# Gastrointestinal Carcinoma and Occurrence of Pleural Plaques on Pulmonary X-Ray


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In many studies of persons exposed to asbestos an overrepresentation of gastrointestinal carcinomas has been found. So called "pleural plaques" (PP) are hyaline or calcified formations of the parietal pleura which are caused mainly by exposure to asbestos. If sufficiently large, they can be seen on a chest roentgenogram. It was therefore decided to investigate whether in a population of patients with gastrointestinal carcinoma these formations were more commonly found on the chest roentgenograms than would be expected.

## Subjects and Methods

A list of all patients from the county of Uppsala with gastrointestinal tumors (esophagus, stomach, small and large intestine and rectum) diagnosed during the five-year period from 1968 to 1972 was obtained from the Swedish Cancer Registry. All cancers are reported to this registry as a matter of routine both by clinicians and by pathologists, and the register is considered to contain 97 to 100% of all diagnosed cases. The latest available data year from this registry was 1972. Miniature chest films of the patients were sought in the archives of the General Health Survey of the county. This health survey has been in operation since the early 1960s and all persons of age 15 and above living in the county are invited to take part every second to third year. The participation rate is between 65 and 75%. The miniature chest film is of very good quality, and in the author's experience pleural changes are just as easily diagnosed in these small films as in full size roentgenograms. For every patient whose films were found, three controls were chosen. The archive is organized according to date of birth and the controls comprised the nearest persons with a film taken the same year as the latest film available for the cancer patient (later films being left in the file) and of the same sex. Thus, all the controls were born in the same year, usually in the same month, and in many cases even on the same day as the patients. They were taken randomly from one or both sides of the patients in the archive (i.e., somewhat younger or older) and were examined by the author without knowledge as to which films represented carcinoma patients and which did not.

Only PP fulfilling the criteria in Table 1 were accepted. For almost all male cases their occupation was stated on the card accompanying the x-ray, and this was recorded.

## Results

*Male Cases.* — There were 482 men in the list from the Cancer Registry, 61 with benign lesions only (Table 2). Miniature films were found for 386 (80.1%) of them and thus there were 1,158 controls. The number of persons with PP among the tumor patients was 13 (3.4%) and among the controls 20 (1.7%), the difference being significant at the 2% level (chi-square test). The distribution among the different gastrointestinal regions is given in Table 3.

*Female Cases.* — Of the 420 women in the Cancer Registry, 320 with chest x-rays were found, giving 960 controls. Two women with PP were found, one patient and one control. No conclusions could be drawn from these findings.

## Discussion

The etiology of the various forms of gastrointestinal cancer is far from clear. Epidemiological data, however, point to some external agent(s) as being responsible. Cancer of the colon, on the one hand, is common in Scotland, Denmark, Canada and New Zealand, while it is rare in Chile, Finland, Japan and Israel.[1] On the other hand, cancer of the stomach is common in Finland, Chile, Japan and Iceland.[2,3] If Japanese, who run the Japanese high risk of cancer of the stomach and low risk of cancer of the colon, move to the U.S. and in the process also modify their food habits, they will tend to have children with risks more similar to those of the U.S., i.e., the gastric

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**Table 1. — The Roentgenological Criteria* for Definite Pleural Plaques Used in This Study.**

1. Bilateral Changes
2. Typical Changes, i.e., uneven, situated mainly in the flanks and the diaphragm. If only seen in the flanks, at least 5 mm thick on a normal-sized chest x-ray. Diaphragmal plaques, if the only finding, not accepted unless bilaterally calcified
3. Clear costodiaphragmatic sinuses
4. Progression in a 5-year period if x-rays are available

*All criteria must be fulfilled (except number 4, if no earlier x-rays are available)

**Table 2. — Total Population Distribution by Gastrointestinal Region and Sex.**

| | Male | (Benign) | Female | (Benign) | Male/Female |
|---|---|---|---|---|---|
| Esophagus | 30 | (2) | 9 | (0) | 3.3 |
| Stomach | 183 | (3) | 137 | (1) | 1.3 |
| Small intestine | 11 | (0) | 6 | (0) | 1.8 |
| Large intestine | 133 | (14) | 182 | (10) | 0.7 |
| Rectum | 125 | (32) | 86 | (20) | 1.5 |
| Total | 482 | (61) | 420 | (31) | 1.1 |

cancer rate will go down[2] and the colon cancer will go up.[4]

