

## 9th Seah Cheng Siang Memorial Lecture: Gastric Cancer—Where are we now?†

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### Abstract

*Gastric cancer, the second most common cancer in the world, kills about one million people a year, almost half of whom are Chinese. Chinese, Japanese and Koreans as well as east Europeans top the list with over 40 per 100,000 population per year, with a wide margin over Americans, Indians and Zimbabweans in whom the rates are below 1 per 100,000. The excellent prognosis of early gastric cancer is well established, and survival of cancer involving beyond the submucosa remains poor and there is little new in management. However, recent years have witnessed a breakthrough in the understanding of causative factors and molecular genetic abnormalities in gastric cancer that should pave the way for prevention, early detection and prognostication.*

*Established carcinogens for gastric cancer now include Helicobacter pylori and N-nitroso compounds; other causative factors include salt and salted food intake, cigarette smoking, male sex, and familial genetic abnormalities. H. pylori infection increases cancer risk by about 5 in a 10-year period. Diet high in salt carries a relative risk of up to 6, and a highly significant correlation between 24 h urinary salt content and incidence of gastric cancer has been shown in 24 countries. The risk from smoking and male sex is under 2. Many N-nitroso compounds, which come from nitrites, which in turn come from nitrates in food following bacterial transformation in a hypochlorhydric environment, are established carcinogens in animals, but their risk for human gastric cancer is still debatable.*

*The intestinal type of gastric cancer, according to Correa's hypothesis, develops from chronic inflammation leading to intestinal metaplasia, dysplasia and cancer, and is more associated with H. pylori and early gastric cancer. The diffuse type of gastric cancer does not go through these precancerous conditions and moves straight from inflammation to cancer. Associated with inflammation are an increase in proliferation and apoptosis, and this fine balance between proliferation and apoptosis may be uncoupled by genetic mutations. It is believed that as a result of the accumulation of molecular genetic abnormalities, a cancer eventually develops and metastasizes. p53 mutation, cyclin overexpression (especially in intestinal type), microsatellite instability, down regulation of E-cadherin (especially in diffuse type), and telomerase reactivation are some prominent examples. These molecular abnormalities have the potential for screening, early detection and prognostication.*

*Fruits and vegetables, green tea, α-tocopherol and other micronutrients such as selenium have been shown to reduce the risk for gastric cancer. In fact, it has been reported that diet consisting of vegetables and fruits, low in salt, together with the avoidance of cigarette smoking would prevent two-thirds to three-quarters of gastric cancer. Furthermore, eradication of H. pylori, and for that matter future vaccination, has the theoretical potential of preventing gastric cancer, and the potential use of COX2 inhibiting NSAID in inducing apoptosis may reverse precancerous conditions of the stomach. Both approaches are being intensely studied.*

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