· Colerectal Cancer-related Research ·

#### Epidemiologic trend of and strategies for colorectal cancer

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The incidence and mortality of colorectal cancer (CRC) show increasing tendancy worldwide. It was predicted that the new cases in 2007 would be approximate 1 200 000 and the death cases would be 630 000, a total increase of 27% and 28% and an annual increase of 3.9% and 4.0%. respectively, compared with the figures in 2000. In addition, the incidence of CRC varies regionally and changes over the time. In previously identified high-incidence areas, there are three tendencies; one is to keep rising such as in UK, one is to be stable such as in New Zealand, and the third one is to decrease such as in US and Western Europe. In previously identified lowincidence areas, the incidence of CRC is increasing, such as in Japan, Hong Kong, Singapore, Hungary, Poland, Israel, and Puerto-Rico, especially in Japan, where the incidence increases the fastest. Similarly, the incidence of CRC is increased by 4.2% annually in Shanghai, China, which is faster than the average increasing rate of the world. Since 1991, the average increase in mortality of CRC is 4.7% every year. The increasing number of female patients and the shift of the tumor location to the right side are also noticed for CRC in recent years. We summarized that CRC is a disease caused by synergism of environment and diet, life style and heredity. It was suggested that CRC can be prevented effectively through developing a regular life style, having proper diet, actively participating in the screening for cancers, and removing the pre-cancer lesions.

Key words: colorectal cancer, epidemiology trend, strategy

Colorectal cancer is one of the most common tumors in digestive system and it severely threatens health. In all tumors of the digestive system, colorectal cancer is said to be the easiest for prevention and treatment. However, up to this date, the incidence rate and the mortality rate of colorectal cancer around the globe continue to rise. In 2007, the number of newly reported cases of colorectal cancer had approached 1.2 million, while the mortality rate reached 630,000. When compared to the statistics of the year 2000, these rates had respectively raised by 27% and 28%, which in terms of annual averages, the increases are 3.9% and 4.0%. In addition, colorectal cancer has significant characteristics of exhibiting variations in regional distribution, and these variations can change over the time. By analyzing and comparing these changes, we may find the pathogenic factors for colorectal cancer and thus make prevention and treatment possible.

# Changes in the incidence rate and mortality rate for colorectal cancer

The global incidence rate of colorectal cancer continues to rise. 1-6 In 1980, the number of new cases of colorectal cancer was 572,000. numbers of cases of colorectal cancer in year 1985, year 1990, year 2000, and year 2002, were 678,000, 782,900, 945,000, and 1.023 million, respectively. By year 2007, the number had reached 1.2 million, which was increased by 109.8% compared with that in 1980 and yielded an annual average increase of 4.0%. The number of mortality rate continues to increase annually: 437,000 in 1990, 492,000 in 2000, 529,000 in 2002, and 630,000 in 2007. In the period of 17 years, the mortality rate had increased by 44.2%, with an annual average increase of 2.6%.

According to published data by the International Agency for Research on Cancer of WHO (IARC), the number of new case of colorectal cancer around the globe in 2002 took up 9.4% of all cancer cases. The incidence of colorectal cancer ranks the fourth place males and the third in females. The number of death is equivalent to half of the total number of onsets. The number of surviving patients with colorectal estimated to be 2.8 million, secondary to patients with breast cancer.<sup>6</sup> In the world, the incidence rate and the mortality rate in male patients with colorectal cancer are the highest in Hungary, which are 56.6/100,000 and 35.6/100,000, respectively. The highest incidence rate of colorectal cancer in females is in New Zealand, which has reached 42.2 out of 100,000, while the mortality rate is the highest in Hungary, reaching 21.2/100,000.6

Colorectal cancer has the characteristics of obvious regional variation, where the difference in the incidence rate between the highest and the lowest areas varies at least 25 fold. This variation changes over the time. The incidences of some regions originally with low incidence rates, such as Africa, Asia, parts of Latin America, and some European countries, are now increasing. Countries and territories with the most rapid increase in colorectal cancer are Japan, Hong Kong, Singapore, Hungary, Poland, Israel, and

Porto Rico. Especially in Japan, the incidence rate of colorectal cancer for males in 2002 was as high as 49.3 out of 100,000, which was significantly higher than the incidence rate in North America (44.4 out of 100,000); the incidence rate for females was also increased to 26.5/100,000.<sup>6</sup> This trend was primarily observed in colon cancer. The case numbers of colorectal cancer in 2005 in Japan, for both sexes, were increased by 9.5 fold and 7.5 fold respectively compared with those in year 1975. These numbers are estimated to rise 12.3 fold and 10.5 fold by year 2020.<sup>7</sup>

