Contribution from descriptive studies to the etiological knowledge of colorectal cancer

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It has been estimated that there are half a million new cases of colorectal cancer in the world every year, corresponding to 8.6% of all new cancers [1]. On a world-wide basis, colorectal cancer ranks fourth, whereas it is the second most common tumor in northern and western Europe representing some 13% of all new cancer cases. In southern and eastern Europe colorectal cancer ranks third and fourth respectively comprising around 10% of all new cancer cases.

Based on knowledge of the distribution and frequency of colorectal cancer in defined populations, clues may be gathered to create hypotheses concerning environmental associations which may be determinants of the disease. As a corollary, a hypothesis of the etiology of colorectal cancer must be in accordance with the occurrence of the disease. This paper deals with features of the descriptive epidemiology of colorectal cancer. There is, however, a gradual transition from descriptive to analytical epidemiology.

Variation in incidence

In both high and low risk populations, the incidence of colorectal cancer increases exponentially with increasing age similar to the age dependency of most other epithelially derived tumors [2]. The level is the same for colon cancer in males and females, while male rectal cancer rates are 1.5 times higher than female rates, features found constantly in various parts of the world [3]. There are, however, distinct age-sex differences in incidence throughout the large bowel. In the coecum and ascending colon, rates are approximately equal in men and women of young and middle-age, while rates are higher in older women than in older men. In the transverse colon, young men have higher rates than young women while the rates are approximately similar for men and women of middle and older age. The converse pattern is seen for the left side of the large bowel (descending, sigmoid colon, and rectum), where the male/female rate ratio increases with increasing age, the male predominance becoming increasingly important for distal sites of the bowel [4].

International comparison of standardized incidence rates shows that colorectal cancer is a disease of affluent societies in North America, Europe, Australia and New Zealand. An approximate 7-fold difference in incidence rates is seen for colon cancer. A similar variation is seen for rectal cancer, which internationally follows the same distribution as colon cancer.

These international patterns are not attributable to variation in genetic factors as demonstrated by the study of migrants from low to high incidence areas. Japanese who migrate from Japan to the west coast of the United States thus adopt the high incidence rates of the host country within two generations [5]. There is an indication that the incidence rates approach those of US Whites already during the first generation, and changes of life-style in adulthood may thus influence the risk of colon cancer.

Evidence that colorectal cancer is a disease of affluency is further corroborated by the finding of positive gradient with social class in low incidence areas [3].

International correlations

The international distribution of colorectal cancer points to the role of diet in the disease etiology, in particular to a westernized diet rich in meat and fat and poor in fibre and cereals. Support for this hypothesis has been provided by several studies in which the incidence or mortality of colorectal cancer in a country has been correlated with national statistics on food consumption and nutrients. Armstrong and Doll [6] thus found the strongest correlations with meat and fat, and also a negative correlation with cereals. Although indicative, such correlation studies cannot provide persuasive evidence of causality.

The observations are however in line with a low risk of colorectal cancer among Seventh Day Adventists–i.e. vegetarians–both in the United States and Denmark [7, 8]. Low risks of colorectal cancer have also been observed among Mormons, who by religious prescription are supposed to lead a healthy life-style, and who eat a cereal-rich diet [9].

Both internationally and within the United States, beer consumption is known to correlate positively with the incidence of rectal cancer [10]. Just as for the dietary correlations, specifically designed analytical studies are needed for determining whether the relationship is causal. Analytical studies have so far shown inconsistent results [11].

Dietary comparisons between Denmark and Finland

Within Scandinavia the incidence of colorectal cancer is 3 to 4 times higher in Copenhagen than in rural Finland, with rural Denmark and Helsinki taking intermediate positions. This situation has been explored in two population-based comparisons of diet and the concentration of fecal components, believed to be associated with colon cancer risk. A positive

association of colorectal cancer incidence exists with acid steroid concentration, which is a result of daily acid steroid excretion into the lumen of the gut and the faeces [12]. In accordance with these faecal characteristics, there were no differences between the populations in total daily fat intake (which is associated with faecal acid steroid excretion in bile), but an inverse gradient for dietary fibre intake with incidence in particular for the pentoses fraction, which has a bulking effect on the stools. There is thus some evidence that dietary fibre protects against colorectal cancer occurrence; other dietary factors differ also between these populations, notably the intake of beer although not consistently over the incidence gradient– and milk, which is a source of dietary calcium, recently suggested to be protective against the disease.

Conclusion

The epidemiologic characteristics of colorectal cancer both internationally and within countries, supported by studies of migrants, indicate that factors associated with a westernized, affluent life-style may play a role in etiology. It has been hypothesized that high dietary fat intake, in particular in the form of meat, leads to an increase in faecal bile acid concentration which within the gut lumen may be converted to secondary bile acids. These have tumor promoting or cocarcinogenic properties. The international correlation with meat and fat intake corroborates this hypothesis. Similarly it has been suggested that low risk populations are characterized by a high dietary fibre intake, which may have a bulking effect on the stools, thus leading to a rapid mouth-anus transit time and a dilution of cocarcinogens present in the faeces. Some support for this hypothesis has been produced notably from population comparisons undertaken in Denmark and Finland.

It should be noted, however, that such populations may differ substantially on other characteristics than the ones noted and correlations or population comparisons are insufficient to provide persuasive evidence of causality. The clues provided by observations on the occurrence and distribution of colorectal cancer and by correlation studies must be explored in studies of individuals (such as case-control, cohort, and intervention studies) before the etiology of colorectal cancer can be finally established.

Summary

Contribution from descriptive studies to the etiological knowledge of colorectal cancer

Incidence of colorectal cancer increasing exponentially with age is confirmed but sex-age differences in incidence throughout the large bowel are shown. Observations of incidence within countries indicate that colorectal cancer is a disease of affluent societies. Furthermore, it is hypothesized that a high dietary fat intake leads to an increase in faecal components associated with colon cancer risk.

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