Review Article

Environmental and Lifestyle Risk Factors of Gastric Cancer

Yeong Yeh Lee MD FRCP[1,2], Mohammad H. Derakhshan MD FRSPH•[1]

Abstract

Effective prevention and early diagnostic strategies are the most important public health interventions in gastric cancer, which remains a common malignancy worldwide. Preventive strategies require identification and understanding of environmental risk factors that lead to carcinogenesis. *Helicobacter pylori (H. pylori)* is the primary carcinogen as this ancient bacterium has a complex ability to interact with its human host. Smoking and salt are strong independent risk factors for gastric cancer whereas alcohol is only a risk when it is heavily consumed. Red meat and high fat increase the risk of gastric cancer however fresh fruits, vegetables (*allium* family) and certain micronutrients (selenium, vitamin C) reduce the risk, with evidence lacking for fish, coffee and tea. Foods that inhibit *H. pylori* viability, colonization and infection may reduce cancer risk. Obesity is increasingly recognized as a contributory factor in gastric cardia carcinogenesis. Therefore, modest daily physical activities can be protective against cancer. Foundry workers are at risk for developing gastric cancer with dust iron being an important cause. Other risk factors include Epstein-Barr virus (EBV), possibly JC virus and radiation but the effects of these are likely to remain small.

Keywords: Environmental, lifestyle, risk factor, stomach cancer

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Introduction

Gastric cancer remains an important burden for public health, particularly in less developed countries including Middle and Eastern Asia, South America and Eastern Europe, being responsible for 70% of cases worldwide (Figure 1).[1] Mortality rates remain high[1] with disease usually detected late in its course; at this stage treatment strategies are often not useful. Therefore, primary prevention and early detection strategies remain the most important public health interventions.[2] However, these strategies require identification and understanding of risk factors that lead to carcinogenesis.

With gastric cancer, a disease that is traced to ancient civilizations, the risk appears to evolve over time as a possible result of change in dietary and lifestyle factors. Improved sanitation, refrigeration and effective eradication strategies of *Helicobacter pylori* (*H. pylori*) have led to significant reduction in incidence of this cancer in the recent past[3] but the fact that this disease remains prevalent in modern times suggests that other environmental risk factors are involved in sustaining this condition.

The current review aims to discuss these environmental and lifestyle factors that are responsible for maintaining the burden of gastric cancer, as well as protective factors, with emphasis on developing countries, unless there is no available quality evidence.

Helicobacter pylori (H. pylori), the "death germ"

Before 1984, peptic ulcer disease as a global public health burden, was assumed to be associated with acid and stress.[4,5] Marshall and Warren in 1984 were first to describe the association between peptic ulcer disease and *H. pylori*,[6] and it has since been associated with gastric cancer[7] as well. There is strong evidence for *H. pylori* being a class I carcinogen that causes gastric cancer,[8,9] its eradication has since resulted in hope for the control this debilitating disease.[10] Developed countries, including Australia, that have improved socio-economic and living conditions during the formative years of their populations have reported both a lower prevalence of *H. pylori* and incidence of gastric cancer.[11] Those populations that presumably began with an extremely low prevalence of this infection, such as the ethnic Malays in Malaysia, have also shown a rare occurrence of stomach cancer and its precancerous lesions, further proving their causal relationship (Figure 1).[12–14]

The most common subtype of adenocarcinoma associated with *H. pylori* infection is the non-cardia intestinal type, which is related to corpus-dominant gastritis and precancerous lesions that include atrophic gastritis and intestinal metaplasia.[15] Within the cardia there can be two distinct etiological subtypes of cancer, one of gastric and the other of esophageal origin.[16] The gastric subtype behaves similarly to the non-cardia intestinal subtype which is associated with *H. pylori* infection.[17,18] The development of precancerous lesions in *H. pylori*-infected individuals is thought to arise from chronic inflammation[19] but more recently there is a role for genetic variations[20,21] as well. Eradication of infection in clinical trials with the aim to reduce the cancer incidence has been somewhat inconclusive.[10] Notwithstanding, these studies suggest that *H. pylori* is only a triggering factor in this multi-step disease, and that *H. pylori* should be eradicated early in life for disease prevention to be successful.

