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From the Ludolf Krehl Clinic Heidelberg
(Medical School Clinic)
Director: Professor Dr. R. Siebeck

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By

Dr. H. W. Wedler, Chief Physician of the Clinic
(died March 20, 1943)

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In the last twelve to fifteen years, both German and foreign medical literature has recorded such a wealth of experience regarding asbestosis that we have a wide knowledge of the endangerment of asbestos workers and a clinical picture of their occupational disease as well as its progress. Of course, there are still many questions yet to be answered regarding its pathogenesis--clarification to be expected from animal experimentation and chemical-physical research. On the other hand, our knowledge of asbestosis' complications and attendant diseases rests on a less broad and firm foundation. In this area the author has recently made a great contribution in the area of the relationship of pulmonary tuberculosis to this coniosis. Equally illuminating and important is the question of the relationship of asbestosis to lung cancer, whose frequency in cases of asbestosis has been repeatedly discussed in the past few years. This relationship is of interest not only from the viewpoints of public health or of insurance law; rather, it also impacts the field of general medicine because it manifests a new example of exogenous cancer origin. Although the absolute number of such observations is small, in view of the rarity of this disease it is so remarkable, that a summarizing

presentation is in order. It is also desirable because there is not yet any such work in the literature from the clinical side.

We first present a summary of previously-reported cases of lung cancer coupled with asbestosis, then add to them the most recent experiences and point out the peculiarities of this syndrome and its clinical diagnosis.

The first mention of a carcinomatous tumor in the asbestos dust lung was made by Gloyne in a treatise in 1933 dealing with the pathological anatomy and histology of asbestosis. There he discusses the complications of asbestosis which are said to be in causal connection with it (purulent bronchitis, broncho-pneumonia, tuberculosis, emphysema, bronciectases) as well as accompanying diseases which, according to the knowledge of that time, had nothing to do with the influence of dust. Among the latter, he mentions an observation which he dismisses as follows: "There has also been one case of squamous carcinoma of the pleura. There is no evidence at the moment that this was in any way related to the asbestosis."

In 1935, Gloyne contributed two further cases of lung cancer with asbestosis, but he believed that an etiological connection of both diseases could not be asserted at that time. Certain histological aspects, however, seemed to him to suggest to such a connection.

The first of these two observations concerned a woman, 35, who had been an asbestos spinner for eight years, and who, after that, lived still another nine years without exposure to asbestos dust. As the autopsy showed, she died of moderate asbestosis, a clot in the right heart, splenic infarction and meningeal bleeding. A walnut-sized tumor

(which had not been detected clinically) was found on the base of the right upper lobe of the lung, extending up to the apex and the thickened pleura. There were no metastases present. The horny plate-epithelium carcinoma had its starting point at a small bronchus.

The second observation by way of autopsy also concerned a woman, age 71. Fifteen years prior to her death she had worked for six months, and then again for thirteen months, in the typically extremely dust-laden mattress and preparation department in an asbestos factory. Anatomically, Gloyne found a medium advanced asbestosis with a partially disintegrated tumor in the right lower lobe of the lung, ascites and thrombosis of the vein of the left leg. There were likewise no metastases. Histologically, this was also a horny plate-epithelium carcinoma.

In both cases the cancer was not so widespread as to constitute the sole cause of death. The same could be said of the asbestosis.

That same year (1935), a communication by Lynch and Smith came from the U.S.A. about lung cancer with asbestosis which also contained a detailed case history. The described patient, 57, who was to be a cotton weaver for twenty-two years and then, until his admission to the hospital, had been an asbestos weaver for another twenty-one years, had complained of shortness of breath for five years. After having had, three years prior to his death, intermittent pains in his back and the last three ribs on the right, these pains reappeared during the last months of his life. His physical condition declined, he coughed, lost appetite, ran temperatures and suffered from bloody sputum and dyspnea on exertion. The

clinical finding was characteristic of asbestosis. The breathing sound low over the lung on the right was weakened. The clinical diagnosis indicated asbestosis and chronic indurating pneumonia with callosity on lower right. Aside from the asbestosis with right-sided pleuritis and bronchiectases, a cavity of disintegration was pathologically-anatomically found in the right lower lobe which was macroscopically believed to be tuberculosis. Microscopically, however, it turned out to be a plate-epithelium carcinoma. Metastases were not present. The description of hyaline nodules in the lung is unusual for a case of asbestosis. The carcinoma had started from a bronchus with a metaplastic epithelium. The authors thought of the chronic irritation of the bronchia as the cause. They characterized the connection between cancer and asbestosis as a "possible relationship" and drew parallels to other kinds of occupational lung cancer.