In China, the incidence rate of colorectal cancer is also increasing. Taking Shanghai as an example, the incidence rate of colorectal cancer between year 1973 and 1993, was increasing at an annual pace of 4.2%, which is significantly higher (2%) than the global average level. From the national population sampling survey of 1/10 of the entire population from 1990 to 1992, the corrected average mortality rate for colorectal cancer was 4.54 out of 100,000, which was increased by 28.2% compared to that of 3.54/100,000 in 1977. This placed the mortality rate of colorectal cancer in the fifth place among all cancers.8 According to the recent data from WHO, the incidence rate of colorectal cancer in 2005 had increased by 70.7% in China since 1991, yielding an average increase of 4.71% per year. 9 Also, based on our own statistical analysis, the number of onset and the mortality rate in 2005 were 172,000 and 99,000, respectively, which surpass the rates in the United States. The incidence rates for males and females were 15.0 /100,000 and 9.7/100,000, respectively. The mortality rates for males and females were 8.6 /100,000 and 5.4/100,000.10

The onset of colorectal cancer in high incident regions shows three trends: 1) continuous increase, such as UK; 2) stable, such as New Zealand; 3) decrease, such as the United States, Western Europe, and Northern Europe. The country with the most rapid declination in both the incidence rate and the mortality rate is the United States.<sup>2</sup>

The trend for the onset of colorectal cancer is different in UK compared with the United States. Since 1971, the incidence rate of colorectal cancer in UK started to increase slightly, with an annual increase of 35,000 new cases. However, its mortality rate is decreasing. The mortality rate at the end of the 90s of the 20th century was decreased by half, comparing to that in 50s of the 20th century. The early five-year survival rate in the 70s of the 20th century was only 20% and it was increased to 45% by the mid-90s of the 20th century. 11 Similar to most European countries, the mortality rate of colorectal cancer in females has dropped more than in males. This is supposed to be related to oral ingestion of contraceptive drugs and substitute hormonal therapy.<sup>11</sup>

The incidence rates of colorectal cancer in Australia and New Zealand are stabilized at a higher level. In 2002, the WHO reported that the incidence rate for males was 48.2/100,000 and for females was 36.9/100,000.6

The incidence rate and the mortality rate of colorectal cancer in the United States, period of rapid increase, started to slow down at the 70s of the 20th century. By the 90s of the 20th century, the incidence rate for colorectal cancer between 1990 and 1994 was reported to drop annually by 1.9%.12 From the mid-90s of the 20th century to year 2004, the incidence rate continued to decrease. The decrease in the mortality rate was even more significant. mortality rates for male and female patients with colorectal cancer in 2004 were 21.57/100,000 and 15.15%, respectively, which were separately decreased by 29.90% and 25.37% compared to data in 1990.13 In the United States, both the incidence rate and the mortality rate of colorectal cancer rank the third in both females and males. The incidence rate and mortality rate in males are only secondary to prostate cancer and pulmonary carcinoma; while those are only secondary to breast cancer and pulmonary carcinoma in females. 13

### Distribution of patients accordingly to sex and age

There are more male patients with colorectal cancer than females, but the trend shows that the number of female patients is increasing rapidly.

The onset age for colorectal cancer is also increasing, where the incidence rate increases along with aging.

For the global average incidence rate of colon it is 16.6/100,000 for males and 14.7/100,000 for females. For the average incidence rate of rectal cancer, it is 11.9/100,000 for males and 7.7/100,000 for females.14 If the data are statistically analyzed together, incidence rate for males would be 20.1/100,000; the incidence rate for females would be 14.6/100,000; the mortality rate for males would be 10.2 /100,000; and the mortality rate for females would be 7.6/100,000.6 Generally, ratio of males to females is 1.2:1. In developed countries, the incidence rates of colon cancer are similar in males and females, or even higher in females. As for the rectal cancer, the incidence is higher in males than in females. For example, in 2008 in the United States, it was estimated to have 53,760 new cases of males and 54,310 new cases of females with colon cancer, and 23,490 new cases of males and 17,250 new cases of females with rectal cancer.13