Certain virulence factors present in the bacterium have been found to influence the risk of developing cancer. The best studied of these factors include cytotoxin associated gene A (*cag*A), an active form of vacuolating cytotoxin gene (*vac*A), and more recently the duodenal ulcer promoting gene A (*dup*A).[22] While these virulence factors are commonly present in high risk populations including Iran,[23] they may be associated by chance (a type 1 error),

Authors' affiliations: [1]Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK. [2]School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.
•Corresponding author and reprints: Mohammad H. Derakhshan MD FRSPH, Section of Gastroenterology, Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK.
E-mail: Mohammad.derakhshan@glasgow.ac.UK
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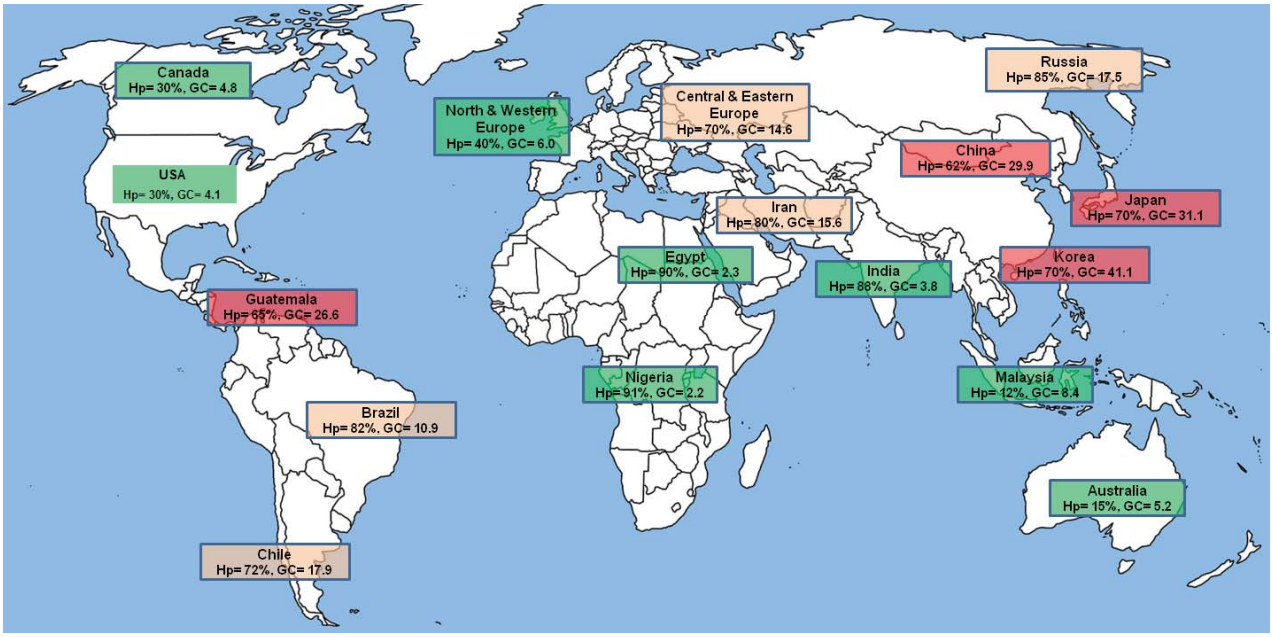

Figure 1. Prevalence of *H. pylori* infection (Hp, in %) and incidence of gastric cancer in 2008 (GC, world age-standardized rates per 100,000) in selected countries.

Note: Incidence of gastric cancer in countries with World Age Standardized Incidence Rate (WASR) <10 is denoted in green, 10 to 20 in orange, and <20 (20 /100,000 person-year) in red. The reported incidence rates are based on overall incidence of gastric cancer in males and females of the entire population within a country; they may not represent incidence variations within an individual country. Estimates of incidence rates extracted from updated Globocan database.[115] Estimates of *H. pylori* infection rates have been extracted from the World Gastroenterology Organization database[116] and Malekzadeh et al.[117] All figures are approximate.

where heterogeneous characteristics of these factors are partly being responsible for the error.[24]