In 1936, Egbert and Geiger reported another such observation which they--with the exception of Gloyne's brief reference in 1933--believed to be the very first of this kind. The man, 41, had been an asbestos weaver for eighteen years. After nine years of work and following pneumonia, he had retained a cough and shortness of breath. Eight months prior to a brief treatment in the hospital, he got severe, paroxysmal backaches. He had grown thin, was hardly mobile on account of his pains, had a cough, cyanosis and shortness of breath as well as bloody-purulent sputum. Aside from the asbestosis, X-ray detected a focus in the lower part of the left lung, which focus resembled an atelectasis or a pneumonic process, but could be recognized as a tumor, because of metastases present in the pelvis and in the spinal column. During the

autopsy not only asbestosis, but also a 5:5:4 cm measuring acinous cancer in the left lower lobe were found. The cancer had established metastases in the lungs, the left-side glands of hilus and aorta, the right adrenal gland (suprarenal body), the musculature of the abdomen, the pelvis, the spinal column and the skull. The origin of the tumor was a large branch of the bronchus in the left lower lobe. Thus, an etiologic connection between the two illnesses seemed likely, namely, "That the irritating effects of the inhaled asbestos particles may in this case have been a significant factor concerned in the developement [sic] of the primary lung cancer seems sufficiently plausible to be worth of consideration."

In 1936, Gloyne was able to add a further observation to his previous three. He found a dedifferentiated carcinoma of the left lower lobe with asbestosis whose vector was 59 years old and had worked for twenty-one years in the asbestos trade.

Sparks related in 1938, without any particular details, that Gloyne had encountered in his autopsies six cases of lung cancer with asbestosis. Baader learned through a letter from Gloyne that these six cancer cases resulted from fifty performed autopsies.

Nordmann amplified our knowledge that same year with two new cases of cancer with asbestosis which he had dissected in Hannover within a short interval. The first patient was 35 years old. From her seventeenth to her twenty-sixth years, for exactly seven (7) years [sic], she had worked in the carding, spinning, and weaving departments of an asbestos plant. Four to five years prior to death she began to suffer from a cough and shortness of breath. Nine months before her death she began to receive medical treatment, the suspicion being that she had

tuberculosis. Hornig made a diagnosis of probable cancer in the left lower lobe with marked asbestosis, because clinically there were signs of atelectasis, and tomographically the main bronchus had been displaced. Anatomically, it was a horny plate-epithelium carcinoma with a walnut-sized deterioration cavity which was connected to the bronchus of the lower lobe. There were pleura callosity and metastases in liver and kidneys.

The second observation concerned a man, 55, who had worked for seven years (from his 36th to his 43rd year) in the preparation of an asbestos plant. Thirteen months prior to his death he grew considerably thinner and brought up bloody sputum. Originally, it was suspected that he had contracted tuberculosis. There was a muffled and weakened breathing sound over the lower left lung. X-rays disclosed opacity there. The treating physicians diagnosed asbestosis with lung cancer. The autopsy confirmed this. In the left lower lobe the cancer had, in connection with the main bronchus, deteriorated down to walnut size and was interrelated to the pericardium, the left ventricular wall, the diaphragm, the peritoneum of the left upper abdomen, the retroperitoneal tissue behind the spleen, the lymph nodes there and the lower thoracic upper lumbar vertebral column. Histologically, it again concerned a horny epithelium carcinoma. A beginning bronchial carcinoma was also found in the right lower lobe of the lung.

Nordmann added to these observations a thorough evaluation of the new point which seemed proof to him of an occupational cancer. He was the first one to speak clearly of an occupational cancer of asbestos workers.

Wedler drew attention in 1939 to another observation in Germany which originated from Bohne, but had not been previously made known. The man, 58, had worked ten years (1925-1935) in an asbestos plant, part of that time as a master workman. Only a few years after having been exposed to dust, he began to experience difficulty with his respiratory organs. In 1928 he was sent for two months to a health resort. Several times thereafter he went to a sanitarium, although no mycobacteria tuberculosis were found. Due to an increasingly worsening condition he quit his job three months prior to his death. In the hospital he showed signs of general emaciation, cyanosis and a catarrh which was especially noticeable over the lower part of the lungs. There were numerous asbestos particles in his sputum but no mycobacteria tuberculosis. The erythrocyte sedimentation was strongly accelerated (57/95). On the left, over the ninth rib a chestnut-sized tumor (grown together with the skin) was found in the forward axillar line. It was removed and found to be a cancer metastasis. The X-rays showed signs of asbestosis as well as an increase in markings in the right upper region. According to the evidence at my disposal, there was no diagnosis of a lung cancer intra vitam. The patient expired of heart failure soon after the excision of the metastasis. The findings of the postmortem examination were described as follows: "The lungs were tightly grown together with the chest wall. The heart was not enlarged, the musculature was of a brown-reddish color and of a somewhat flaccid consistency. The left lung was full of blood and fluid, the lower lobe of solid consistency and slate color. Upon removal, the right lung tore in the area of the middle lobe. Its tissue looked yellow-reddish and completely decayed and evidenced

extended cavity and node formation. The upper lobe was rich in blood and fluid, of firm consistency and free of air. The lower lobe was of a slatish, grey-reddish color and firm consistency. It too was free of air. The microscopic examination of the lungs showed typical cancer tissue in the right middle lobe, whereas the lower lobe presented all changes which are characteristic for asbestosis. Asbestos particles were found in all samples."

