Aetiology of Cancer in Asia

Sohee Park¹, Jisuk Bae², Byung-Ho Nam¹, Keun-Young Yoo²*

Abstract

Cancer has become the leading cause of death in many Asian countries. There is an increasing trend in breast, prostate and colon cancers, which are considered as typical of economically developed countries. Although breast and prostate cancer rates are still lower than in western countries, they are particularly rapidly increasing. In this paper, we review recently published literature to identify important etiologic factors affecting the cancer risk in Asian populations. Infectious agents such as Helicobacter pylori, hepatitis B and C viruses, and human papillomavirus were shown to be associated with elevated risks of stomach, liver and cervical cancer, respectively. Tobacco smoking was shown to be significantly associated with higher lung cancer risk and moderately increased all cancer risk. Excessive alcohol drinking appeared to increase the risk of colorectal cancer in Japanese and breast cancer in the Korean population. Betel nut chewing was associated with higher risk of oral and esophageal cancer. In terms of diet, various studies have demonstrated that high caloric and fat intake was associated with breast cancer risk, salted food intake with stomach cancer, aflatoxin B1 with liver cancer, and low fruits and vegetables intake with breast and lung cancer. Environmental exposure to indoor and outdoor air pollution, arsenic, radon, asbestos and second hand smoke was shown to increase the lung cancer risk. Reproductive factors such as late age at first childbirth, early menarche, late menopause, oral contraceptive intake, and short duration of lifetime lactation were shown to be associated with breast and/or colorectal cancer. Cancer has clearly become an emerging health threat in Asia and cancer control programs should be actively implemented and evaluated in this region. Various strategies for cancer control have been developed in some Asian countries, including the set-up of national cancer registries, cancer screening programs, education programs for health behavior change, eradication of Helicobacter pylori and vaccination for hepatitis B and C viruses, and human papilloma virus high risk forms. However, more attention should also be paid to low- and medium-resource Asian countries where cancer incidence rates are high, but neither intensive research on cancer for planning effective cancer control programs, nor easy implementation of such programs are available, due to limited financial resources.

Key Words: Asia - cancer - etiology - risk factors

Introduction

Trends in cancer incidence and mortality

Cancer is becoming a serious health threat in many Asian countries and it has become the leading cause of death in Asian Pacific countries such as Japan and Korea. Most commonly diagnosed cancers in Asia are in the order of lung, breast, colon and rectum, and the leading causes of cancer deaths are lung, stomach and liver. In year 2000, there were over 3 million new cancer cases and over 2 million cancer deaths in Asia and projections suggest that the number of new cancer cases in Asia will increase to 7.1 million by year 2020 if existing prevention and management strategies remain unchanged (Mackay et al., 2006).

There is an increasing trend in breast, prostate and colon cancer, which are regarded as the cancer of economically developed countries (Yang et al., 2004). Although breast and prostate cancer rates are still lower in Asian countries than in western countries, the rates have been increasing rapidly (Figure 1a, 1b). Age-standardized prostate cancer mortality rates showed an apparent increase ranging from 50% in Thailand to 260% in Korea over the last several decades (Sim et al., 2005). Colon cancer incidence rates in Asia have gradually caught up with the rates of western countries (Figure 1c). In particular, there was a rapid increasing trend in both incidence and mortality from colorectal cancer in Japan from 1960 to 1990, where the per capita consumption of meat and animal fat showed an apparent increase during this period (Yiu et al., 2004; Bosetti et al., 2005). Although this correlation of national data does not provide evidence...
for a causal relationship, it motivates the hypothesis that increased risk of colorectal cancer may be attributable to a change in diet. The incidence and mortality rates of stomach and liver cancer are very high in Japan, Korea and China, but stomach cancer rates have been steadily decreasing and liver cancer rates have recently begun to decrease (Ngoan et al., 2002; Chen et al., 2006). Lung cancer is the leading cancer-killer in Asia and specifically the lung cancer incidences in women have been increasing in Japan.

In this paper, we review recently published literature to identify important etiologic factors affecting the cancer risk in Asia, but since this topic covers large literature, the references we cite here are not exhaustive.