Gene variants in *H. pylori*-susceptible hosts can also determine whether one has increased risk for developing gastric cancer. Among the recent reported gene variants include *ATG16L1*[25] in the Western population; *NOD1* and *NOD2*,[26] *COX-2*[27], and *MDM2*[28] in the Chinese population; *IL-10*[29] in Koreans; and *MTHFR*[30] and *iNOS*[31] in Iranians. Whether these gene variants are useful risk markers in infected individuals is unknown and population studies are clearly needed for their assessment. In addition to gene variations, the epigenetic event is also contributory. More recently, epigenetic silencing of *FOXD3*[32] by *H. pylori* has been found to promote gastric carcinogenesis with its occurrence being an early event. Certain gene variants may also protect against developing gastric cancer by reducing susceptibility to *H. pylori* infection, among these include *DNMT-1* in the Chinese;[33] *uPA* in the Japanese;[34] and *C7orf10*, *TSTD2*, *SMG7*, and *XPA* in the Malay.[35]

The evidence thus far suggests that interplay between host and strain factors is important in determining the risk of developing cancer in *H. pylori*-infected individuals. Subsequent development of gastric cancer in these individuals would also require an understanding of mediators that are involved in the pathogenesis, of which phosphorylation of certain protein kinase C isozymes,[36] has recently been found to be among them.

The bane of smoking

Smoking is a risk factor for many cancers. As many as 14 types of cancers including gastric cancer have been found to be associated with smoking in a cohort study of 34439 British doctors over 50 years.[37] In a large population-based study in Europe (EPIC), 17.6% of gastric cancer cases were attributed to smoking.[38] Likewise, a pooled analysis of two population-based cohort studies in Japan has indicated that compared to those who never smoked, the relative risk for gastric cancer in current smokers was 1.84 and for past smokers, it was 1.77.[39] A meta-analysis did not find any difference in smoking risk between Caucasian and Asian studies.[40] Another meta-analysis has suggested that smoking increases risk for both cardia and non-cardia cancers with a relative risk of 1.87 (cardia) and 1.60 (non-cardia).[41]

The cancer risk in past smokers can remain up to 14 years after cessation of smoking.[39] The effect of smoking on gastric cancer is dose-dependent and additive in the presence of other risk factors, including alcohol.[42,43] However, passive smoking did not seem to increase the risk.[44] In addition to tobacco, opium has been recently found to be associated with a higher risk of gastric cancer.[45] There is a striking male predominance in gastric cancer hypothesized to be the result of a greater number of male smokers, however studies suggest that this is not the case.[46] Instead, the male predominance is related to intestinal histological subtype and is due to marked delay in the development of this type of tumor in females prior to 50–60 years of age.[47]

While the exact mechanisms are unclear, it is likely that formation of oxygen radicals and increased apoptosis associated with smoking induces precancerous changes in the gastric epithelium, further promoting the progression of carcinogenesis.[48,49]

Salt, a necessary menace

Salt has influenced the existence of humans since the beginning of civilization. It has played important socioeconomic, cultural and military roles in the history of mankind such that its harms are often ignored. Salt has been first reported to be a risk factor for gastric cancer in 1959.[50] Since then a number of ecological, case control and cohort studies have confirmed the role of salt in gastric carcinogenesis.[51] The higher the level of salt consumption,

Table 1. Selected recent publications on environmental and lifestyle factors associated with an increase in risk of gastric cancer.

