

Cancer aetiology and prevention biology essay

[Science](#), [Biology](#)



A number of vitamins and minerals associated with cancer aetiology and prevention. To avoid superficial coverage of material - a vitamin and mineral associated with both aetiology and prevention will be chosen and discussed. Reasons for choosing - Iron - haemochromatosis common, iron deficiency anaemia also common - could prevent supplementation, possibly iron deficiency and overload cause cancer? interesting. No protective properties. Vitamin A - carotenoids supposed to be antioxidants (supposed to be less potent than vitamin A, but cancer?). Protective against certain cancers. Not liver cancer even though stored there? Selenium - number of cancers involved, recent SELECT study, bad press lately, Vitamin D - huge press about it,

Aetiology:

1. Iron:

intro to apc loss pdf – NB to tie all together...

haemochromatosis etc

Iron is an essential mineral required for (KY'S NOTES - roles, where found in body, storage etc, amount absorbed) [Thomas Briony]. However, excess iron intake or storage has been demonstrated to have a role in the aetiology of a number of different cancers, particularly of the colon and liver. The colon is particularly susceptible as only 10% of dietary iron is absorbed resulting in luminal exposure with the potential to cause direct oxidative damage to the colorectal lumen. Hepatocellular carcinoma (HCC) is very strongly associated with hemochromatosis and other iron-overload diseases. (SACN)

Current Evidence:

A number of epidemiological studies have been undertaken, establishing a link between iron and colon cancer. A recent meta-analysis has demonstrated a consistent and significant association between high intakes of heme iron from meat and the increased risk of colon cancer. Five prospective cohort studies published between 2004 and 2010 were included, with data on 566, 607 individuals and 4, 734 cases of colon cancer. The overall relative risk of colon cancer was 1.18 in the individuals with the highest intake of heme iron compared to those with the lowest intake (pdf). The meta-analysis had a number of limitations, including that the studies did not all consider the same factors. For example, calcium has a proven role in animal models in inhibiting certain carcinogenic activities of heme iron in the colon (20, 21, 22). This was taken into consideration in two out of the five studies, which both demonstrated higher associations between heme iron and colon cancer than the other three studies (17-18). This experimental evidence examining the carcinogenic effect of heme iron in rats is consistent with the epidemiological studies, with a significant correlation between the number of aberrant crypt foci, a putative precancer lesion, per colon and the concentration of heme iron in the diet (Pierre F). The risk of HCC relating to hereditary hemochromatosis (HH) was first quantified in a cohort study in 1985, which concluded that there was a 200-fold increased risk of HCC in patients with GH (Bradbear). Studies since this initial study have confirmed the high association and shown increased risks of 20-200, occurring predominantly where liver cirrhosis was already present. (Kris). A population-based cohort study performed in Sweden in 2003 is believed to indicate the

true incidence and prevalence of HCC in HH. The study included 1847 Swedish patients with HH using nationwide, population based health and census registers. As it was a population-based study, it was possible to establish an overall standardized incidence ratio of HCC in the population. It found that patients with HH were at a 20-fold risk of liver cancer with an almost unaltered risk of all other cancers (Elmberg).

Research (Mechanisms):

The mechanism for iron's role in the aetiology of colon cancer is largely unknown, but a number of hypothesis were discussed in a meta-analysis in 2011 (pdf). They are based on iron having a catalytic role in the formation of carcinogenic N-nitroso compounds known to cause DNA damage and adduct, which contribute to p53 and K-ras mutations. This is hypothesised to initiate and promote tumour growth (46). It is also believed to have a catalytic effect on the formation of cytotoxic and genotoxic aldehydes by lipoperoxidation. (61) ? similar in HH?/? More recently, research carried out by Cancer Research UK scientists in 2012 found bowel cancers were 2-3 times more likely to develop in mice after adenomatous polyposis coli (APC) gene deletion that were fed high amounts of iron compared to mice who still had a working APC gene or those with gene deletion but a low intake of iron. Following deletion of the gene, proteins inducing iron accumulation are expressed, leading to a cancer signalling cascade. It was also found that increased luminal iron (but not systemic) promoted tumorigenesis (APC Pdf).