**Etiologic Factors for Cancer**

1) **Infectious Agents**

_Helicobacter pylori (HP), hepatitis B virus (HBV), hepatitis C virus (HCV), and human papilloma virus (HPV) are important risk factors for the development of gastric, liver, and uterine cervical cancer in Asia._

**Helicobacter pylori (HP) and gastric cancer**

The International Agency for Research on Cancer (IARC) classified Helicobacter pylori (HP) as a group 1 human carcinogen for gastric cancer in 1994. The infection rates of HP in the world population is approximately fifty percent, and in Asian countries these rates are considerably high (Prinz et al., 2006). In 2001, the Helicobacter and Cancer Collaborative Group (Helicobacter, 2001) conducted a pooled analysis on the association between HP seropositivity and gastric cancer risk in 12 nested case-control studies within prospective cohorts. Four out of these 12 studies were from Asian countries including Japan, China (2 studies) and Taiwan, and of these the Chinese and Taiwanese studies showed risks of less than 2.0, which were lower than the overall pooled risk estimate of 2.36.

A nested case-control study in Korea revealed that there was no direct association between HP and gastric cancer risk (OR=1.06, 95% CI: 0.80–1.40) (Shin et al., 2005). It has been suggested that factors other than HP infection could explain the diversity of gastric cancer incidence in Asian region. Azuma (2004) investigated the distribution of CagA strain, and classified two major CagA subtypes, namely the East Asian and the Western type (Azuma, 2004). The prevalence of the East Asian CagA-positive strain was shown to be associated with the high mortality rates of gastric cancer in Asia. A Korean study on the association between HP and gastric cancer by the virulence factors (CagA and VagA) further suggested that CagA seropositivity was significantly associated with a higher risk of gastric cancer among HP-infected subjects (OR=3.57, 95% CI: 1.05–12.14) (Gwack et al., 2006).

Although there is an inconsistency, there is an abundance of epidemiological evidence suggesting that HP eradication is able to reduce the risk of gastric cancer, especially among subjects without atrophic gastritis or intestinal metaplasia (Malfertheiner et al., 2005).

**Hepatitis B virus (HBV), hepatitis C virus (HCV) and liver cancer**

Chronic infection with HBV and/or HCV is a well-
known risk factor for hepatocellular carcinoma (HCC) (Tsukuma et al., 2005). HBV and HCV carriers are at 20-fold and 25-fold higher risk of liver cancer than non-carriers, respectively. However, only small fractions of chronic HBV carriers are expected to develop HCC in their lifetime. The inter-individual variation in the risk and age at onset of HCC among chronic HBV carriers can be attributed to the variability in aflatoxin exposures and lifestyle factors such as alcohol consumption and cigarette smoking (Srivatanakul et al., 2004).

Although chronic HBV infection is a major cause of HCC, there is wide variation in the proportion of HCC attributable to HBV (Muir, 1996). A number of studies have implicated that HCV infection is an important risk factor for HCC. In addition, co-infection of HCV and HBV have been reported to have an additive effect on the risk of HCC (Tsai et al., 1997).

Liver flukes and liver cancer

Liver flukes such as *Clonorchis sinensis* (CS) and *Opisthorchis viverrini* (OV) have been suggested as the risk factors for liver cancer including cholangiocarcinoma (CCA) and hepatocellular carcinoma (HCC). As for CCA, the variation in geographical distribution is related to the infestation rate of liver flukes; the incidence of CCA is relatively high in Indochina countries such as Thailand, an endemic area for OV and Far East Asia, an endemic area for CS (Srivatanakul et al., 2004).

It has been known that the role of liver flukes in carcinogenesis is related to chronic inflammation induced by prolonged infestation. Preventive strategies such as the intake of cooked fish and hygienic caution should be implemented to reduce the risk of CCA in the endemic areas of liver flukes.

Human papillomavirus (HPV) and cervical cancer

Uterine cervical cancer is the second most frequently diagnosed female cancer worldwide and the persistent infection with a high risk “oncogenic” type of HPV is a well-established risk factor for invasive cervical cancer. An international comparison study showed that there was large variation in the overall and age-specific HPV prevalence rates across countries. There is a high prevalence of HPV in Asia, especially in India and China (Moore et al., 2004; Franceschi et al., 2006). An effective HPV vaccination program for pre-adolescent girls may reduce mortality from cervical cancer by 80%, however, high cost of vaccine, poor awareness of linkage between HPV infection and cervical cancer, and social stigmatizing for a sexually transmitted disease are barriers to be overcome (Lee et al., 2007).

