Review

The Decreasing Burden of Gastric Cancer in Japan

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Gastric cancer in Japan, previously the top killer cancer, has recently shown decreased incidence and mortality rates. Epidemiological studies have demonstrated that environmental factors are closely associated with stomach oncogenesis, as evident from the geographical differences seen throughout Japan in both incidence and mortality. Moreover, Japanese immigrant populations gradually exhibit the lower incidence and mortality rates of gastric cancer in their chosen country. Likewise, younger generations in Japan have lower mortality rates than older generations at the same age, which may be accounted by the dramatic lifestyle changes in Japan after World War II. In addition to exploring and learning from the impact of these environmental factors, deliberate strategies to further lower the incidence and mortality rates of gastric cancer must include aggressive eradication programs for Helicobacter pylori and dietary education in both school curricula and for the general adult population to lower the intake of causative agents such as salt and increase the intake of beneficial agents such as fruits, vegetables and seaweeds. The dietary education should be coupled with better motivation for the general population to undergo regular screening with improved techniques. In the future, changes in these environmental factors and progresses in the diagnosis of and therapeutic strategies for gastric cancer will lead to further decrease in the incidence and mortality rates of this disease in Japan. ——— gastric cancer; incidence; mortality; dietary factors; Helicobacter pylori

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Gastric cancer previously had the highest rates of incidence and mortality in Japan (Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour, and Welfare, Japan 2003; Osaka Medical Center of Cancer and Cardiovascular Disease, Department of Cancer control and Statistics 2004). As for the mortality rate, it has gradually decreased from the 1970s, and lung cancer overtook gastric cancer in 1997 in men, though the latter is still to date in first place in women (Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour, and Welfare, Japan 2003). However, gastric cancer is still one of the most common cancers and an important disease in the clinical and public health fields in Japan.

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Recent findings of gastric cancer incidence and mortality rates

Because the enforcement period is longest in Japan and the registry precision (Death Certificate only [DCO]) has been relatively constant, the Osaka Cancer Registry (Pref. Osaka 2004) is suitable for observation of the secular changes of the incidence rates of gastric cancer in Japan. These data indicate that the age-adjusted incidence rates of gastric cancer have decreased gradually and steadily (Osaka Medical Center of Cancer and Cardiovascular Disease, Department of Cancer control and Statistics 2004) (Fig. 1), but the number of gastric cancer patients has increased (Osaka Medical Center of Cancer and Cardiovascular Disease, Department of Cancer control and Statistics 2004) (Fig. 2), which demands that

![Fig. 1. Trends of age-adjusted incidence rates of gastric cancer in Osaka prefecture (standard population: 1985 Japanese model population).](image1)

![Fig. 2. Numerical trends of gastric cancer incidence in Osaka prefecture.](image2)
more attention needs to be paid to this disease. Especially in the clinical field, the large number of patients represents a very important problem because of health expenditure; so despite decreased incidence and mortality, the clinical importance of the existence of gastric cancer remains unchanged in Japan. Regarding the mortality, a similar dissociation between rates and the

Fig. 3. Trends of age-adjusted mortality rates from gastric cancer in Japan (standard population: 1985 Japanese model population).

Fig. 4. World trends of age-adjusted gastric cancer incidence rates in males (standard population: world population).
Fig. 5. World trends of age-adjusted gastric cancer incidence rates in females (standard population: world population).

Fig. 6. World trends of crude mortality rates from gastric cancer of men.
number are recognized, which also emphasizes the importance of gastric cancer (Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour, and Welfare, Japan 1999, 2003) (Fig. 3). Additionally, the age-standardized mortality ratios (SMRs) (Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour, and Welfare, Japan 2003) have decreased but gastric cancer death in the older generation (over 80 years old) is increasing.

When we compare Japan with other countries by incidence and mortality rates, it is clear that the incidence and mortality rates of gastric cancer around the world have decreased gradually in a similar fashion as in Japan (Waterhouse et al. 1982; Muir et al. 1987; Parkin et al. 1992, 1997; World Health Organization Mortality Database) (Figs. 4, 5, 6 and 7), which may be partially explained by the progresses in therapeutic strategies and the increase of early stage detection as well as the decrease in incidence rates.

