

Precancerous Gastric Disease

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IN THE DEVELOPMENT of this particular subject, two aspects are emphasized: first, the morphologic changes present in the stomach and their precancerous features, and second, the environmental or hereditary features that may go along with the development of this condition.

MORPHOLOGIC FEATURES

Mucosal Atrophy and Achlorhydria

The old concept of the abnormal mucosa has really not been improved upon. Sir Arthur Hurst and others referred to the abnormal mucosa, the achlorhydria, the atrophic change. Studies have continued along that line in an effort to determine whether that atrophic change is there preceding the gastric carcinoma or whether the atrophic change and the achlorhydria may go along with the development of the gastric carcinoma and even be accentuated afterward.

Many studies have been done attempting to determine the degree of achlorhydria in patients with either a gastric polyp or a gastric carcinoma. There is undoubtedly a high incidence of achlorhydria in gastric carcinoma. In our own experience, complete achlorhydria was present in 65 per cent, an additional 20 per cent had hypo-acidity, and the remainder had normal acidity. Therefore, gastric carcinoma is compatible with some degree of acidity. There is, however, some alteration in the acid-secreting cells in association with the development of gastric carcinoma. It may be an abnormal mucosa that merely goes along with an abnormal growth process, or it may precede such. There is some evidence suggesting the development of carcinoma in the presence of a normal degree of acidity with achlorhydria developing at a later date.

Likewise, there is evidence that in the presence of a gastric carcinoma there may be an atrophic change in the gastric mucosa, and as the disease progresses the degree of atrophy increases. It is generally believed that the achlorhydria and the atrophic gastritis are merely manifestations of an abnormal mucosa upon

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which a carcinoma develops and that they do not necessarily precede the development of the gastric carcinoma. Therefore, whether the sequence was atrophy and/or achlorhydria first, followed by the gastric carcinoma, is undecided. This indecision does not establish any etiologic concept for gastric carcinoma; it merely indicates that more has to be done along such lines in order to determine why such individuals develop abnormal mucosa upon which such transition may take place.

Gastric Polyp

The gastric polyp for many years has been looked upon as a precursor. Whether or not it is truly precancerous or whether there are two distinct types—merely benign polyps, and cancerous polyps—is not established. There are those who believe that benign gastric and colonic polyps never develop into carcinoma. Gastric polyps in observations extending over a period of nine or ten years have shown no evidence of malignant change. In all probability there are many benign polyps that never become cancerous. However, there is reason to conclude that a small percentage probably undergo transition to cancer. The principal problem revolves around the initial diagnosis. The clinical inability to make the differential diagnosis enforces polypectomy because we cannot determine whether the polyp is benign or malignant.

It has been conclusively demonstrated by Mandred Comfort that in individuals with gastric polyps there coexists an exceedingly high incidence of achlorhydria. Therefore, here again there is some mucosal abnormality, perhaps atrophy, with associated secretory suppression; in addition, a polyp exists or develops in that abnormal mucosa. It is suggested that in the background there exists some factor producing such abnormality that could bring about the three features of atrophy, secretory suppression, and polypoid change.

Pernicious Anemia

In patients with pernicious anemia there is necessarily a concomitant, causal, or resultant achlorhydria. Some young individuals with early pernicious anemia may have a small amount of free hydrochloric acid; in general, however, any patient who has pernicious anemia will not have free hydrochloric acid. Studies on such individuals indicate them to be increased gastric cancer

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risks. The occurrence of gastric carcinoma is probably twelve times more frequent than among the general population. Figures based on follow-up studies by x-ray at postmortem are confirmatory. Here again is abnormal gastric mucosa manifest in achlorhydria and atrophic changes, and the frequent development of either carcinoma or a polyp.

Gastric Ulcer

The presence of a gastric ulcer is also an indication of abnormal mucosa. A debate has always revolved about whether a gastric ulcer may undergo malignant transition. That a few ulcers become malignant does not convey much significance to the real issue.

The management of a patient with a gastric ulcer depends on whether or not the ulcer is benign or malignant when first observed. The differential diagnosis can and should be established within a matter of a few weeks or, at the most, months, settling the issue at that time and not creating concern as to whether or not this lesion may undergo transition to malignancy. It is my contention that an ulcer develops in a gastric carcinoma and not the reverse. Unless one has the opportunity to observe gastroscopically a carcinoma and later visualize an ulcer developing in that same area, or vice versa, there cannot be conclusiveness. While the controversy persists, the reports on benign lesions becoming malignant diminish and the problem has truly resolved into whether or not a lesion was malignant in the first place.

Comment. All of the morphologic changes I have mentioned have significance in developing the thesis that abnormal mucosa occurs upon which a gastric carcinoma may develop. We still have a long way to go in knowing what that abnormality is, how long it must be present, and then how long the gastric carcinoma takes to develop.