2) Lifestyle

Potential explanations for large geographic differences in cancer incidences may be due to genetics or lifestyle and environment. For example, adaptation of “western” lifestyle which is a combination of decreased parity, delayed childbearing, early menarche, high total caloric or fat intake and sedentary life pattern has been considered as the primary reason for increasing trends of cancer in breast, colon, rectum and prostate in Asian countries. An international comparison has shown that the breast cancer incidence rates have markedly increased in Asian countries. “Westernized” lifestyle changes in fertility and diet have been hypothesized as an explanation for these increases (Althuis et al., 2005). Several migration studies have further supported this hypothesis in breast cancer (Ziegler et al., 1993; Stanford et al., 1995; Pike et al., 2002). Some risk factors related to lifestyle such as smoking have shown consistent results in various studies conducted in Asian populations but several factors showed weaker evidence as discussed below.

Smoking and alcohol

Smoking is a primary lifestyle-related, avoidable risk factor for cancer. International ecological studies showed that countries with high cigarette consumption had higher lung cancer incidence rates (Kobayashi et al., 2000). Moore and Tsuda (2002) have intensively reviewed the smoking-related research in Asian-Pacific countries (Moore et al., 2002). The association of cigarette smoking with cancer risk appears to differ by cancer sites and gender. There are recently published series of systematic review on smoking and cancer risk based on cohort and case-control studies in Japan (Inoue et al., 2005; Mizoue et al., 2006; Nagata et al., 2006; Wakai et al., 2006). The authors reported that there is convincing evidence that current tobacco smoking moderately increases the risk of total cancer (about 1.5 times). In lung cancer, smoking was a strong risk factor (OR=4.39 in men; OR=2.79 in women) (Yamaguchi et al., 2000). However, the effect of smoking on other cancers is not conclusive. Smoking was also reported as a possible risk factor for breast cancer (Nagata et al., 2006), but not enough evidence showed for the risk of colorectal and liver cancer (Mizoue et al., 2006; Tanaka et al., 2006). Korean and Japanese studies showed similar results with elevated risk of lung cancer for current smokers (RR=4.0 in men; RR=2.2 in women) (Jee et al., 2004). Jee et al (2004) reported that smoking was also associated with an elevated risk for other cancers such as esophagus, stomach, pancreas, larynx, bladder and leukemia.

Second hand smoke was reported to moderately increase the risk of lung cancer incidence and mortality. In the Shanghai women’s health study, high proportion of study participants (83.1%) were exposed to second hand smoke from their husbands, at work and from family members in early life. Non-smoking women who were exposed to second hand smoke showed moderately higher risk of lung cancer mortality than those unexposed (HR=1.79) (Wen et al., 2006).

Excessive alcohol drinking is another avoidable risk factor for cancer. A meta-analysis in Japan reported that even moderate drinkers (<46 g/day) had a higher risk of colorectal cancer and this finding was different from a pooled analysis of studies in Western countries (Mizoue et al., 2006). Alcohol drinking also increased the breast cancer risk in Koreans (Yoo et al., 2006).

Along with tobacco smoke and alcohol consumption, betel nut chewing which is very common in South-East Asia, was also identified as human carcinogens by the
International Agency for Research of Cancer (IARC). A Taiwanese study reported that those who chewed betel nut with a piece of betel inflorescence or swallowed betel-quid juice had a significantly higher risk of esophageal cancer (OR=4.2 and 3.3, respectively). Betel nut chewing plays a relevant role in the development of esophageal squamous cell carcinoma, and interacts with smoking and alcohol drinking (Wu et al., 2006). The betel nut chewers had an increased risk of esophageal cancer ranging from 2.4 to 27.4 times that of non-chewers in India, depending on different combinations of betel nut chewing pattern (Phukan et al., 2001). On the contrary, a review article in mainland China has reported that the prevalence of oral cancer among betel quid chewers was low (0.02% to 0.05%) in Hunan and Hainan, while the betel quid chewing was very common in these provinces. They suggested that betel quid chewing habits differ across geographic areas, which may affect the magnitude of associated cancer risk (Zhang et al., 2007). A cancer incidence study in Pakistan also identified ‘smokeless tobacco use’ as a potential risk factor for oral and pharyngeal cancer (Bhurgri et al., 2003).