The risk for the onset of colorectal cancer increases with aging. In developed countries, 90% of patients are 50 years or above. In the UK, the peak onset age is 70 years, while 5% to 10% of patients are 80 years. 14 The peak onset age in the Unite States is 75 years, while less than 6% of patients are under the age of 40.15,16 However, in the developing countries, the onset age is younger. The incidence rate of colorectal cancer in Egypt is low, with an average onset age of 40 years, while 38% of patients are below 40 years and only 15% of patients are older than 60 years.<sup>17</sup> In Thailand, the average age for patients of colorectal cancer is 61.2 years and 83.9% of patients are above 50 years. 18 In Philippine, the average onset age in patients of colorectal cancer is 55.3 years, while 17% of patients are below 40 years. 18 In Korea, the average onset age of colon cancer was 57.4 years and 55.6 years for rectal cancer.19 The ratio of males and females with colorectal cancer in China has significantly changed in recent 20 years. In the 80s of the 20th century, the ratio was 1.5 to 1. In the 90s of the  $20^{\text{th}}$  century, the ratio was 1.26 to 1 (p < 0.05).<sup>20</sup> In Beijing between 1993 and 1997, the incidence rate of colorectal cancer for males was 9.8/100, 000 and 10.3/100,000 for females. The mortality rate for males was 5.1/100,000 and 5.7/100,000 for females. These data suggest that the incidence rate and the mortality rate of colorectal cancer in females had been increased more than in males.<sup>21</sup> From 1998 to 2002, the incidence rate of colorectal cancer for males in Beijing was 24.2/100,000 and 23.3/100,000 for females. In Shanghai, the incidence rate for males was 40.7/100,000 and 40.4/100,000 for females. This suggests that the incidence rates of colorectal cancer for females and males are very close in major cities.<sup>22</sup> In the 2003 annual report regarding the mortality rate due to malignant tumors on population of approximately 50 million in 33 counties and cities of China, it was surprised to observe that nearly 1/3 of cities and counties demonstrated equal incidence rates of colon cancer between females and males or even higher in females (Table 1), while the results from eight cities and counties showed a similar tendency for rectal cancer (Table 2).23

Previous studies had reported that the onset age for colorectal cancer in China was 12 to 18 years younger than that in European countries and US. However, recent statistics suggest that there is a tendency of increased onset age for colorectal cancer in China. The medium onset age for rectal cancer patients in Shanghai was 61 years and 64 years for patients in Guangzhou. In Tianjin between 1981 and 2000, the statistics showed that the medium onset age of colon cancer was 64 years (males, 64 years; females, 65 years), while approximately half of the patients had the onset at ages between 54 and 72 years. Li et al.20 reported that the average onset age for colorectal cancer in the 80s of the 20th century was 56.83 years, while the age was 59.66 years in the 90s of the 20th century.

## Right shift in the position of colorectal cancer lesions

As early as 40 years ago, scholars noticed the right shift in the position of colorectal lesions. Since 1985, the global incidence rate of intestinal cancer dramatically has been increased. <sup>4,24</sup> Takada

et. al.25 analyzed the age, sex, and position of colorectal cancer at the time of diagnosis over a period of 20 years between 1974 and 1994 in Japan, and found that the percentage of elderly patients, 70 years or above, had been increased, especially in females. The ratio of colon cancer on the right side had been increased, while that of the rectal cancer continued to decrease. Also, they found that the ratio of right colon cancer in males was relatively stable, which was dominant in females. Based on the statistical data of colorectal cancer between 1970 and 2000 as reported by the US Bureau of Veterans Affairs, Cucino et al.<sup>26</sup> discovered that the ratios of white females and males with right colon cancer were increased by 16% and the black males by 22%.

Table 1 Worldwide age-standardized mortality rates for colon cancer per sex in 2003 in some cities and counties of China

	or cinna		
City/ county	Male(1/100 000)	Female (1/100 000)	
Guangzhou City	7.8	7.8	
Qidong City	0.8	2.1	
Yangcheng County	2.3	2.8	
Yanting County	0.3	0.3	
Yangzhong City	1.9	2.1	
Jiashan County	5.7	5.7	
Ma'anshan City	1.6	2.5	
Changle City	1.6	2.8	
Linqu County	1.7	2.4	
Feicheng City	0.5	0.5	
Linzhou City	1.9	2.0	

From Chen Wanqing et al. China Cancer, 2007, 16 (8):586-597.