Many investigations have revealed a higher rate than that expected for gastrointestinal cancers among persons exposed to asbestos. As early as in 1951 Gloyne[5] reported 102 autopsy cases of asbestosis collected over some decades, and there were eight cases of gastrointestinal cancer included among them even though the average age of the patients was only 35.5 years. In 1964 Selikoff, Churg and Hammond[6] reported on 632 insulation workers who had been followed from 1943 to 1962. Among them there were 29 with gastrointestinal cancer, while the expected number was 9.4. These workers have been followed further, and in 1973, 41 deaths of gastrointestinal cancer had occurred against 13 expected, i.e., 2 to 3 times the expected figure.[7] The time from first exposure to asbestos to diagnosis of the cancer was more than 20 years in most cases. Specifically, gastric cancers were six times as numerous as expected, and cancer of colon three times as numerous.[8]

Mancuso,[9] in 1965, also found an approximately doubled risk for asbestos workers in a U.S. plant manufacturing asbestos brake linings, and Newhouse[10] found a significant increase of gastrointestinal cancers in males in a London asbestos textile factory. In 170 male insulation workers from Belfast followed from 1940 to 1960, Elmes and Simpson[11] likewise found an increase in the incidence of gastrointestinal cancer, and in Russia Kogan et al[12] reported the same. An increasing number of gastrointestinal cancers with increasing exposure to asbestos has also been noted in Canada.[13] A tendency to a higher mortality has been found in Sweden[14] as well as in U.S. districts with shipyards, where especially during World War II, asbestos has been used extensively.[15] In reviews of the above articles and others, Schneiderman[16] and Miller[17] concluded that there are no doubts about the increased risk of gastrointestinal cancer among persons exposed to asbestos, and that the induction period is usually more than 20 years.

The occurrence of PP may be regarded as indirect proof of exposure to asbestos. With strict roentgenological definitions of PP (Table 1), 80% of PP carriers will readily admit to asbestos exposure, and of the rest a large portion will probably have been exposed unknowingly.[18] Very few false positive cases will be found with these criteria if comparison is made with the autopsy findings, but on the other hand a large portion will be missed.[19] The criteria have been used in earlier investigations and in one patient group with bronchial carcinoma[20] and in one with laryngeal carcinoma[21] a highly significant increase of PP carriers was found. Thus, if exposure to asbestos does have any influence on the occurrence of gastrointestinal malignancies, there ought to be a higher frequency among such patients than among controls. Since the occurrence of PP differs in different age groups, and the incidence is rising,[18] the controls are very important.

In the present investigation there were three controls of the same sex and age with a roentgenogram taken in the same year, and the films were scrutinized without knowledge as to which represented cancer patients and which represented controls. The frequency of PP among the male controls, 1.7%, is similar to the expected value from 1976 in the county.[20] Among the patients with gastrointestinal cancer the frequency of PP was 3.4% and the difference is statistically significant at the 2% level. As for the different gastrointestinal regions, there was a tendency towards higher figures for the esophagus and the stomach. Apart from the total figures, it was only for cancer of the stomach that the differences were statistically significant.

How does asbestos reach the gastrointestinal tract? The most plausible way is, of course, by swallowing, and the major part of any inhaled dust deposited in the upper digestive tract will be quickly transported to the gastrointestinal regions.[22] Evans and Morgan and co-workers[23,24] showed that 30 to 68% of inhaled radioactively-labelled

**Table 3. The Distribution of All Male Patients with Available Chest Films and Those with PP in Gastrointestinal Regions.**

| | Total | (Benign) | Number of PP Observed | (Benign) | Expected | Obs/Exp |
|---|---|---|---|---|---|---|
| Esophagus | 21 | (2) | 1 | (0) | 0.35 | 2.8 |
| Stomach | 148 | (1) | 6 | (0) | 2.5 | 2.4* |
| Small intestine | 8 | (0) | 0 | | — | — |
| Large intestine | 108 | (13) | 3 | (2) | 1.8 | 1.7 |
| Rectum | 101 | (30) | 3 | (0) | 1.7 | 1.8 |
| Total | 386 | (46) | 13 | (2) | 6.6 | 2* |