**Dietary factors**

There have been tremendous reports on food or nutrients and their association with cancer risk. High total caloric and fat consumption was reported to increase the risk of breast and colorectal cancer. Some Asian diet may play a protective role in cancer risk and these have been more intensively studied recently.

**High total caloric and fat intake:** Red meat and animal fat consumption was found to increase the breast cancer risk in a number of epidemiological studies in Asia (OR=3.84 in Malaysia; OR=5.1 in Taiwan; OR=8.47 in Indonesia; OR=2.9 in China) (Yuan et al., 1995; Wakai et al., 2000; Lee et al., 2005; Kamarudin et al., 2006). High red meat or animal fat intake are also associated with the risk of colorectal cancer (OR=1.5–2.2) (Seow et al., 2002; Chiu et al., 2003). The amount of fat intake may differ by various cooking methods. Deep-frying is known to increase the fat content in the food. Furthermore, a case-control study conducted in Philippines showed an associated risk of breast cancer with the consumption food boiled in coconut milk in their adolescence (OR=2.78), and this was thought to be due to high total caloric and animal fat contents in coconut milk (Kotopoulos et al., 2006).

**Low fruit and vegetable intake:** Although some inconsistencies were found, epidemiologic studies showed that low consumption of fruits and vegetables is associated with cancer risk in Asian countries. High consumption of Chinese white turnips, dark yellow-orange or green vegetables and fruits was shown to reduce the breast cancer risk (ORs ranging from 0.65 to 0.79 for highest quartile group) (Hirose et al., 2003; Malin et al., 2003; Sauvaget et al., 2003). Studies also reported its association with lung cancer risk. After controlling for smoking and occupational exposures, people with low yellow and light green vegetables were at a higher risk of lung cancer in southern China and Hong Kong (OR=2.26, 2.39) (Forman et al., 1992). However, population-based cohort studies in Japan found no association between lung cancer and fruits and vegetables (Liu et al., 2004). A case-control study in India reported that prostate cancer risk can be reduced in men with high fruits and vegetables consumption (OR=0.4) (Sunny, 2005). On the other hand, the association with colorectal cancer risk has been inconsistently reported (Sato et al., 2005).

**High Salt Intake and gastric cancer:** Higher intake of salt and salted food is known to increase the risk of gastric cancer and the prevalence of HP infection (Correa, 1992; Tsugane et al., 1993; Tsugane et al., 2004; Tsugane, 2005). Besides their effect on HP infection, salt and salted food also acts synergistically to promote the development of gastric cancer.

**Aflatoxin B1 (AFB1) and Liver Cancer:** Although chronic HBV infection has been well documented as the most important risk factor for HCC, dietary exposure of AFB1 has been implicated as another major cause. The AFB1 binding to DNA may be a critical step in hepatocarcinogenesis. The extent of the AFB1 binding to DNA may depend on various endogenous factors and concurrent exposure to other environmental agents such as alcohol drinking and cigarette smoking (Yu et al., 1996). A synergistic interaction between AFB1 exposure and HBV infection on HCC risk also has been reported in several epidemiological studies (Chen et al., 2001). HBV infection may affect AFB1 adduct formation through alteration of AFB1 metabolism. On the other hand, the immunosuppressive actions of AFB1 may modulate HBV infection. Food safety procedures to control AFB1 contamination could offer strategies for lowering HCC rates in Asia.

**Soy intake and green tea consumption (protective):** Soy intake and green tea consumption represent protective Asian diet that has drawn much attention recently. Soybeans are a rich source of isoflavones and a main type of plant estrogens. Epidemiological studies showed significant associations between high soy intake and the reduced risk of breast cancer (OR=0.46 for highest quartile group) (Yamamoto et al., 2003; Hirose et al., 2005). There has been an attention in soy product which may, in part, give an explanation for large international differences in breast cancer incidence rates. However, this protective effect of soy intake was questioned by Wu et al (1998) when they found the effect was weakened in US-born Asian Americans compared to non-US-born Asian Americans. It was suspected that soy intake may be a marker of other factors associated with the degree of westernization that are causally associated with the breast cancer risk (Wu et al., 1998; Wu et al., 2000). In relation to the colorectal cancer risk, animal studies have shown that soyfoods and isoflavones inhibited the formation of aberrant crypt foci, however the findings from epidemiologic studies have not been consistent (Toyomura et al., 2002). Further evaluation will be needed for the conclusive protective effect of soybeans.

