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Stomach Cancer - it's causes and treatments

Stomach cancer is a worldwide killer, causing the deaths of around 1 million people per year, with around 9000 of those being in the UK. Whilst incidence is decreasing in the developed world this is due to better diet rather than better treatment so it is important that effective treatment is available.

It is a multifactorial disease, having many risk factors and predisposing factors but no definitive causes. This account outlines some of the risk factors of stomach cancer and then goes on to detail current treatments.

Prevalence and types of stomach cancer

The significance of stomach cancer varies worldwide, with different reports describing it as either the 2nd or 4th largest cancer worldwide, accounting for just under 9% of new cases but nearly 11% of deaths each year. However it should be noted that overall incidence rates have been decreasing since the 1930s, but this is mainly due to a larger drop in distal stomach cancer, which is unfortunately coupled with an increase in cancer of the cardia and gastro-oesophageal junction (see figure 1 for the structural divisions of the stomach).

There are two main forms of stomach cancer, diffuse and intestinal, with the diffuse type affecting more of the non typical individuals, eg females and younger (see risk factors below). Diffuse and intestinal stomach cancers differ both in location and causative factors. 90% of stomach cancers are adenocarcinomas derived form the glandular tissue.

Risk Factors

As stomach cancer is multifactorial there are no causative factors as such, rather risk factors and predisposing factors, the most significant of which is Helicobacter pylori infection. Helicobacter pylori (H Pylori) is a bacterium that has consistently been linked with stomach damage including ulceration and cancer. Infection rates for H pylori closely mirror those for stomach cancer, both geographically and epidemiologically. However it should be noted that H pylori is acquired in childhood and many sufferers are asymptomatic. H pylori infection has been classified as carcinogenic to humans since 1994 but the effects are indirect and due to the damage caused to the gastric mucosa. It has been shown that normal gastric mucosa is not associated with stomach cancer. Thus infection with H pylori is considered 'necessary but not sufficient' to cause stomach cancer. The relative risk of H pylori infection is 2.5, and prevalence is almost double in developing countries, compared to the developed Western world. One of the most compelling arguments for the involvement of H pylori in stomach cancer comes from a Japanese study in which no individuals without the bacterium developed stomach cancer, compared to 2.9% of those with the bacterium, even those who were asymptomatic for ulceration and dyspepsia.

H pylori infection damages the gastric mucosa, which predisposes the individual to carcinogenesis. Whilst initial levels of H pylori in atrophic gastritis (which often leads to cancer) are high, by the time that the more significant damage that leads to cancer has occurred, H pylori levels have dropped, due to the unsuitable gastric conditions.

The progression from regular H pylori infection to stomach cancer involves several stages, through metaplasia and dysplasia to carcinoma. These final stages have largely unknown causes so it is imperative that the disease is caught at the earlier H pylori infection and gastric atrophy stages so that effective intervention may occur.

It has been suggested that around ½ of gastric cancers are associated with H pylori infection, possibly due to the different effect that H pylori infection has on younger people. One of the reasons why H pylori may be implicated in stomach cancer is that it reduces the bioavailability of vitamin C, known to be protective against many types of cancer, including that of the stomach.

There are a number of other recognised risk and predisposing factors for stomach cancer, as detailed below:

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Male Age 60+

Pernicious anaemia,
hypogammaglobulinaemia,
previous gastric surgery,
achlorhydria,
blood group A,
high salt intake,
high nitrate intake,
familial history,
smoking,
poor fruit and vegetable intake,
occupational hazards

Treatment

The successful treatment of stomach cancer depends heavily on the early and accurate diagnosis, as might be expected. Surgery may be curative or palliative, depending on whether it seeks to remove all of the cancer and associated tissue. Surgery is the most effective way of treating stomach cancer, but has a poor long-term prognosis, with only 34% of patients surviving past 5 years. If the cancer is detected early, however, survival can be better than 90%. In advanced stages of the disease surgical resection cannot remove all of the metastases, perhaps contributing to the poor prognosis.

Chemotherapy

5-fluorouracil based chemotherapy is recommended in advanced stage stomach cancer that cannot be treated with surgery. However, even though it represents the most effective chemotherapy currently available, median survival rates are only in the region of 6-10 months. Other suitable drugs for the advanced stage cancer include doxorubicin and cisplatin, which have a response rate of between 19 and 86% as single agents. However more success on the chemotherapeutic front comes from combination therapy, with the most commonly used combination therapy being 5-fluorouracil and cisplatin, with an over 50% success rate being reported in a 2005 study. It has also been suggested that COX-2 inhibitors might be chemoprotective in stomach cancer, acting to inhibit the apoptosis and possibly consequent carcinogenesis aggravated by the COX-2 enzyme.

Conclusion
Whilst H pylori has a significant impact on the development of stomach cancer it is not necessarily causative. Instead it is deemed as producing an environment conducive to carcinogeneis. Basically anything that can damage the gastric mucosa will greatly increase the chance of stomach cancer developing.