Factor	Study (Ref.)	Year	Region	Design	HR, OR or RR (95% CI)
Helicobacter pylori (H. pylori)					
	Cavaleiro-P et al.[8]	2011	Asia, Europe, US	Meta-analysis	RR 1.1 (0.8,1.4) cardia RR 3.0 (1.9, 4.7) non-cardia
	Wang et al.[9]	2007	Asia, Europe	Meta-analysis	OR 3.4 (2.1, 5.3)
Smoking					
	La Torre et al.[40]	2009	Global	Meta-analysis	HR 1.5 (1.3, 1.7)
	Ladeiras-l et al.[41]	2008	Global	Meta-analysis	RR 1.9 (1.3, 2.7) cardia RR 1.6 (1.4, 1.8) non-cardia
Opium					
	Shakeri et al.[45]	2013	Iran	Case-control	HR 3.2 (1.9, 5.1)
Salt					
	D'Elia et al.[52]	2012	Japan, Europe, US	Meta-analysis	RR 1.7 (1.2, 2.4) (high intake) RR 1.4 (1.0, 1.9) (moderate)
Alcohol					
	Duell et al.[57]	2011	Europe	Cohort	HR 1.6 (1.1, 2.6) (heavy)
	Tramacere et al.[59]	2012	Global	Meta-analysis	RR 0.9 (0.8, 1.1) (vs. none)
Meat (total)					
	González et al.[63]	2006	Europe	Cohort	HR 3.5 (2.0, 6.3)
Dietary heme iron					
	Jaksyn et al.[64]	2012	Europe	Cohort	HR 1.1 (1.0, 1.3)
Fat (oleic acid)					
	Chajès et al.[68]	2011	Europe	Cohort	HR 1.7 (1.0, 2.9)
Chili pepper					
	Bonequi et al.[69]	2011	Latin America	Meta-analysis	OR 1.9 (1.4, 2.7)
	Mathew et al.[70]	2000	South India	Case-control	OR 7.4 (4.0, 13.5)
Obesity					
	Yang et al.[98]	2009	Global	Meta-analysis	Only cardia: OR 1.5 (1.3, 1.8)
Foundry working					
	Ahn et al.[103]	2010	Korea	Cohort	SRR 2.1 (1.1, 4.0)
Uranium mining					
	Kreuzer et al.[89]	2012	Germany	Cohort	ERR/Gy 0.3 (-1.3, 1.9)
Epstein-Barr virus (EBV)					
	Murphy et al.[108]	2009	Global	Meta-analysis	Pooled prevalence 8.7% (7.5, 10.0)
JC virus					
	Murai et al.[111]	2007	Japan	Case-control	10× higher DNA load

Ref= reference, HR= hazard ratio, OR= odds ratio, RR= relative risk, CI= confidence interval, US= United States, SRR= standardized rate ratio, low-LET= low linear energy transfer, ERR/Gy= excess relative risk per unit of radiation exposure (in Gy).

the higher the risk of cancer, a finding particularly observed in the Japanese population.[52] Preservation of food with salt is an ancient human practice. While this practice is still common in the less developed parts of the world, the introduction of refrigeration has significantly reduced salt preservation. This reduction is believed to be one of the primary reasons for the decreased incidence of gastric cancer in the developed world.[53] The exact mechanism for salt as the cause of stomach cancer remains elusive. It may act synergistically with *H. pylori* infection, as has been shown in case-control and animal studies, through mechanisms that include potentiation of *cagA* expression, changes in mucous viscosity, enhancing damage and inflammatory response in the epithelium and hypergastrinemia with subsequent loss of parietal cells.[54] More recently, polymorphism of angiotensinogen has been found to be associated with salt sensitivity, and while M235T polymorphism was not shown to be significantly different between gastric cancer cases and controls, other salt sensitivity genes have yet to be studied.[55]

Alcohol, the heavier drinker a greater risk

Alcohol, as an independent risk factor for gastric cancer has not been supported by evidence. In 2007 the International Agency for Research on Cancer (IARC) working group has suggested that alcohol might be associated with increased risk, however confounding factors that include smoking and dietary habits could not be ruled out.[56] More recent evidence from epidemiological studies lack support for alcohol as an independent risk factor, with the exception of heavy alcohol consumption. In the European (EPIC) study of 444 subjects with gastric cancer, heavy alcohol consumption (≥60 g/day) increased the risk with a hazard ratio of 1.6, however the risk was confined to the intestinal subtype of non-cardia cancer.[57] A similar result was reported in a Chinese study of 391 subjects with gastric cancer, which showed that heavy drinkers (>4 drinks or >50 g/day) had increased risk with a hazard ratio of 1.4. However, the risk was greater for spirits compared to beer.[58] Like-

Table 2. Selected recent publications on environmental and lifestyle factors associated with "protection" against gastric cancer and *Helicobacter pylori (H. pylori).*