Green tea has a number of compounds, including polyphenols, that have chemopreventive properties, and in vivo and animal studies have reported its preventing role from cancer. While animal studies have shown the protective effect of polyphenols in green tea, there is large variation among the results from epidemiological studies.
High green tea consumption was associated with the reduced risk of breast cancer in Chinese women (OR=0.59–0.87) and Japanese-American women (OR=0.53) (Wu et al., 2003; Zhang et al., 2006) but not in Japanese women (Suzuki et al., 2004). A Japanese case-control study reported a significant protective effect for stomach (OR=0.69) and rectal cancer (OR=0.46) (Inoue et al., 2001). However, no association was found for prostate cancer (Kikuchi et al., 2006). A recent meta-analysis reported that the evidence for a protective effect of green tea on colorectal cancer risk was insufficient in epidemiological studies (Sun et al., 2006). The role of green tea in chemoprevention should be evaluated further in humans.

Physical inactivity

Low physical activity has shown to be linked to a significantly increased risk of breast and colorectal cancer in numerous studies. A Japanese study has reported a significantly reduced risk of female breast cancer among those with high physical activities (Hirose et al., 2003). Other studies also have suggested that regular and frequent physical activity over a long time period were associated with lower risk of colon cancer in Chinese (OR= 0.52) (Hou et al., 2004) and with distal colon and rectal cancer in Japanese (OR=0.5–0.7) (Isomura et al., 2006). Weaker evidence was reported in prostate, lung and endometrial cancers and there was insufficient evidence for other sites of cancer (Kruk et al., 2006). There are limitations in studying the effect of physical activity because the methods are various in the assessment of physical activity including its frequency, duration and intensity. Nonetheless, animal and experimental studies strongly support the decreased risk of breast and colon cancer. In relation to physical activity, obesity is a major public health problem worldwide. In Asian countries with accelerated economic growth, less physical activity along with diet change towards high caloric and fat intake has increased the prevalence of obesity.

Sexual behavior

Age at first intercourse, lifetime number of sexual partners and high parity were found to be important factors for invasive cervical cancer, especially through oncogenic HPV infection, in many Asian countries (Chichareon et al., 1998; Hsieh et al., 1999; Thomas et al., 2001; de Boer et al., 2006; Kanato et al., 2006). Besides the risk caused by their own sexual behavior, women’s risk of developing cervical cancer is also attributable to the sexual behavior of male sex partners. Women whose husbands had multiple sex partners were at a significantly higher risk of HPV infection and cervical cancer (OR=1.42, China) (Zhao et al., 2006). A study of massage parlor and a brothel in Bangkok, Thailand, revealed that the risk of invasive cervical cancer in monogamous women was associated with their husband’s lifetime visits to prostitutes (OR=3.2, for >280 visits vs. none) and suggested that commercial sex workers in Bangkok serve as reservoirs of oncogenic HPV and cervical cancer for monogamous Thai women (Thomas et al., 2001). Furthermore, sexual behavior of young and unmarried women tend to be more risky, in terms of having unprotected intercourse and having multiple sexual partners, hence more attention will be needed to educate the teenagers (Kanato et al., 2006).

3) Reproductive Factors

Late age at first child birth, early menarche, late menopause, oral contraceptive intake, and shorter duration of lifetime lactation are known to increase the risk of breast cancer. Epidemiological studies have shown consistent results in these risk factors in many Asian countries (Yoo et al., 1992; Zheng et al., 2000; Lee et al., 2003; Kamarudin et al., 2006; Sim et al., 2006; Yoo et al., 2006). One interesting note is that the breast cancer patients are relatively younger and age-specific breast cancer rates show somewhat different patterns in Asian countries compared to those in western countries. For example, there is an inverted U-shape risk of breast cancer with age in Korea, showing a steep increase until forties and a slow decrease in later ages (Yoo et al., 2002).

Some studies suggested that reproductive factors are also associated with colorectal cancer risk in Japanese (Yoo et al., 1999; Tamakoshi et al., 2004). Such reproductive factors include menstrual regularity, early menarche, late age at menopause, first pregnancy, and number of abortions. It was hypothesized that reproductive events may affect the carcinogenesis in the large bowel through hepatic function and bile acid formation. However, the results have been rather inconsistent in other studies, hence evaluation will be needed to make a firm conclusion.