* = Significance on the 5% level (chi-square test)

asbestos dust will be deposited in the gastrointestinal tract in rats initially, and after 30 days more than 70% will have been excreted in the feces. Gloyne[25] showed that asbestos bodies could be found in the feces of asbestos workers, and since it is hard to imagine asbestos body formation taking place in the gastrointestinal tract, they must have come from the bronchi. Cunningham and associates[26] have shown that the amount of fecal asbestos is significantly increased among asbestos workers. Most of the ingested asbestos fibers traverse the entire tract, but some of them will probably penetrate into the intestinal cells. Webster[27] fed asbestos to baboons and found a small portion of it later in their ashed gut. Westlake,[28] on feeding rats with asbestos, found asbestos needles in their large intestine cells, and Storeygard and Brown[29] found some fibers in rat jejunal wall one hour after asbestos ingestion. After injection into rat stomachs, chrysotile fibers could be isolated two to four days later from many organs.[30] Despite these findings, both Davis[31] and Gross et al,[32] stated that asbestos fibers do not penetrate into the gastrointestinal cells. Other authors, however, believe such penetration possible.[32 33 34] In a long-term study Gibel and co-workers[35] showed that rats which consumed asbestos daily had significantly more tumors than did control rats, including carcinoma of the kidney and lung, and papilloma of the stomach.

In humans fibers have been demonstrated widely disseminated in the spleen, liver, kidney and gastrointestinal tract,[36 37] but these, of course, might have been transported there via the blood from the lungs. Chatel et al[38] investigated 42 men occupationally exposed to asbestos and found asbestos fibers in the gastric fluid in five cases. Electron microscopic examination of biopsies obtained at gastroscopy in some of these men gave negative results, but in one case where the whole stomach was available for study after operation for a malignant tumor, many naked small fibers were found. Asbestos bodies are seldom found in the intestinal wall; Rosen et al[39] found no such bodies in the colon of 21 patients with primary malignancies of the colon.

There has been public anxiety that ingestion of asbestos in food or drink can occur and lead to gastrointestinal cancer. Asbestos fibers can be found in small quantities in practically all kinds of beverages[30 26] even in fresh, unpolluted water near asbestos deposits. Beer and wine are often passed through asbestos filters, and consequently asbestos fibers can be found in the finished products.[40] Water polluted from asbestos mining operations or simple dumping of asbestos, or from being passed through asbestos pipes, has been shown not to be associated with a higher prevalence of gastrointestinal carcinoma, but the observation time might well have been too short.[41 42 43] Wigle et al[44] report that in two communities in Quebec the incidence of cancer of the stomach among men is twice the expected value, but this is explained by probable occupational exposure to asbestos.

Asbestos fibers can also be found as an ingredient in many processed foodstuffs. The most discussed of these is the talc-coating of rice, which is done mainly for aesthetic purposes.[45] Merliss[3 46] suggested that it is this coating that explains the seven-times greater-than-expected prevalence cancer of the stomach in Japan but Haenszel et al[2] found no support for this theory in epidemiological studies. Electron microscopic investigations have revealed talc, but not asbestos, in gastric carcinoma cells from Japanese patients in one study[47] and both talc and asbestos, as well as other particulate matter, in another[48] but this does not, of course, prove any relationship.

There is a correlation between low socioeconomic status and occurrence of gastrointestinal carcinoma.[49] For example, Enterline[50] reported a doubled incidence of gastrointestinal cancer in a population of coalworkers and related this to socioeconomic factors. If this was the main reason for the higher prevalence of gastrointestinal carcinomas among carriers of PP in the present investigation, it might be expected that there would be some significant differences in the stated occupations between the patients and their controls, but with the exception of construction workers in relation to carcinoma of the stomach this was not the case. Many persons exposed to asbestos are in fact skilled workers and cannot be regarded as a group belonging to a low socioeconomic class.

In conclusion, there is a slight but significant excess of typical pleural plaques in patients with gastrointestinal carcinoma, particularly carcinoma of the stomach. This is in accordance with many other reports, in which exposure to asbestos has been linked to an approximately doubled risk of gastrointestinal carcinoma.

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## Forging New Connections

To sustain a balanced effort between the search for new knowledge and uses for the old, we must build a collaborative partnership among research and educational institutions, the government, and the private sector. Industry must become a full partner — not merely a "user" and especially not an adversary. New connections must be forged between academic and industrial research centers. A wide range of cooperative programs must be emplaced, and, as in any true partnership, the needs of both parties must be taken into account. For healthy science, the vital ingredients in the delicate process of creation (especially freedom of choice and a stable floor of support) must be preserved, and, meanwhile, industry has a right to a fair balance between risk and reward.

— From "Opinion: Epidemic of Life" by James D. Ebert, in *Bioscience*, August 1980.