PROSPECTS FOR THE PREVENTION OF DIGESTIVE TRACT CANCERS IN SINGAPORE (SECOND DIGESTIVE DISEASES FOUNDATION LECTURE, 1988)

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SYNOPSIS

For the purposes of this paper, the digestive tract will include the following sites:
(a) Oral cavity (including lip and tongue),
(b) Oesophagus,
(c) Stomach,
(d) Small intestine,
(e) Colon and rectum.

Together the above sites constitute 30.0% of all cancers in males and 25.3% in females (1978-82 figures). In general, the oral, gastric and oesophageal cancers are declining in Singapore, while colorectal cancer is rapidly increasing, similar to the situation in the West. For each primary site, the pattern of the disease, the main risk factors and the potential for prevention will be presented.

The major strategy in primary prevention is to eliminate known risk factors, which are mainly environmental — diet (e.g. salted foods, nitrates and nitrosamines in food, fat, deficiences in vital micronutrients), alcohol, tobacco smoking and chewing. Fresh fruits and vegetables, especially the cruciferous and carotene-rich ones, are protective against cancers and should be included in the daily diet. .

KEY WORDS: Digestive cancers, prevention, Singapore

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INTRODUCTION

For the purposes of this paper, we will restrict the digestive tract to comprise the following:

Site	ICD* Code
(a) Lip	140
(b) Tongue	141
(c) Mouth	143-5
(d) Oro- & Hypo-pharynx	146, 8
(e) Oesophagus	150
(f) Stomach	151
(g) Small intestine	152
(h) Colon	153
(i) Rectum	154

Together they constitute a major group of malignancies which must be given adequate attention in any cancer control programme.

THE SITUATION IN SINGAPORE[1]

A conservative estimate of digestive tract cancers in Singapore shows that they account for 30.0% of all cancers in males and 25.3% in females (Table 1). This is in line with general estimates in many countries all over the world. Although the overall totals may be the same, there are some interesting variations for individual sites. By comparing between high-risk and low-risk populations, useful clues can be generated in the search for causal factors.

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Table 1
DIGESTIVE TRACT CANCERS IN SINGAPORE, 1978-1982

Male			Female	
%	No		No	%
0.05	5	Lip	1	0.01
0.7	71	Tongue	35	0.4
0.9	92	Mouth	38	0.5
1.0	105	Pharynx	31	0.4
4.3	439	Oesophagus	150	1.9
12.3	1238	Stomach	645	8.1
0.2	17	Small Int.	18	0.2
5.7	572	Colon	651	8.2
5.8	487	Rectum	442	5.6
30.0	3026	Total	2011	25.3

Oro-pharyngeal cancers (including lip and tongue) are generally rare in Singapore. The highest incidence (around 10 per 100 000) occurs among the Indians, as is the case in the Indian subcontinent. There are very few cases among the Chinese, and the overall trend is on the decline.

Oesophageal cancer is one of the important sites but its incidence has been declining markedly in the last 15 years — by about 4% in Chinese males and 6% in Chinese females. This is mainly a cancer of the Chinese, especially the Hokkiens and Teochews.

Gastric cancer is still a frequent site, second only to lung. It is also declining (by 1 to 2%) but not to the same extent as oesophagus. The Hokkiens and Teochews are similarly at high risk.

Cancers of the small intestine are very rare, and will therefore not be discussed.

Colon and rectum are the two sites which have shown dramatic increases in incidence over the last 15 years. Much of the increases (by 3 to 5%) are found in the Chinese, but there are no dialect group differences. It is anticipated that very soon colo-rectal cancer would be

one of the main primary sites of cancer in Singapore.

PRINCIPLES OF CAUSATION

In cancer-causation, we are dealing with a complicated process which is still being unravelled and which will remain the subject of intense research for a long time to come. There are three types of agents involved:

(a) initiators — which affect the genetic material in the cell to cause permanent change,
(b) promoters — which facilitate the subsequent growth of cancer,
(c) inhibitors — which can suppress the growth of cancer.

Very often we do not know enough about initiators. However, with sufficient knowledge about promoters and inhibitors, we can prevent clinical occurrence of cancer. It is not the definitive answer, but at the present level of knowledge, it is a step forward.

Although there are some genetically determined precancerous conditions, e.g. familial polyposis, etc., they are rare. By and large, most the risk factors are environmental in nature, related to what we eat, drink or smoke. The main agents in digestive cancers are dietary which have been estimated by various prominent researchers as being responsible for 10-70% of all cancers.[2]

INTERNATIONAL VARIATION AND RISK FACTORS

Oro-pharyngeal Cancers:

In Asia, this group of cancers is closely associated with people from the Indian subcontinent, irrespective of the present place of domicile.[3] Various aetiological studies have incriminated the chewing of tobacoo, betel leaves, betel nut, slaked lime and other substances in various combinations. There is evidence to suggest that tobacco is the main culprit, and tumours tend to occur on the side where the quid is kept in the mouth.[4] Other related habits include chutta smoking (reverse smoking) and bidi smoking (uncured tobacco). Diets deficient in β-carotene, vitamins A and C are also contributory.

In Western countries, other risk factors identified include alcohol (as a promoter) and solar radiation (mainly for lip cancer).

Oesophageal Cancer

Studies in geographic pathology have shown an "oesophageal cancer belt" stretching from Turkey, through N.E. Iran, southern republics of USSR, to Northern China.[5] In China, the high risk provinces include Sichuan, Henan and Shanxi, where the disease has been known for more than 2000 years.[6] In Singapore, the Hokkiens and Teochews have high incidence. Here the rates are generally declining, probably due to improved methods of food preservation which have resulted in a reduction of dietary carcinogens or precursors for carcinogen-formation.