**Epidemiological studies in environmental factors**

*Secular changes in the incidence and mortality rates*

After World War II, gastric cancer incidence and mortality rates have gradually decreased in Japan, which suggests the influence of environmental factors. Indeed, environmental factors such as dietary habits dramatically changed in Japan after World War II (Figs. 1 and 3) due to the changes in diagnostic/therapeutic level or lifestyle, including dietary habits among the different areas in Japan.

*Geographic distribution*

The SMRs among the 47 prefectures in Japan show that SMRs are higher in northern Japan than those in southwestern Japan (Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour, and Welfare, Japan 2003) (Fig. 8). Rather than congenital factors (most Japanese are of the same
ethnic origin), the reason for this may be the geographically-related differences in lifestyle, including dietary habits, among the various geographic regions in Japan.

Research on immigrant residents

Several reports have confirmed that the incidence rates among Japanese immigrant residents gradually become closer to those of native residents. Especially in the USA, the lifestyles of Japanese residents show a tendency to become similar to those of the natives in the place to which the Japanese have migrated; therefore the gastric cancer incidence rates of immigrant Japanese residents approach those of the indigenous residents (Waterhouse et al. 1982; Muir et al. 1987; Parkin et al. 1992, 1997, 2002) (Figs. 9 and 10). Similarly, the incidence rates among

![Fig. 8. The geographic distribution of age-standardized mortality rates according to all prefectures in Japan (2003).](image)

![Fig. 9. Comparison (standard population: world population) of the age-adjusted incidence rates in males between Japanese immigrant residents and indigenous US natives.](image)
Japanese immigrants in Brazil have gradually become closer to those of the Brazilian natives (Tsugane et al. 1990), probably because of the enforced change in lifestyle among immigrant Japanese residents.

**Birth cohort analysis**

A birth cohort analysis of the gastric cancer mortality rates in Japan has shown that the older generations have higher incidence rates when compared with each successive birth cohort at the same ages (Statistics and Information Department,
Minister’s Secretariat, Ministry of Health, Labour, and Welfare, Japan 2003) (Figs. 11 and 12). The diverse generation-associated lifestyles may be the reason behind this.

Thus, epidemiological findings have shown that environmental factors exert a stronger influence than congenital factors in Japan (Kono and Hirohata 1996; Kobayashi et al. 2002; Machida-Montani et al. 2004; Inoue and Tsgane 2005) and the rest of the world (Galanis et al. 1998; Hyun et al. 2002; Kelley and Duggan 2003; Crew and Newgut 2006; Forman and Burley 2006).

**RISK FACTORS ASSOCIATED WITH GASTRIC CANCER**

A review report which summarized many of the previous studies regarding the association between lifestyle and gastric cancer was published in Japan (Major cancer and lifestyles by The Japanese Society of Cancer Epidemiology [Japan Society of Cancer Epidemiology 1997]) (“Japanese review”), referring to another such report from the USA (Food, nutrition and the pre-

### TABLE 1. Risk factors and preventive factors of gastric cancer (Japan Society of Cancer Epidemiology, 1997).

<table>
<thead>
<tr>
<th>Preventive factors</th>
<th>Risk factors</th>
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<tbody>
<tr>
<td><strong>Convincing</strong></td>
<td>salt and pickles</td>
</tr>
<tr>
<td><strong>Probable</strong></td>
<td>Nitrite intake</td>
</tr>
<tr>
<td><strong>Possible</strong></td>
<td>atrophic gastritis</td>
</tr>
<tr>
<td>fruits and vegetables</td>
<td>broiled meats and fish</td>
</tr>
<tr>
<td>use of refrigerators</td>
<td><em>H. pylori</em> infection</td>
</tr>
<tr>
<td>yellow-green vegetables</td>
<td>tobacco smoking</td>
</tr>
<tr>
<td>green tea</td>
<td>alcohol drinking</td>
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</table>
vention of cancer: a global perspective by World Cancer Research Fund & American Institute for Cancer Research [American Institute for Cancer Research 1997] (USA review) (Table 1). The authors review the risk factors of gastric cancer based on the “Japanese review”.

