

Structural Alterations in the Rat Oesophagus Epithelium after Ingestion of the Transkei Diet

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SUMMARY

Maize, beans and wild vegetables, grown in the Transkei and prepared in the traditional manner, were fed to rats from weaning until death, when the oesophagus was examined histologically. The diet appeared to induce degenerative changes in the oesophagus epithelium, which were followed by alterations of a preneoplastic nature. Recent evidence for the involvement of the staple diet in the aetiology of oesophagus carcinoma is discussed.

S. Afr. Med. J., **48**, 2361 (1974).

The numerous aetiological investigations into the cause of oesophageal carcinoma usually incriminate the excessive use of tobacco and alcohol. Yet not all hard-smoking and drinking communities have a high rate of oesophageal cancer, and certainly in one of the highest cancer rate areas in the world, along the Caspian Sea in Iran, virtually no use is made either of tobacco or alcohol. Environ-

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mental chemists well know that today we are living in an increasingly carcinogen-contaminated environment and, as may be expected, many neoplastic diseases are on the increase.

It would be rather surprising if an organ such as the oesophagus was exposed to a single source of carcinogens. Chemical carcinogenesis is dose-related and the important total dose will be culminative from many sources. There will always be a variable 'background' exposure. If it is high enough, single additional sources of carcinogens can be of critical importance in precipitating frank neoplasia.

MATERIAL AND METHODS

Diets are variable and this is an obvious line of investigation when attempting to assess the 'background' exposure. The most common constituents of the Transkei diet are maize, beans and wild vegetables (*imifino*). These locally-produced foods were collected, prepared in the traditional manner and fed to rats from weaning until death. Eighty rats received maize and beans alone and a further 80 received *imifino* in addition. Ten rats received maize and beans which were produced in the Transvaal, and a further 10 received balanced rat feed. Rats died throughout the 3-year experimental period and occasionally small aliquots were killed to provide representative material. The oesophagus was dissected, fixed in formalin, and approximately six transverse sections along its length were prepared for histological examination.

RESULTS

No gross abnormalities were found, but on careful histological examination a subtle but severe sequence of changes had occurred, which markedly altered the histological structure of the oesophagus in the majority of animals. Rats receiving balanced rat feed were unaffected, and those that consumed Transvaal maize and beans exhibited only slight changes. Both groups on the Transkei diet were markedly affected, but alterations were consistently more advanced in the group receiving *imifino* in addition.

Considerable variability existed, but in general cellular degenerative changes were prolonged and were followed by changes that could be classed as premalignant, though not irreversibly so. Vacuolation, condensation of chromatin, pyknosis and necrosis of basal epithelial cells, from which the carcinomas arise, were prolonged and seen at most stages in the Transkei diet groups. After one year the epithelium of many animals became exceedingly thin and sparsely populated with basal cells. After approximately two years of life the epithelium of most animals was thickened and some animals showed parakeratosis, hyperkeratosis, basal cell hyperplasia, dysplasia and/or single scattered cells or foci of anaplastic cells. Occasionally sub-epithelial accumulation of macrophages or oedema was present, and fibrosis was not infrequent in older animals. Two animals receiving the full diet had small papillomatous outgrowths near the cardiac junction, which caused some stenosis and proximal distension.

DISCUSSION

Although no carcinomas were produced, the study clearly demonstrated that the diet contains a factor which is toxic to the basal epithelial cells. The majority of site-specific carcinogens are in fact toxic to the predilected tissue.

Nitrosamines are the most potent known oesophageal carcinogens, and are no exception in this regard. When high doses were injected subcutaneously into rats, we found that they may die on about the fifth day from fatty degeneration of the liver, but if they survive this crisis the oesophagus becomes necrotic, gangrene sets in and death occurs about two weeks after the injection of nitrosamine. Small weekly injections do not elicit any clinical signs, but within days toxic effects on the oesophageal epithelium are demonstrable histologically and are soon followed by a variety of premalignant changes which progress to frank carcinomas about 6 months later.

These acute effects are the basis of current short-term attempts to demonstrate the possible presence of carcinogens in foods. Maize is produced in the Transkei in a high oesophageal cancer locality, using controlled experimental fertilisation regimens. Aliquots have been fed to rats for 2-4 weeks, after which the number of basal epithelial cell nuclei in one transverse section, made from the middle of the oesophagus, which exhibits degenerative changes, were counted. In the studies completed to date, some associations with the nutritional state of the plant and the number of degenerating cells in the oesophagus epithelium appear to be emerging.

The earlier associations between deficient soils, stunted plant growth and oesophageal cancer in the Transkei, are now well known. It is interesting to note that we have observed extensive signs of abnormal plant growth along the Caspian Sea in Iran, a locality which also has an extraordinarily high incidence of oesophageal carcinoma. Here the problem is essentially one of salinity in the soil, the degree of which correlates well with the cancer rate. In several parts of the world, including the USA, the disease is increasing among lower socio-economic groups, and the increasing use of lower grade carcinogen-rich plant material as food appears currently to be the most logical explanation.