ENVIRONMENTAL AND HEREDITARY FEATURES

Geographic Incidence

The environmental and hereditary features constitute a different aspect of this whole concern. Geographic differences have been studied intensively in recent years, with the conclusion that a geographic incidence-variation exists for gastric carcinoma. This is included in discussing precancerous gastric disease because knowledge of what is going on in the different geographic areas may indicate some factor that is common to a group of individuals;

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an environment, diet, or radiation exposure that predisposes that population segment to the development of a gastric carcinoma.

In a study of the southern section of the country (Texas) as compared with a mid-northwestern area (Michigan), a greater incidence of gastric carcinoma in our colder climate was found as compared with the warmer climate. (The two major studies were done in Dallas, Texas, and in Detroit, Michigan.) This distinct difference has been present year after year; it is not just happenstance. In Japan the incidence of gastric carcinoma is almost twice that in this country: About 37 per 100,000 individuals in Japan have a gastric carcinoma, whereas the average in the United States is around 18 or 20. Among the Japanese residing in Hawaii and in Los Angeles, the incidence of gastric carcinoma is higher in the native-born than in the Hawaiian-born or American-born Japanese. Yet in all three locations the Japanese have a higher incidence of gastric carcinoma than the white population of the United States. So here is some racial tendency modified by some other factor. Whether it is completely hereditary, racial, or the result of a change in dietary habits is debated; the latter is most often indicted. Other comparative mortality studies have been done in the Netherlands and England. In England the incidence of gastric carcinoma is distinctly higher than in the Scandinavian countries. Whether or not that is due to difference in diet actually has not as yet been established. We do not yet know whether it is the type of food or whether it is the type of environment. We merely have made observations that permit speculation on available information. There is, however, something of significance that creates the difference in incidence of gastric carcinoma in comparable areas.

One pleasing feature about the incidence of gastric carcinoma in this country is the fact that it is definitely decreasing. The United States Public Health Service has analyzed the incidence of gastric carcinoma in the Detroit hospitals, for example, going back fifteen years. Within recent years, a definite decrease in the incidence of gastric carcinoma is evident in that community. The change is not explained. It can hardly be merely an improved ingestion of vitamins or more beef.

Age and Sex

From the standpoint of age, gastric carcinoma has of course been reported in youth, but the curve ascends straight, without

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leveling off at any age segment as it may in other diseases. One might speculate, therefore, whether something is injected into our life that is the carcinogenic agent. The actual incidence may depend upon the amount of carcinogen injected over a long period of time, thereby producing the disease in a certain person; not injecting that amount permits the escape of another person.

Interestingly enough, a significant sex-related difference exists in the sites of carcinoma in the gastrointestinal tract. The incidence of carcinoma in the upper digestive tract is much higher in males over females. In the pharynx, the esophagus, and stomach, the incidence of carcinoma is much higher in the male than it is in the female. As one descends the intestinal tract to the colon, an equalization for sexes is approached.

Blood Group

There have been observations indicating a very convincing relationship of the blood group to the incidence of gastric carcinoma. There has been some emphasis made on lesions in the lower part of the stomach being more common in one blood group. This may indicate a predisposing factor.

Heredity

There are two conflicting reports on heredity. The Minnesota group decided that there was no hereditary component in the incidence of gastric carcinoma. In the Netherlands it was concluded that the incidence of gastric carcinoma in the relatives of patients with gastric carcinoma was four times greater than in the nonrelative group. Carcinoma of other organs in this group of relatives had no greater incidence than in the average population.

Comment. Our geneticist feels that there is probably no proved relationship or proved increased incidence from the environmental standpoint. Sociologically, it is true that the urban people have more gastric carcinoma than those residing in rural countries. Unmarried women and unmarried men have less gastric carcinoma than married persons. There are various features that seem to have some, but indefinite, bearing.

PERIOD OF DEVELOPMENT

Great interest has been focused on the length of time a gastric carcinoma takes to develop. There is evidence indicating that some gastric carcinomas may have a long quiescent existence. A mass

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survey for gastric carcinoma on individuals 40 years of age and older, entering the Johns Hopkins Outpatient Department was conducted. From this group were selected 23 individuals with early defects in their stomachs ideally demonstrable by x-ray. Morgan personally followed that group for three years, and in that period there was very little change in the size of lesion. He did not pursue it beyond that time because of lack of funds and outside interest. That he did not is regrettable, for we have no present knowledge of how long it takes a carcinoma to develop.

We may someday find some carcinogenic agent in our environment that has been present for a long period of time. The carcinoma itself may be present for a long time, and hence we may have an ample interval of time during which we could make the diagnosis. The hope at the present time is to discover that "something" which influences the development of a gastric carcinoma after the diagnosis has been made. Certainly, surgery, at the present time the only curative approach, is not the ideal. Perhaps by utilizing some of the precursor lesions, some of the abnormal cells, some of the factors that we do know, admitting that this knowledge is modest, we can hope that over a period of time more work will be stimulated to be done on this subject and that someday we will have that necessary information about the development of this disease and, thence, its adequate management.