**Helicobacter (H.) pylori**

Since *H. pylori* was discovered (Warren and Marshall 1983) and its pathogenesis was reported (Marshall et al. 1985), many researchers have taken notice of various factors associated with the development of this disease, especially carcinogenesis, and have conducted many biological studies (Anti et al. 1998; Honda et al. 1998; Sugiyama et al. 1998; Watanabe et al. 1998; Zhang et al. 1998; El-Omar et al. 2000; Peek et al. 2000; Wang et al. 2000). At the same time, many epidemiological studies have been published in the international literature. Though some reported that *H. pylori* infection correlated with gastric cancer (Forman et al. 1991; Nomura et al. 1991; Parsommet et al. 1991; Hansson et al. 1993) and some that it did not (Webb et al. 1996; Kim et al. 1997), a meta-analysis has revealed the association (Eslick et al. 1999). Likewise in Japan, a great deal of epidemiological research on the relationship has been carried out (Hirayama 1986; Hirohata and Kono 1997; Kobayashi et al. 2002; Ngoan et al. 2002; Kelley and Duggan 2003; Saubaget et al. 2003). Hirayama and other researchers insisted that green-yellow vegetables had a particular preventive effect (Hirayama 1986; Ward and Lopez-Carrillo 1999; Kobayashi et al. 2002; Ngoan et al. 2002; Kelley and Duggan 2003; Saubaget et al. 2003). Plausible mechanisms, in which vitamin C, vitamin E and beta-carotene play important roles, have not yet been sufficiently examined from an epidemiological aspect.

**Dietary factors**

**Vegetables and fruits.** Vegetables and fruits are considered convincing preventative factors against gastric cancer (American Institute for Cancer Research 1997). Many epidemiological studies have been conducted focusing on the association between vegetables, fruits and gastric cancer in Asia (Hyun et al. 2002) and around the world (Galanis et al. 1998; Ward and Lopez-Carrillo 1999; Nishimoto et al. 2002; Stefani et al. 2004). Similarly in Japan, a great deal of epidemiological research on the relationship has been conducted (Hirayama 1986; Ward and Lopez-Carrillo 1999; Sauvaget et al. 2003). Plausible mechanisms, in which vitamin C, vitamin E and beta-carotene play important roles, have not yet been sufficiently examined from an epidemiological aspect.

**Salt and salty foods.** There are many reports which illustrate that exposure to salt and high consumption of salty foods accelerate carcinogenesis in gastric cancer (Ward and Lopez-Carrillo 1999; Kelley and Duggan 2003; Stefani et al. 2004; Türködogan et al. 2005; Tsugane 2005). It is assumed that the spread of the use of the refrigerator led the change in food-storage methods away from curing with salt into cold storage, and the reduction of salt consumption because of this lowered the incidence rates of gastric cancer. A case-control study revealed that the lower were the incidence rates (American Institute for Cancer Research 1997). Intra-Japanese ecological studies have shown that Iwate prefecture has low incidence rates even though it is in the Northeast region of Japan, which is the area with the highest rates (Fig. 8). Nakaji et al. (1991) compared the dietary habits among people in Iwate with those among residents of Aomori prefecture (a prefecture with one of the highest gastric cancer incidence rates in all of Japan), and reported that the...
consumption of salty food among Iwate people was lower than that among Aomori people. Furthermore, Takemori et al. (1993) reported a significant correlation between daily salt intake and the SMRs of gastric cancer in Japan. In addition, it has been reported that effect of salt intake on gastric cancer incidence was found in Mongolian gerbils with *H. pylori* infection but not in those without infection (Nozaki et al. 2002).