Factor	Study (Ref)	Year	Region	Design	HR, OR, or RR (95% CI)
Total vegetables, onion, garlic					
	González et al.[72]	2006	Europe	Cohort	HR 0.7 (0.3, 1.2) total vegetable HR 0.7 (0.4, 1.3) onion, garlic
Toenail selenium					
	Steevens et al.[75]	2010	Netherlands	Cohort	RR 0.9 (0.8, 1.1)
Plasma vitamin C					
	Jenab et al.[78]	2006	Europe	Cohort	OR 0.5 (0.3, 0.9)
Zinc element in drinking water					
	Nakaji et al.[83]	2001	Japan	Cohort	OR 0.6 (men)
Vitamin E, carotenoid (α & β)					
	Pelucchi et al.[84]	2009	Italy	Case-control	OR 0.5, (0.5, 0.4)
Fish					
	Wu et al.[86]	2011	Global	Meta-analysis	RR 0.9 (0.7, 1.1)
Coffee and black tea					
	Gallus et al.[87]	2009	Italy	Case-control	OR 0.9 (0.7, 1.2) coffee OR 0.9 (0.6, 1.4) black tea
Green tea					
	Myung et al.[88]	2009	Japan, China, US	Meta-analysis	RR 1.6 crude RR 1.0 adjusted
Special foods against *H. pylori*					
	Lee et al.[89]	2012	Malaysia	Case-control	HR 0.09 (0.1, 0.7) "Budu" HR 0.2 (0.1, 0.6) "*Centenella asiatica*" HR 0.02 (0.01, 0.1) Local tea
Physical activity					
	Huerta et al.[95]	2010	Europe	Cohort	HR 0.7 (0.5, 0.9)
	Sjödahl et al.[96]	2008	Norway	Cohort	HR 0.5 (0.3, 0.9)
Human T lymphothrophic virus type 1 (HTLV-1)					
	Matsumoto et al.[109]	2008	Japan	Case-control	HR 0.4 (0.2, 0.7)

Ref= reference, HR= hazard ratio, OR= odds ratio, RR= relative risk, CI= confidence interval.

wise, a recent meta-analysis suggested a higher risk for non-cardia but not cardia-type gastric cancer with heavy alcohol consumption.[59]

The mechanism for alcohol-induced carcinogenesis is likely to involve a chronic inflammatory response from direct toxic effects of ethanol metabolites and cytokines that subsequently impair the gastric mucosal barrier and increase absorption of nitrosamines.[60] Toxins including acetaldehyde and acetate arise from metabolism of ethanol via the enzyme alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), both prone to genetic variants that can increase the levels of these toxins. A recent study from Korea has shown a four-fold higher risk for gastric cancer in heavy drinkers with *ALDH2 *1/*2* heterozygotes compared to non-drinkers.[61] Acetaldehyde can be further increased by bacterial overgrowth in the oral cavities of alcoholics.[62]

Diet: Balancing risk and protection

Probable high risk diets: Meat, fat and possibly chili pepper

The risk of non-cardia but not cardia gastric cancer increases with higher intakes of total, red and processed meat in *H. pylori*-infected subjects, with an absolute risk of 0.3% in ten years in those having the highest quartile of total meat intake.[63] Heme iron, mostly abundant in meat, is the main precursor for endogenous nitrosamine production and formation of free radicals, both of which are important carcinogens. Studies have shown a 70% increase in the risk of gastric cancer with the highest quartile of dietary heme iron; this effect was only significant at the lowest levels of plasma vitamin C.[64,65]

Although dietary fat is associated with increased risk of gastric cancer, there is limited prospective evidence.[66,67] Prediagnostic profiling of fatty acid with high concentrations of oleic acid, α-linolenic acid and di-homo-γ-linolenic acid has been found to be associated with increased risk of gastric cancer in the EPIC-EURGAST study.[68]

Certain populations, including those in Latin America and South India, have reported increased risks for gastric cancer with high consumption of chili pepper.[69,70] However, the actual carcinogenic potential is likely to be small and there is the possibility of contamination of capsaicin-containing foods with known carcinogens.[71]