In contrast to breast cancer, early age at first child birth was found to increase the risk of cervical cancer (Guo et al., 1994). In addition, women with multiple parities were at higher risk of cervical cancer than nulliparous women. A hospital-based case-control study in India showed that early age at first marriage was a single independent risk factor for cervical cancer. This study also suggested that the rapidity of multiple pregnancies was a more important factor than the parity itself in increasing the cervical cancer risk (Mukherjee et al., 1994).

4) Environmental Carcinogens

With rapid industrialization and economic development, the air quality has worsened in Asian countries and outdoor air pollution has become a concern. For instance, the levels of polycyclic aromatic hydrocarbons (PAHs), well-established human carcinogens, are high in major cities in Asia, compared to western countries. Although not conclusive, studies have reported there exists an association between outdoor air pollution and cancer risk, mortality and other health problems (Chen et al., 2004). Besides outdoor air pollution, indoor air pollution is known to elevate the risk of lung cancer. In rural areas of China, coal stove has been commonly used for heating or deep-fry cooking in a house with poor ventilation. Studies in northeast China showed that there was a two-fold elevated risk of lung cancer for those involved in smoky outdoor environments, long use
of coal-burning stoves and high indoor air pollution. (Xu et al., 1989; Wu-Williams et al., 1990). Similarly, compared to using unprocessed biomass (crop residues, wood, sticks, and twigs), using coal for heating and cooking was linked to an elevated risk of lung cancer (OR=1.29) among residents in the rural area of China (Kleinerman et al., 2002).

Arsenic exposure has also been associated with cancer. Data from an arseniasis-endemic area of Taiwan suggested that high mortality rates from bladder and lung cancer were observed in highly arsenic-exposed villages, with significant dose-response relationship. In China, a three-fold increased risk of lung cancer was reported in smelter workers that were exposed to inorganic arsenic (Wu-Williams et al., 1990). Liver cancer mortality also appeared to be associated with arsenic exposure (Morales et al., 2000).

Radon and asbestos are other known environmental factors to elevate the risk of lung cancer. Miners were intensively studied to show a significant association between radon and lung cancer. Residential radon exposure also appears to be able to increase lung cancer risk, as shown for example in studies in China (Wang et al., 2002; Lubin et al., 2004) and Pakistan (Matiullah et al., 2000).

Radon and asbestos are other known environmental factors to elevate the risk of lung cancer. Miners were intensively studied to show a significant association between radon and lung cancer. Residential radon exposure also appears to be able to increase lung cancer risk, as shown for example in studies in China (Wang et al., 2002; Lubin et al., 2004) and Pakistan (Matiullah et al., 2000).

### Prevention Measures

Many Asian countries are rapidly reaching an aging or aged society and we expect more cancer cases occurring in the future. Moreover, cancers of “westernized” lifestyle, such as breast, prostate and colon cancers, are significantly increasing in Asian countries, and this implies that so-called “protective Asian lifestyle” involving healthy diet and more physical activity may no longer exist. In addition, better diagnosis will only increase the number of newly diagnosed cancer cases further in Asia and cancer will become an emerging health threat in this part of the world.

Various strategies for cancer control have been developed in Asia, including the set-up of national cancer registries, cancer screening program, education program for health behavior change, eradication of HP and the vaccination for HBV, HCV and HPV.

#### 1) Cancer Screening

As a “secondary prevention” of cancer, early detection for cancer cases through screening program is important. Many studies in Asia have shown the effectiveness of cancer screening in reducing cancer mortality rates. To control high stomach cancer incidences in Japan, mass screening program was introduced in 1960 and there was substantial evidence showing that the screening program played an important role in reducing the gastric cancer mortality rates (Tsubono et al., 2000). Since 1982, Japan has begun a national cancer screening program in the cancer of stomach, lung, colon, rectum, breast and cervix.

The Korean government began to implement a national cancer-screening program in 1999, which covers the same five cancer sites as in Japan.