Table 2 Worldwide age-standardized mortality rates for rectal cancer per sex in 2003 in some cities and counties of China

City or County	Worldwide age-standardized mortality rate (1/100 000)	
	Male	Female
Tianjin City	2.8	3.0
Yangzhong City	2.5	5.2
Jiaxing City	2.7	3.3
Ma'anshan City	2.6	3.9
Linzhou City	2.4	4.3
Ganyu County	1.1	1.5
Yangcheng County	1.3	1.3
Qidong City	4.8	4.9

From Chen Wanqing et al. China Cancer, 2007, 16(8): 586-597.

Li et al.<sup>20</sup> analyzed the national reference data of colorectal cancer between 1980 and 1999 and found that the cancer position had significantly changed over the past 20 years. In the 80s and the 90s of the 20th century, the cancerous lesions mostly occurred in the rectum, even though the percentage of rectal cancer was decreased from 71.2% in the 80s to 66.7% in the 90s (p < 0.001). The percentages of cancer in transverse colon and ascending colon were significantly increased. At the same time, the percentage of right colon cancer had increased from 10.9% to 15.2% (p < 0.001).<sup>20</sup>

### The study on risk factors for colorectal cancer

Although the true cause of colorectal cancer remains obscure, the risk factors for the onset of colorectal cancer have been well investigated. In China, over the past 20 years, the research has always assumed that colorectal cancer is the product of synergic effects from the environment, diet, lifestyle, and genetic factor. Carcinogenic compounds in combination with cellular genome mutation contribute to the development of cancer.

Dietary factor. High cholesterol diet. As early as 30 years ago, Armstrong et al.27 first described a positive relationship between the incidence rate and the mortality rate with the diet of high cholesterol, meat, and animal proteins. Later, more data suggest that high cholesterol diet is a risk factor for the onset of colorectal cancer. In the 21st century, clearly pointed out that overindulgence of cholesterol and animal proteins, specifically the red meat, is the primary risk factor for colorectal cancer. 1,2 Immigrant epidemiology data showed that when residents of the low incident region migrate to the high incident region, the first and the second generations of immigrants, due to the change in the diet, had a higher incidence rate of colorectal cancer than indigenous residents. This phenomenon was significantly noticed among immigrant Japanese in Hawaii of the United where the incidence rate of colorectal cancer was 2.5 times higher than that in Japan and the incidence rate was even much higher than that of the local whites (38.4/100,000 vs. 27.6/100,000), especially for females, which reached 51.2 /100,000 vs. 30.8/100,000.<sup>6,28</sup>

The mechanism of how high cholesterol diet induces colorectal cancer remains unclear. It is speculated that lipid may cause the carcinogenic effect by generating oxidized compounds and fatty acid. The incidence of colorectal cancer is related to the concentration of secondary bile acids in intestine. Bile acids can be transformed into carcinogenic compound, known as methylcholanthrene, by enzyme. In the population of intestinal carcinoma with high cholesterol diet, there is an elevated level of bile acids in stool compared with normal individuals. Fat and cholesterol (bile acids and salt) can be metabolized to become secondary carcinogenic compounds in intestine (deoxidized bile acids and lithocholic acids), which can promote growth of adenocarcinoma to possess the infiltrative property. Limited ingestion of fat can reduce the quantity of carcinogenic compounds. Bile acid is a carcinogenic promoting agent which can directly damage DNA to induce epithelial growth. Also, it can, through bacteria, promote synthesis of pentane in stool. Fatty acid, especially in ionic state, can stimulate colon to cause inflammatory response, while it can increase DNA synthesis in epithelium of intestinal membrane. It induces and activates ornithine decarboxylase. The fat in diet can also cause transformation of primary bile acids by bacteria in colon into secondary bile acids (such as deoxidized bile acids), resulting in non-specific injury to the intestinal membrane and epithelial growth.

Fibers. Dietay fibers can resist degradation by digestive enzymes in the body. The primary component of dietary fibers is non-glycogen and exists in vegetables, fruits, and grains. Fibers can increase the stool amount and thus, dilute the intestinal carcinogenic compounds. Fibers can also adhere to bile acid salt (which is a carcinogenic promoting agent for colorectal cancer) and be degraded by bacteria into short-chain fatty acids that can reduce the pH level, which is not suitable for tumor growth. In the United States, there are at least 60 research

reports that support the protection of high fibrous diet against colon cancer. By comparing the patients taking the highest and the lowest amount of fibers, the risk level is estimated to be reduced by 43.0%. In addition, 13 control researches on colorectal cancer suggest that a daily average ingestion of 13g fibers can reduce 31.0% incidence rate of colon cancer in the United States. Scholars collected stool weight from 20 different populations of 12 countries and conducted risk analysis for the development of colon cancer from aspects of fibers, habit, stool quality, and passage time of stool. They discovered that the average daily weight of stool is in a negative relation to the risk of developing intestinal carcinoma and this is positively related to the ingestion quantity of fibers in the diet. The amount of stool is increased with ingestion of fibers. High fibrous diet (18g/d) can yield a daily excretion of 150g which further would reduce the risk of intestinal carcinoma.<sup>28, 29</sup>

