questionnaires can provide good estimates, they may not capture all the detail about cooking techniques that is necessary to determine HCA and PAH exposure levels. In addition, individual variation in the activity of enzymes that metabolize HCAs and PAHs may result in exposure differences, even among people who ingest (take in) the same amount of these compounds. Also, people may have been exposed to PAHs from other environmental sources, not just food.

Numerous epidemiologic studies have used detailed questionnaires to examine participants’ meat consumption and cooking methods.[27] Researchers found that high consumption of well-done, fried, or barbecued meats was associated with increased risks of colorectal[28–30],...
pancreatic\textsuperscript{[30-32]}, and prostate\textsuperscript{[33,34]}, cancer. However, other studies have found no association with risks of colorectal\textsuperscript{[35]} or prostate\textsuperscript{[36]} cancer.

In 2015, an independent panel of experts convened by the International Agency for Research on Cancer (IARC) determined consumption of red meat to be “probably carcinogenic to humans” (Group 2A), based largely on data from the epidemiologic studies and on the strong evidence from mechanistic studies. However, IARC did not conclude that HCAs and PAHs were associated with cancer incidence.

**Guidelines report**

Currently, no Federal guidelines address the consumption of foods containing HCAs and PAHs. The World Cancer Research Fund/American Institute for Cancer Research issued a report in 2007 with dietary guidelines that recommended limiting the consumption of red and processed (including smoked) meats; however, no recommendations were provided for HCA and PAH levels in meat.\textsuperscript{[37]}

**Ways to reduce HCA and PAH formation in cooked meats**

Even though no specific guidelines for HCA/PAH consumption exist, concerned individuals can reduce their exposure by using several cooking methods:

- Avoiding direct exposure of meat to an open flame or a hot metal surface and avoiding prolonged cooking times (especially at high temperatures) can help reduce HCA and PAH formation.\textsuperscript{[37]}
- Using a microwave oven to cook meat prior to exposure to high temperatures can also substantially reduce HCA formation by reducing the time that meat must be in contact with high heat to finish cooking.
- Continuously turning meat over on a high heat source can substantially reduce HCA formation compared with just leaving the meat on the heat source without flipping it often.
- Removing charred portions of meat and refraining from using gravy made from meat drippings can also reduce HCA and PAH exposure.\textsuperscript{[38]}
The relationship between the consumption of HCAs and PAHs and cancer risk in humans

Researchers in the United States are currently investigating the association between meat intake, meat cooking methods, and cancer risk. Ongoing studies include the NIH-AARP Diet and Health Study\[^{28,39}\], the American Cancer Society’s Cancer Prevention Study II\[^{40}\], the Multiethnic Cohort, and studies from Harvard University.\[^{41}\] Similar research in a European population is being conducted in the European Prospective Investigation into Cancer and Nutrition (EPIC) study.

**CONCLUSION**

We know that high cooking temperatures and smoke put mutagenic chemicals into and onto meat. Yet, there are several measures you can take to reduce the number of heterocyclic amines and other carcinogens in the meat you eat.

Keep in mind that just like everything in life, moderation is key. You still can enjoy grilled meats, but just do so in moderation and when cooked at low temperatures. That said women who have had breast cancer may want to limit the amount of grilled, barbecued, and smoked meats they consume, even if they take the measures above to reduce carcinogens.

Finally, instead of thinking about only what you need to avoid, you may wish to reframe and think about the foods you can enjoy which may instead reduce your risk of cancer.

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