Probable protective diets: Fruits, vegetables and micronutrients

The same EPIC-EURGAST study found that increased dietary intake of fresh fruits and vegetables in particular the *Allium* family (e.g., onions, garlic and leek) is associated with reduced risk of gastric cancer, especially the non-cardia intestinal type. *H. pylori* does not modify this effect.[72] The combination of anti-oxidant nutrients in plant food as measured using the total radical-trapping antioxidant potential (TRAP), rather than single nutrients, is more important for the observed protective effect.[73]

Certain micronutrients and minerals may also reduce the risk of gastric cancer, among which selenium is of particular interest.[74] A cohort study from the Netherlands suggests an inverse association between toenail selenium and gastric cancer.[75] Likewise, an ecologic study associates selenium deficiency with a high incidence of gastric cancer in the Ardabil Province of Iran.[76] The main mechanism for the protective effects of selenium is due to its superior anti-oxidant properties, its ability to reduce DNA damage, as well as anti-inflammatory properties and anti-angiogenesis effect.[77]

Vitamin C may be associated with a reduced risk of gastric cancer[78] by inhibiting formation of N-nitroso compounds.[79] Vitamin C may modify the effect of *H. pylori*[80] in gastric carcinogenesis and also reduces the risk of progression of precancerous lesions.[81] Other micronutrients that have possible protective effects include zinc,[82,83] vitamin E and carotenoids.[84]

Foods with a possible protective effect

Fish, a common diet worldwide, provides the vital source of n-3 fatty acids shown to have anti-inflammatory and anti-carcinogenic effects.[85] In a meta-analysis of 5323 cases of gastric cancer, the authors have concluded that high fish consumption lacks conclusive evidence for a protective effect. This conclusion might be due to the difference in types of fish consumed, of which processed and salted fish carry a risk rather than protection.[86]

Coffee and tea (black and green), the two most consumed food beverages in the world, have inconclusive evidence on their association with gastric cancer risk.[87,88] This may be explained by the presence of carcinogenic as well as anti-carcinogenic chemicals in these beverages, difference in dosing/frequency, temperature, limitation of case-control studies, and influence of confounders including *H. pylori* infection which have not been adequately addressed.

Foods that reduce *H. pylori* infection may be protective

Since *H. pylori* infection is the primary carcinogenic agent, dietary factors that contain chemicals which naturally inhibit this infection are therefore potentially protective against gastric cancer. In the ethnic Malays, frequent use of "budu", "pegaga or *centenella asiatica"* and local tea has been found to reduce the risk of infection.[89] Foods such as broccoli sprouts, Manuka honey and omega-3 oil, independently and in combination, have been shown to attenuate inflammation by blocking the release of IL-8 from infected gastric mucosa.[90] Probiotic strains that include *Lactobacillus johnsonii* MH-68, *Lactobacillus Salivarius* subsp. *salicinius* AP-32 appear to suppress *H. pylori* viability *in vitro* and reduce the occurrence of gastritis and risk of infection *in vivo*.[91]

Obesity and physical activity

Gastric cancer tends to affect the poorer classes. Although the reasons are not exactly known, some investigators suggest this may be the result of excessive physical activity, exposure to high risk occupation and having poorer quality diets in comparison to the wealthy.[92] Few studies have examined the association between physical activity and gastric cancer. A prospective study suggests an increase in relative risk for gastric cancer with excessive physical activity.[93] A case-control study however did not support this finding,[94] and likewise, the recent and larger EPIC study has found an inverse association between non-cardia distal cancer and time spent on cycling and sports activities, which was not observed in the cardia-subset.[95] A modest amount of physical activity is likely beneficial for protection against gastric cancer.[96]

A rising trend in obesity and sedentary life-style has raised concerns that both would be major risk factors for many cancers. Unlike colon and esophageal adenocarcinomas in which obesity is a major risk factor,[97] the association between obesity and gastric cancer is not straightforward and is meaningful when only analyzed as subgroups. Yang et al. in his meta-analysis has shown a 55% increase in risk of gastric cardia cancer among overweight and/or obese subjects. The study by Yang et al. did not show an excess risk of gastric non-cardia cancer in obese people.[98] The association of obesity with gastric cancer could not be seen in the Asian population, perhaps due to a higher proportion of non-cardia cancer. An inverse relationship between BMI and atrophic gastritis which has been described in a large-scale study by Watabe et al. might explain the mechanism of inverse or null association between obesity and non-cardia gastric cancer.[99]