In Asian countries, there is a large concern in two major female cancers: breast and cervical cancer. Cervical cancer is the second in importance in developing Asian countries, with high incidence rates, whereas the importance is in the seventh in developed countries (Parkin et al., 2005). By applying routine Pap smear tests, the incidence of invasive cervical cancer has decreased in the developed countries for last fifty years. However, cervical cancer screening has not been established in many Asian countries and the incidence and mortality rates remain still high. Although showing decreasing trends in China and Japan, the cervical cancer incidence rates have been high in Thailand, India and Philippines, which are about 3 times the rates of the USA, Europe or Australia (Table 1). In less developed countries, the cost-effectiveness of screening program has been questioned and the implementation of screening program has been difficult because of the cost. A population-based simulation model using the case data of Thailand demonstrated that well-organized screening programs can reduce cervical cancer deaths in less developed countries at relatively low costs (Mandelblatt et al., 2002). Furthermore, as important as setting up cancer screening programs, appropriate health education is also essential to arrive at the successful secondary prevention, as supported by a report in Thai females (Wiwanitkit, 2006). The cervical cancer program has not been established in other Asian countries such as India and Indonesia (Schapiro et al., 1996; Murthy et al., 2005).

#### 2) Vaccination

Hepatocellular carcinoma (HCC) takes a large part as a cause of deaths in Asian men. Chronic HB infection, a well-known risk factor for HCC, can be approximately 90% preventable with HB vaccination. The global immunization strategy is carried out based on the generally accepted assumption that prevention of the HB-carrier state with vaccine will prevent the disease. National vaccination against HB has been implemented in Taiwan, Thailand, Malaysia, Singapore, Korea and China.
HP is considered for reducing gastric cancer incidence, reduction of stomach cancer. Although the eradication of HPV is now being introduced in Asia. It is still at its early stage, thus reducing the risk of liver cancer.

Most effective in preventing vertical transmission of HB, HBV surface antigen prevalence rate from 2.5% among children born in 1985 to 0.4% among children born in 1989, which showed a dramatic impact in school cohorts born after the implementation of vaccination program (Chang et al., 1997). Mongolia began implementing HB vaccination program in 1991 and Malaysia began the expanded program of immunization in 1989, which showed a dramatic impact in school children. A follow-up study observed a steady decline of HBV surface antigen prevalence rate from 2.5% among children born in 1985 to 0.4% among children born in 1996 (Ng et al., 2005). HB vaccination program was the most effective in preventing vertical transmission of HB, thus reducing the risk of liver cancer.

As part of preventing cervical cancer, HPV vaccination is now being introduced in Asia. It is still at its early stage, however many population-based trials are being conducted to study the cost-effectiveness of HPV vaccination. Lastly, vaccination for HP infection may contribute to the reduction of stomach cancer. Although the eradication of HP is considered for reducing gastric cancer incidence, its effectiveness is questioned since a large proportion of Asian population is infected, yet only a relatively small proportion will develop stomach cancer.

### 3) Health education

For changeable lifestyle risk factors of cancer, education for promoting the healthy lifestyle will be essential. For example, public health policymakers should make an effort to promote the smoking cessation, physical activity and healthy diet such as high consumption of fruits and vegetables, less consumption of salty food and red meat, and reduced alcohol consumption. It is a high priority that risky sexual behavior should be warned against as well.

As an effort to reduce smoking prevalence, for instance, a national health policy against smoking can be developed through raising cigarette price, putting warning label on cigarette cases, banning tobacco smoking at public places and running smoking cessation clinics. Such programs will effectively reduce the incidence and mortality from lung cancer, although the effect of these policies will be seen after a significant number of years. Studies have shown an inverse dose-response relationship between the duration of smoking cessation and lung cancer risk, however the risk of former smokers may never reach as low as that of non-smokers. Thus, in addition to making an effort to promote the smoking cessation, educating adolescents not to start smoking will clearly be very important.

### Conclusions

In this paper, we have reviewed the etiologic factors of cancer that are more likely to be modifiable, as summarized in Table 2. There is also a rapidly evolving research area, namely the molecular cancer epidemiology, which searches for the genetic variations that are associated with the cancer risk. Some genetic variants such as BRCA1 against the risk of breast and ovarian cancer have been already identified. Further studies are underway to investigate the genetic markers and the gene-gene and gene-environment interactions in their impact on cancer risk. Then the prevention strategy for cancer will have to be modified to reflect these future findings.

Cancer has clearly become an emerging health threat in Asia and cancer control programs should be actively implemented and evaluated in this region. Furthermore, much attention should be paid to poor Asian countries with high cancer incidence rates, where neither intensive research on cancer for planning effective cancer control programs will effectively reduce the incidence and mortality from lung cancer, although the effect of these programs will be seen after a significant number of years. Studies have shown an inverse dose-response relationship between the duration of smoking cessation and lung cancer risk, however the risk of former smokers may never reach as low as that of non-smokers. Thus, in addition to making an effort to promote the smoking cessation, educating adolescents not to start smoking will clearly be very important.