In the West, it is a rare cancer except in certain parts of France.[5] In these populations, the main risk factors identified are alcohol and tobacco. As alcohol consumption increases, the incidence also increases. Alcohol is thought to be a promoter by:

(a) enhancing the carcinogenic effects of carcinogens (e.g. from tabacco),
(b) acting as solvent of carcinogens,
(c) increasing susceptibility of certain tissues in the body.

In Asia and other developing countries, the risk factors are thought to be different.[8] Carcinogens (and mutagens) have been suspected in fermented, mouldy or smoked foods, e.g. nitrosamines. High levels of nitrates in the food and/or water can also result in the formation of nitrosamines in the body by bacterial action. At the same time, there is also the likely deficiency of inhibitors like vitamins A, C and riboflavin and trace elements like zinc and selenium. Other suspects not proven include frequent ingestion of hot fluids and mineral (silica) fibres in the food.

Gastric Cancer

This is a cancer of the Japanese, who have the highest incidence in the world. The incidence is also high in Latin America and China.[5] Happily, there is a worldwide decline and again this is likely to be due to better methods of food preservation.

Observations on the Japanese have shown that migrants from high to low risk areas tend to show decreases in incidence only from the second generation onwards, thus underlining the strong influence of environmental factors, possibly in the diet.[7] From various studies, a "high-risk" diet has been identified as follows:

(a) low in fresh green leafy vegetables;
(b) low in fresh fruits;
(c) high in salt;
(d) high in nitrates.

Salted foods tend to cause severe gastritis, affecting the mucous barrier thus allowing the carcinogens to act directly. The nitrate story is less clear; nitrate is present in all human diets and there is no way that we can reduce it. But nitrosation can be blocked by vitamins A, C, E and β-carotene. This is where the intake of fresh vegetables and fruits come in. Other conditions associated with chronic gastritis, like pernicious anaemia, are also known to have higher risks for gastric cancer.

Colo-rectal Cancer

Usually, medical practitioners tend to take the large bowel together but there is increasing (though insufficient) evidence to suggest that the colon and the rectum should be considered separately. They are both cancers of the affluent West and rare in Asia, Africa and Latin America.[5] Singapore and Hong Kong are some of the few Asian populations showing marked increases in incidence in the last two decades. Migrant studies in U.S.A. and Australia have shown dramatic changes within one generation.

In the West, the risk factors have more or less reached saturation point and it is becoming difficult to demonstrate differences between cases and controls. It is still possible in a place like Singapore, where the differentials are still there.[8] We are in the process of analysing a case-control study that has just been completed.

The main leads from medical literature show the following "high-risk" diet:

(a) high in total fat,
(b) low in fibre, especially certain components of dietary fibre,
(c) low in vegetables, especially cruciferous vegetables.

The above items are not conclusively proven as yet.

For example, fibre may be just an indirect indicator of vegetable intake and the active component may be something else like anti-cancer compounds (e.g. indoles) found in cruciferous vegetables,[9] which include cauliflower, cabbage, Chinese cabbage (pakchoy), mustard greens (kaichoy), chye sim, kailan, kangkong, broccoli and brussels sprouts.

It would seem that the main mechanism involves bile acids and their breakdown products. Fat intake increases the secretion of bile acids and mutagens have been known to be formed in the gut due to bacterial action. Fibre may act to remove and reduce the effect of fat and

bile acids. Vegetables act as sources of inhibitors.

CONCLUSION

We have reached the stage in medical research where we do not yet have all the clear answers. On the other hand, we have sufficient knowledge to initate some practical measures which would hopefully lead us to some degree of control in the decades ahead. We cannot and should not wait for all the answers before doing something. Latent periods in cancer causation are long, and even when something definitive is done now, the results will not be seen until 15 or 20 years later.

From the available studies so far, the prudent strategy in terms of digestive cancers would be to bring about some vital changes in our lifestyle, particularly in the diet. In life very few situations are clear-cut phenomena. There will be pros and cons, risks and benefits. It is our responsibility as health professionals to evaluate the findings and make reasonable and balanced recommendations.

The role of diet in causing cancer may be mediated in the following ways:

(a) food items may be carcinogenic,
(b) food items may be vehicles for carcinogens,
(c) diet may contain precursors of carcinogens, which get converted in cooking or in the body,
(d) diet may contain promoters of cancer,
(e) diet may lack inhibitors of cancer.

They are, of course, not mutually exclusive.

The guidelines that are generally acceptable to most medical authorities are as follows:[10]

(1) Maintain total fat intake at 25-30% of calorie intake.
(2) Minimize salt-cured, pickled and smoked foods.
(3) Take alcohol in moderation.
(4) Avoid tobacco in all forms.
(5) Include fresh fruits and vegetables, particularly cruciferous and carotene-rich ones.

Such advice is not new. According to a Chinese medical classic "Ji Sheng Fang" written during the Sung Dynasty (960-1279 A.D.), the following statement was made:

> "One should eat and drink in moderation (not in excess, not at a rapid rate, foods not too hot and not overly hard), maintain an even temperament, eat a good diet and Ye Ge (oesophageal cancer) will not develop".

In these days of high-tech medicine, we would do well to pay some attention to the perceptions of wise practitioners whose only tools were the science of keen observation and the art of applying human knowledge. They are just as valid today as they have always been in the affairs of men

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