High risk occupation - the foundry workers

Workers in iron, steel and dust-prone industries are reported to have elevated risks not just for chronic respiratory diseases and lung cancer but also gastric cancer. The few cohort and case-control studies involving iron foundry workers indicate an excess in total mortality and cancer-related mortality as being associated with gastric cancer, even after adjusted for non-occupational confounders that include smoking, diet and socioeconomic status.[100–102] The risk is higher in those workers with greater exposure to dusts.[103] While it is likely that many chemicals in the dusts may be responsible for carcinogenesis, iron itself is likely a most important element to cause progression of gastric cancer.[104] The mechanisms for iron involvement in gastric carcinogenesis are elusive but studies in hemochromatosis and cirrhotic patients suggest that iron can be deposited in gastric glands, especially in the fundus, and induces gastritis.[105,106] In addition, absorbed ingested dust iron, possibly similar to dietary iron, is associated with endogenous nitrosamines production and formation of free radicals resulting in oxidative damage and inflammation.[64]

Other risk factors - the "unseen"

Viral factor

Viruses are one of the emerging risk factors for gastric cancer. In particular, the Epstein-Barr virus (EBV) which is a ubiquitous γ-1 herpes virus acquired in childhood is known to be associated with several cancers, including lymphoma and nasopharyngeal carcinoma.[107] Epidemiology data suggest an overall low prevalence of gastric cancer associated with EBV and a meta-analysis of 15952 gastric cancer cases has indicated that in EBV-associated carcinoma there was a two-fold increase of risk in men, which was more likely to arise in the cardia and body. The lymphoepithelioma-like histology was determined to be >90% EBV positive.[108]

On the other hand, a Japanese study indicated that in those patients seropositive for human T lymphotropic virus type 1 (HTLV-1), the incidence of gastric cancer has been shown to be lower.[109] Unlike EBV which probably acts as co-factor for *H. pylori*-related carcinogenesis, HTLV-1 induces a less suitable stomach environment for *H. pylori* due to prolonged immunosuppression.

Another potential virus with possible involvement in gastric carcinogenesis is a human polyoma virus, the JC virus. Approximately 90% of the world's population are asymptomatically infected with low levels of JC virus. It is associated with the lethal progressive multifocal leukoencephalopathy (PML) if activated during periods of immunosuppression.[110] Higher levels of JC viral infection are found to be associated with gastric cancer development in the Japanese.[111]

Radiation exposure

The other "unseen" risk factor is radiation exposure. Low dose radiation exposure in uranium miners has been found to have a positive but statistically insignificant association with gastric cancer.[112] Children that were exposed and survived the Hiroshima and Nagasaki atomic bombs were found to have higher mortality from all cancers, with boys developing cancers even at low doses of exposure.[113] In a large case-control study from China, genetic instability as a result of γ-radiation induced chromatid breaks was found to be associated with an increased risk of gastric cancer.[114]

Conclusion

Gastric cancer is one of the most common malignancies worldwide. Despite its declining incidence in developed countries, it remains an important public health burden that is likely due to sustenance by environmental risk factors, both known and unknown (Tables 1 and 2). *H. pylori* remains the primary carcinogen. Although its prevalence has markedly decreased due to improved sanitation and effective eradication strategies, this ancient bacterium still has a survival edge in the stomach. Smoking and dietary salt are strong independent risks for gastric cancer whereas alcohol is most likely a risk only in the presence of heavy alcohol consumption. Red meat and high fat diet increase the risk of developing gastric cancer but fresh fruits, vegetables and certain micronutrients (selenium, vitamin C) are protective, with evidence lacking for fish, coffee and tea. Foods that can inhibit *H. pylori* viability, colonization and infection are potential protective factors. With the rising prevalence of obesity and sedentary lifestyles, modest physical activities are also likely protective. Foundry workers are at risk for developing gastric cancer with dust iron being an important source. EBV, possibly JC virus and radiation are other risk factors, however current evidence suggests they have a minor role in gastric carcinogenesis.

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