**Others.** Other plausible risk factors are N-nitroso compounds (Kamiyama et al. 1987; Tsugane et al. 1992), alcohol consumption (Kikuchi et al. 2002) and green tea (Hoshiyama et al. 2002), but these are still inconclusive because there are some reports in which they were not regarded as risk factors (Tsubono et al. 2001; Sasazuki et al. 2002).

**Tobacco smoking**

Tobacco smoking is the most convincing risk factor for gastric cancer (Trèdaniel et al. 1997; Chao et al. 2002; Engel et al. 2003; González et al. 2003) as well as for esophageal cancer (Enzinger and Mayer 2003), and there are many epidemiological inquiries that have investigated the correlation between smoking and gastric cancer in Japan (Kamiyama et al. 1987; Mizoue et al. 2000; Enzinger and Mayer 2003; Minami et al. 2003; Koizumi et al. 2004). Particularly, the most notable report is the cohort study carried out by Hirayama (1987). It showed the attributable risks of gastric and other sites of cancer caused by habitual cigarette smoking, and clarified that smoking facilitated carcinogenesis in gastric cancer.

**Atomic bomb radiation fallout**

A cohort study of Hiroshima and Nagasaki atomic bomb survivors insisted that exposure to radiation had somewhat promoted the risk of gastric cancer but the effect was extremely small (Tompson et al. 1991).

**Why is the incidence or mortality decreasing in Japan?**

From the above bodies of evidence, the authors think that there are three possible reasons for the higher incidence of or mortality from gastric cancer in Japan than in the rest of the world. The first reason is the high infection rate of *H. pylori* in Japan. Indeed, the infection rate is higher in Japan, as much as 50% for adults (over 20 years old) than those in Western countries; 30% in USA, 40% in UK, and 40% in Italy (The Eurogast Study Group 1993). The second reason is believed to be the high intake of salt. The daily intake of salt was 13.5 g in 1975 and 11.4 g in 2002 in Japan (Section of Nutrition, Bureau of Public Health, Ministry of Health and Welfare, Japan 1978, 2005), while it was 6.8 g in 1970 and 8.6 g in 2000 in the USA (National Center for Health Statistics, USA 1971-1975; National Health and Nutrition Examination Survey, USA 1999-2000). The third reason is the high prevalence of tobacco smoking among Japanese males, which is one of the highest in the world, though it has decreased by 25% or more over 20 years (World Health Organization, Regional Office for Europe 2001; National Center for Health Statistics, USA 2004; Japan Tobacco Inc. [JT] 2005) (Table 2).

As for vegetables and fruits, we cannot compare the intakes of vegetables and fruits between Japan and other countries, because the methodology of nutritional intake survey in Japan is very different from other countries.

**Recent changes in environmental factors in**

**Table 2. Prevalence of smoking (%) compared geographically.**

<table>
<thead>
<tr>
<th></th>
<th>1974</th>
<th>2000</th>
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<tbody>
<tr>
<td>Denmark</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>78.8 (Males)</td>
<td>53.5 (Males)</td>
</tr>
<tr>
<td></td>
<td>16.7 (Females)</td>
<td>13.7 (Females)</td>
</tr>
<tr>
<td>Slovenia</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>42.8 (Males)</td>
<td>25.2 (Males)</td>
</tr>
<tr>
<td></td>
<td>32.2 (Females)</td>
<td>21.1 (Females)</td>
</tr>
</tbody>
</table>
Japan, especially the decline of tobacco smoking in men (JT 2005), the decrease in salt intake (Section of Nutrition, Bureau of Public Health, Ministry of Health and Welfare, Japan 1978, 2005), the increase in the intakes of vegetables and fruits (Section of Nutrition, Bureau of Public Health, Ministry of Health and Welfare, Japan 1978, 2005) will contribute to the decrease in the incidence of gastric cancer in Japan. Because of the progresses in cancer therapeutic and diagnostic techniques and strategies, and the spread of medical screening and other forms of check-up for cancer, the mortality rates of gastric cancer will continue to decrease.

References


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