### Acknowledgements

This work was supported in part by the Research Grant of National Cancer Center, Korea (NCC-0710160). The authors would like to thank Dr. Aesun Shin for her help on reviewing the section of Infectious Agents.

---

**Table 2. List of Etiologic Factors for Cancer in Asia**

<table>
<thead>
<tr>
<th>Etiologic factors</th>
<th>Cancer sites</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious Agents</strong></td>
<td></td>
</tr>
<tr>
<td>Helicobacter pylori</td>
<td>Stomach</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Liver</td>
</tr>
<tr>
<td>Hepatitis C virus</td>
<td>Liver</td>
</tr>
<tr>
<td>Liver flukes</td>
<td>Bile Duct</td>
</tr>
<tr>
<td>Human papilloma virus</td>
<td>Uterine Cervix</td>
</tr>
<tr>
<td><strong>Lifestyle</strong></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Lung</td>
</tr>
<tr>
<td>Betel nut chewing</td>
<td>Oral, Esophagus</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td>Breast, Colorectum</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>Breast, Colorectum, Prostate, Lung</td>
</tr>
<tr>
<td><strong>Diet</strong></td>
<td></td>
</tr>
<tr>
<td>High caloric/fat intake</td>
<td>Breast</td>
</tr>
<tr>
<td>Salted food intake</td>
<td>Stomach</td>
</tr>
<tr>
<td>Alfatoxin B1</td>
<td>Liver</td>
</tr>
<tr>
<td>Low fruit and vegetables</td>
<td>Breast, Lung</td>
</tr>
<tr>
<td>Soy products (protective)</td>
<td>Breast, Colorectum</td>
</tr>
<tr>
<td>Green tea (protective)</td>
<td>Breast, Colorectum</td>
</tr>
<tr>
<td><strong>Environment</strong></td>
<td></td>
</tr>
<tr>
<td>Outdoor air pollution</td>
<td>Lung</td>
</tr>
<tr>
<td>Indoor air pollution</td>
<td>Lung</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Lung, Liver</td>
</tr>
<tr>
<td>Radon</td>
<td>Lung</td>
</tr>
<tr>
<td>Asbestos</td>
<td>Lung</td>
</tr>
<tr>
<td>Second hand smoke</td>
<td>Lung</td>
</tr>
<tr>
<td><strong>Reproductive Factor</strong></td>
<td></td>
</tr>
<tr>
<td>Late age at first child birth</td>
<td>Breast, Colorectum</td>
</tr>
<tr>
<td>Early menarche</td>
<td>Breast, Colorectum</td>
</tr>
<tr>
<td>Late menopause</td>
<td>Breast, Colorectum</td>
</tr>
<tr>
<td>Oral contraceptive intake</td>
<td>Breast</td>
</tr>
<tr>
<td>Short duration of lactation</td>
<td>Breast</td>
</tr>
<tr>
<td>Menstrual regularity</td>
<td>Colorectum</td>
</tr>
<tr>
<td>Number of abortion</td>
<td>Colorectum</td>
</tr>
<tr>
<td>Multiple parity</td>
<td>Cervix</td>
</tr>
<tr>
<td>Number of sexual partners</td>
<td>Cervix</td>
</tr>
<tr>
<td>Sexual behavior of partner(s)</td>
<td>Cervix</td>
</tr>
</tbody>
</table>

In Taiwan, a nationwide HB vaccination program has launched in 1984, and this program has shown to be very successful in preventing HCC (Lee et al., 2003; Su et al., 2007). There was a significant decrease in both the chronic HBV carrier rates and HCC incidence rates among birth cohorts born after the implementation of vaccination program (Chang et al., 1997). Mongolia began implementing HB vaccination program in 1991 and Malaysia began the expanded program of immunization in 1989, which showed a dramatic impact in school children. A follow-up study observed a steady decline of HBV surface antigen prevalence rate from 2.5% among children born in 1985 to 0.4% among children born in 1996 (Ng et al., 2005). HB vaccination program was the most effective in preventing vertical transmission of HB, thus reducing the risk of liver cancer.
References


Sohee Park et al

90, 128-34.