<u>Vegetables and fruits</u>. The WHO proposes that reduction of meat and increase of vegetables and fruits in the diet can reduce the incidence rate of colorectal cancer.<sup>1,2</sup>

A prospective study in the United States demonstrates that in comparison with the population taking a small amount of vegetables and grains, the risk level of colon cancer was reduced by 25.0% in males and 38.0% in females taking a large amount.<sup>29</sup> Scholars focused on the existence of anti-tumor agents in vegetables and fruits when exploring the underlying mechanism. Chemists extracted over 100 or more organic compound, known to suppress mutation and prevent carcinogenesis. Garlic offers the strongest protection against colon cancer of the distal segment.<sup>29</sup>

Trace elements and vitamins. Selenium, zinc, calcium, iron, and fluorine are believed to have importance to the incidence of colon cancer. Selenium can alter the metabolism carcinogenic agents, suppress cellular proliferation, and protect body from oxidation. which are supplemented with more selenium, can reduce the incidence rate of colon cancer and the number of cancerous lesions. The

binding of calcium ion and lipid can form a non-dissolving calcium "soap", which can suppress the effects of fatty acids and bile acids. Researches in Utah and Hawaii discovered that the incidence rate of intestinal cancer was significantly lower in patients with higher ingestion of calcium than those with lower quantity. Anti-oxidizing agents, such as vitamin A, C, and E, can inhibit free radical reaction and thus, prevent DNA injury. Vitamin A, C, and E can reverse the hyperactive epithelial proliferation in colon of patients with adenocarcinoma.<sup>28, 29, 30</sup>

Genetic factors. Family history is considered an important risk factor for colorectal cancer. If there is one person in all first relatives who has colorectal cancer, the risk of having colorectal cancer would double and there is greater risk for all other relatives, too.29 According to the genetic epidemiological study, there is indeed a tendency of familial relation in colorectal cancer. The rates for patient to develop cancer when the first degree relatives having colorectal cancer are: control group 2.7%; colorectal cancer 7.4%; colon cancer 9.4%; left colon cancer 9.6%; right colon cancer 6.7%, and rectal cancer 4.9%. The hereditary rate from the first degree relatives in each group was significantly higher than the secondary relatives. In exception to familial adenomatous polyposis and Gardner Syndrome, hereditary non-polyposis colon cancer (HNPCC) takes up 4.0% to 13.0% of all cases of colorectal cancer. In two generations of the family with HNPCC, at least three individuals developed colorectal cancer and at least one had it before the age of 50 years.9, 31 Six known related genes have been isolated from the HNPCC family, including hMSH2, hMLH1, hMSH6, hWSH3, hPMS1, and hPMS2.9,31 In exception to large intestine, endometrium, stomach, bile duct, and pancreas, as well as digestive system and urinary system, are also susceptible to tumor growth.

Pathogenic factors. Chronic intestinal inflammation, polyposis, and adenocarcinoma. Based on estimation, 3% to 5% of chronic ulcer colonic inflammation can lead to colon cancer. The carcinogenic rate for 20-year history of this disease is 12.5% and 40% for 30-year history.

Some believe that 15% to 40% of colon cancer actually originates from intestinal polyposis, where the pre-carcinogenic stage can take five to For the patients with familial 20 years. polyposis, the adenomatous malignant transformation rate at the age of 25 is 9.4%, at the age of 30 is 50%, and almost 100% at the The medium age for malignant transformation is 36-year-old. Adenocarcinoma can undergo malignant transformation, too. Its carcinogenic rate is related to size, pathological existence of stem, and the level of type, uncontrolled growth. For adenocarcinoma which is less than 1cm, the carcinogenic rate is less than 2%. If the size is over 3cm, the carcinogenic rate will surpass 40%.9,32

Schistosomiasis. Because Zhejiang is the epidemic region for schistosomiasis and it is also a region of high incidence of colorectal cancer, this suggests a correlation between the two. However, there is relatively few evidence from the epidemiological study especially that the disease of schistosomiasis is currently under control. The incidence rate and the mortality rate of colorectal cancer, yet, have not decreased accordingly.