Future Directions:

Metabolic inhibitors represent an important class of anti-tumour agents . Aroylhydrazone and thiosemicarbazone iron chelators have demonstrated marked and selective anti-tumour activity in vitro and in vivo against a wide spectrum of tumours without inducing whole body iron-depletion or disturbances in haematological or biochemical functions (DR Richardson). Calcium salts, vitamin C and polyphenols may also have a role e. g. the addition of vitamin C to processed meats to inhibit the formation of NOC in meat (pdf). Individuals with colorectal adenomas and inflammatory bowel disease are at particular risk of developing colon cancer. As they often present with iron-deficiency anaemia due to intestinal bleeding, common practice is to supplement with high doses of oral iron which is conversely likely to further increase their risk of developing colon cancer. To resolve the anaemia and prevent this risk, a possible future direction would be to supplement systemically with intravenous infusions of iron and provide iron chelation therapy (APC pdf).

Selenium

lung cancer <http://www.ncbi.nlm.nih.gov/pubmed/22073154>General cancer <http://www.ncbi.nlm.nih.gov/pubmed/22004275>Prostate cancer <http://www.ncbi.nlm.nih.gov/pubmed/22648711>Cancer <http://www.ncbi.nlm.nih.gov/pubmed/21563143>Bladder <http://www.ncbi.nlm.nih.gov/pubmed/20807831>GI cancer <http://www.ncbi.nlm.nih.gov/pubmed/19145725>GI, Bladder, Prostate, LungNot skin, prostate

Intro:

Selenium has been considered to possess anticancer effects since the early 1970s, when Dr Passwater identified it as a mineral that appeared to reduce cancer incidence (possibly delete). Numerous mechanistic studies, animal studies, epidemiological studies and clinical supplementation trials have since confirmed this observation, although results have also been controversial from other studies (3).

Current Evidence:

A meta-analysis of 9 randomised controlled supplementation trials in 2011 found selenium supplementation to have a 24% preventive effect on cancer incidence. This protective effect was increased further in populations with a low baseline serum selenium level and in high-risk populations for cancer (Lee EH). Another meta-analysis examining prospective observational studies found that this risk was more pronounced in men than in women (Dennert). Selenium has been particularly associated with a reduced risk of cancer of the bladder, the lungs and the gastrointestinal tract. A meta-odds ratio was calculated based on seven epidemiological studies examining selenium status and the risk of bladder cancer, resulting in a 39% protective effect, predominantly in women (bladder). The gender difference in relation to bladder cancer is hypothesised to be due to differences in excretion rates, half-lives and sensitivity to selenium (Patterson B). The relationship between selenium and lung carcinogenesis risk is more controversial. The protective effect of selenium only appeared to be present in populations with lower baseline selenium status, with an increased risk of lung cancer seen in those with higher selenium status, when supplemented (Heidi). Of the RCTs, the

large Nutritional Prevention of Cancer trial found a 57% reduced incidence of lung cancer (Reid) while the Selenium and Vitamin E Cancer Prevention Trial (SELECT) study found a 12% increased risk associated with selenium supplementation (Lippman). Therefore, although selenium may be effective for lung cancer prevention among individuals with lower selenium status, it should not be used prophylactically for lung cancer prevention (Heidi). A large number of studies have shown an inverse relationship between selenium and prostate cancer risk (Hurst). This has become controversial following the conflicting results of the SELECT trial, which was terminated prematurely following identification of an increased risk of prostate cancer of up to 22% with selenium supplementation (Eric). GI – potentially found to decrease risk. (Bjel)

Research:

Selenium occurs in over 30 selenoproteins as selenocysteine. Glutathione peroxidase enzymes (GPx) are important selenoproteins with potent antioxidant activity against hydrogen peroxide and lipid peroxidation, as are thioredoxin reductases, important in regulating DNA expression, both believed to be involved in the prevention of cancer (gibney). Primarily, these two systems are associated with exerting selenium's antineoplastic effects (rayman mechanism). By protecting cells externally and internally from damage by free radicals, GPx prevents the activation of oncogenes (Sch). Thioredoxin reductases have a role in carcinogen metabolism, controlling cell division and may enhance p53 activity, resulting in either DNA repair or apoptosis (Smith). Other functions associated with selenium which may contribute to its chemoprotective effects include its role in thyroid function

and T cell immunity (Ashton). More recent laboratory investigations have proposed that selenium has additional mechanisms capable of preventing cancer development, including growth inhibitory, proapoptotic activity for selenometabolites in premalignant cells (Ip)

Future Directions:

At present, a new study examining the efficacy of selenium in the prevention of cancer in 33, 000 European individuals, The Prevention of Cancer by Intervention with Selenium (PRECISE) clinical trial, is at the pilot study stage (<http://clinicaltrials.gov/show/NCT00022165>). When examining the NPC and the SELECT trial, both with conflicting results, it is important to observe that different forms of selenium were used. Therefore, it is suggested that selenized yeast may give rise to peak anticancer effects (Rayman type) Think about side effects – type two DMit only provides an assessment of efficacy and risk regarding the use of selenium as an individual agent rather than as part of a combined therapeutic strategy for cancer chemoprevention. several studies also have shown that it has strong anticancer effects with a selective cytotoxicity on malignant drug-resistant cells while only exerting marginal effects on normal and benign cells. (google)