Crohn Disease. The predilection sites for Crohn Disease are the terminal end of ileum and ileocecal region, even though the entire digestive tract is susceptible to it. The Crohn Disease in colon takes up 40% of all cases. Generally, it is believed that the carcinogenic rate of Crohn Disease is lower than the chronic ulcer colonic inflammation, but it is still four to 20 times higher than the normal population. percentages of carcinogenesis in different positions of the digestive tract for Crohn Disease are: 25% for small intestine, 70% for colon, and 5% for others. Approximately 10% of Crohn disease is in multiple locations, and thus, the prognostic outcome is poor.33

Influence by other diseases. The incidence of rectal or sigma carcinoma after local radiotherapy on cervical cancer has been reported. The latent period for carcinogenesis is generally 10 years or longer. The risk of carcinogenesis increases along with the increasing dosage.<sup>33</sup> There was also a report of colon cancer carcinogenesis after the

surgical removal of gall bladder, which was about 1.5 times higher than the normal population.<sup>33</sup>

Lifestyle and others. Exercises. In the 90s of the 20<sup>th</sup> century, some scholars noticed a significant difference in the incidence rate of colorectal cancer for professions which require long-term sitting or intensive body strength. <sup>34,35</sup> Recently, the WHO also confirms that exercise is beneficial in reducing the incidence rate of colon cancer, especially for colon cancer. <sup>1, 2,36</sup>

Overweight and obesity. In recent years, it is believed that overweight and obesity are the risk factors for colon cancer. Data suggest that when comparing populations of the body mass index of more than 29 and that of less than 21, the risk of developing colon cancer is relatively increased by 1/2. Active exercises to maintain a healthy body can reduce the incidence of colon cancer. 35,36

Epidemical strategy and measures to control colorectal cancer. Colorectal cancer usually starts as adenocarcinoma and has long progression period. If it is possible to discover and remove pre-carcinogenic lesions, carcinogenesis can be effectively prevented. In addition, there are many researches pathogenic factors for colorectal cancer provide evidences for prevention. Moreover, the therapeutic effect for early stage colorectal cancer is good, which can completely cure the disease. It is said that colorectal cancer is a tumor which can be completely prevented and cured. However, it is a dilemma that the incidence rate and mortality rate of colorectal cancer continues to rise. There are several measures we would suggest to handle this disease

Health education on cancer prevention. General population must understand the pathogenic risk factors of colorectal cancer. They must also know the prevention measures and early discovery, in order to live a healthy lifestyle and actively participate in screening.

Appropriate and balanced diet. Many research data suggest that diet of high cholesterol and animal proteins with high energy, as well as inadequacy in fibers, would induce colorectal cancer. Therefore, prevention of colorectal cancer starts with dietary control, where the dietary structure must be managed to establish a good

dietary habit.

Active treatment of pre-carcinogenic lesion. The pre-carcinogenic state of colorectal cancer is fairly straightforward, which includes adenocarcinoma, familial adenomatous polyposis, and ulcer colonic inflammation. If these lesions can be removed as early as possible, it can greatly reduce the incidence of colon cancer.

Establishment of a good lifestyle and behavior. General population must be encouraged to actively participate in exercises. In addition to a balanced diet, alcohol consumption and smoking should be prohibited. Active participation in sport activities can increase the body immune. Overweight or obesity should be controlled as well.

Periodic routine follow-up. Stool blood test and inquiry of disease history, in addition to selective colonoscopy, can greatly improve the detection of pre-carcinogenic lesions and allow the removal of these diseases. Screening can also discover the tumor in an early stage, which allows the early removal to achieve a good result. In the United States, the current five-year survival rate for patients with colon cancer is only 64%, while the early detection and removal allows a five-year survival rate of 90%. Screening is the most effective way for the early detection and diagnosis of colorectal cancer.

Since the mid-90s of the 20th century in the United States, the incidence and mortality rates of colorectal cancer have started to drop, due to the promotion of a balanced diet, the screening program, the immediate removal of pre-carcinogenic lesion, and exercise. The WHO does not recommend pharmaceutical prevention, such as non-steroid anti-inflammatory drugs, including aspirin and COX-2 inhibitors.<sup>1,2</sup>

In order to implement the above-mentioned measures, large health resources must be devoted to prevent colorectal cancer.

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