Vitamin A

AETIOLOGY: VITAMIN A Beta carotene lung and gastric <http://www.ncbi.nlm.nih.gov/pubmed/19876916> Lung <http://www.ncbi.nlm.nih.gov/pubmed/18689373> Lung <http://www.ncbi.nlm.nih.gov/pubmed/18429004> Mechanisms <http://www.annualreviews.org/doi/abs/10.1146/annurev-pathol-011110-130303> All cancers – lung and

<https://assignbuster.com/cancer-aetiology-and-prevention-biology-essay/>

gastric full <http://onlinelibrary.wiley.com/doi/10.1002/ijc.25008/full> Retinoic receptors in lung <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2483255/Protective> cervical <http://www.ncbi.nlm.nih.gov/pubmed/22005522Lung> <http://www.ncbi.nlm.nih.gov/pubmed/21738614>

Intro:

The role of vitamin A in the prevention and treatment of cancer has been extensively researched due to its antiproliferative effects at a cellular level, with the potential to induce apoptosis of cancer cells [25]. In a meta-analysis of English and Chinese studies, both performed vitamin A and the carotenoids have been demonstrated to be protective towards cervical cancer (Zhang) and towards breast cancer in another meta-analysis (Eliasson). Despite this plausible role in the treatment of cancer, studies have largely produced inconclusive or negative results (American cancer society). In particular, beta-carotene (although normally considered less potent than performed vitamin A and with the added antioxidant properties associated with decreasing oxidative stress with the potential to cause cancer) has been shown to increase the risk of lung cancer among smokers (Heidi).

Current Evidence:

Studies undertaken to assess the role of beta-carotene in the aetiology of lung cancer have demonstrated that this role is exclusively present in individuals already at a high risk of lung cancer, e. g. active smokers, those with a significant smoking history or those who were exposed to asbestos. A

study examining the relationship between dietary beta-carotene and lung cancer risk in U. S. non-smokers ironically found beta-carotene to be 30 % protective for lung cancer (Susan). A meta-analysis from 2008 examined four large randomized studies reporting on the effect of beta-carotene and the incidence of lung cancer in high-risk populations. It included the ATBC (The effect) and CARET (omen) studies and demonstrated a 24% increased risk of lung cancer associated with beta-carotene supplementation among participants who were current smokers and 10% among those with a significant smoking history (Tawee)In 2010, a meta-analysis of 9 randomized control trials (RCTs) showed that the incidence of lung and gastric cancers were significantly increased in individuals supplemented with 20–30 mg beta-carotene per day. An increased risk of 20% of developing gastric cancer was seen in smokers, while this increased to 54% in asbestos workers compared to the placebo group (Nathalie). Retinoids also useless

Research (Mechanisms):

The exact mechanism of the carcinogenesis is not fully understood. The high oxygen concentration of the lungs combined with exposure to lung irritants and conditions of high oxidative stress may result in carotene acting as a pro-oxidant (gibney). A high concentration of beta-carotene is another contributing factor, as anti-oxidant vitamins C, E and beta-carotene were demonstrated in vitro to activate free radical production with increasing concentration in peripheral blood mononuclear cells (de Oliv). The type of radicals involved also determines the fate of beta-carotene (van Held). Carotenoid cleavage products, including highly reactive aldehydes and epoxides, are formed during oxidative attacks in the course of antioxidative

action. They increase oxidative stress by impairing mitochondrial function, resulting in cellular damage and carcinogenesis (Siems).

Future Directions:

The most recent National Health and Nutrition Examination Survey found that 37% of vitamin and mineral supplements contained beta-carotene (Balluz). Recent surveys in Europe investigating the use of multi vitamin supplements have demonstrated large increases in their use in recent years (Reinert). Lung cancer patients surveyed on their use of complementary and alternative therapies revealed that multi vitamin combinations were the most common therapy used, with 17% of patients using them (Micke). Considering that 90% of lung cancer is attributed to smoking (cancer research UK <http://www.cancerresearchuk.org/cancer-help/type/lung-cancer/about/lung-cancer-risks-and-causes>), it is apparent that healthcare professionals need to be more vigilant in advising patients about the adverse effects of supplements containing beta-carotene.