According to Baader (1939), six authors in the years 1935-1938 saw fourteen cases of cancer with asbestosis. No details are included with this information, so that unlike the previous data, as discussed above, these reports cannot be fully confirmed.

There followed in 1941 an extensive clinical and pathological-anatomical report from Wedler and Linzbach regarding another pertinent case history, which set forth the entire course of the disease. The 60 year old man had worked from 1921 to 1939, a total of eighteen years, in an asbestos factory. He was exposed to a heavy concentration of dust (in the preparation phase) for only the first three years. His first symptoms appeared shortly after his commencement of work. In 1938, he already manifested an uncomplicated, severe asbestosis, which had developed rapidly. In the course of his final years of life, there appeared an increasing shadow (over the right diaphragm) in the right lower lobe of his lung, along with clinical signs of an atelectasis and later decay as well as severe neuralgiform pains in the appurtenant area of intercostal nerves. His sputum was bloody. All signs pointed toward cancer, which had already been clinically diagnosed. The autopsy confirmed the diagnosis of a decaying horny plate epithelial carcinoma,

which originated in the right lower lobe bronchus. No metastases were present.

In the meantime in Germany, there were two further observations, which until now have not been presented in the literature.

The first case was seen by Teutschlaender, who had already orally reported the case twice. From a personally-written report, I have gleaned the following: In 1938, Teutschlaender performed an autopsy on a 40 year old woman who had worked sporadically in an asbestos factory for ten years. The clinical diagnosis of her read as follows: "Lung tumor on the right side? Cirrhotic pulmonary involvement right? Vicarious emphysema on the left side. Ascites. Severe cachexia." At the autopsy, no tuberculosis was found, but instead a very widespread asbestosis with numerous asbestos particles and a right-sided pleurablastoma, which histologically was determined to be a pseudoalveolar mesothelioma. In the peritoneum there was widespread tumor dissemination with ascites. The left pleural cavity contained 50 cm3 of fluid. Compensatory emphysema of the left lung. The cachexic woman died of circulatory insufficiency as a result of lung disease.

The second observation comes from Alwens. The autopsy was performed by Fischer-Wasels. My contact with the case was as a consulting specialist.[1] The 60 year old man (August 13, 1881, to September 19, 1941) had worked, up until one-half year before his death, for forty-two years in an asbestos rubberizing factory. In January 1941, he fell ill with increasing shortness of breath and weight loss with signs of left-sided

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[1] May also mean "expert" as in "expert witness." Impossible to tell from context. [Translator's Note.]

pleural fluid. Absolute dullness, increased breathing sounds and right-sided displacement of the heart. Sputum contained numerous asbestos particles. Numerous tumor cells were found in the gelatinous reddish fluid which was repeatedly drained through tap. Over the bottom of the right lung isolated rhonchi could be heard. Erythrocyte sedimentation increased rapidly. No tuberculin bacilli were found in the sputum. An X-ray disclosed asbestosis of medium degree and a primary tumor was suspected in the right hilus. The autopsy disclosed a mild asbestosis with a diffuse primary muciferous glandular cell carcinoma of the left pleura of mainly adenomatose character and metastases on the abdominal side of the left subphrenic space, the membrane of the small pelvis and the musculature of the chest. The autopsy report of the thoracic organs is set forth here in full, since no report has previously been made of it.

Thoracic autopsy: Panniculus adiposus moderately developed. Thorax is moderately rounded and elastic. Costal cartilage is easy to cut through. The diaphragm on the right-hand side in at the height of the fifth intercostal space; on the left side it is folded down and goes far into the peritoneal cavity. Its lower pole there is lower than the pelvic ridge. During the pneumothorax test nearly 3000 ccm of a yellowish-brown, ropy fluid was taken from the left pleural cavity. The entire mediastinum is displaced to the right. The heart is hanging drop-shaped in the mediastinum; its left edge is situated in the center line of the body. The right lung, with the exception of minor rope-shaped concretions, is free in the pleural cavity. In the pleura costalis are four palm-sized, solid, white, sinewy plates with occasional bulbous, solid, white nodules. A big radiate scar is seen in the pleura of the right upper lobe of the

lung. On the pleura of the right lung one recognizes a fine, moderately tenacious, grey, felt-like coating. The right lung itself is of appropriate size and of medium air and fluid content. The pleura and scision show a moderately strong, black, net-shaped marking. The lung tissue, moreover, is a red color. Focal diseases are not to be seen. In the lower lobe branch of the right pulmonary artery a small brown-red blood plug is clinging to the intima. The pulmonary arteries are empty. The left pleura is in its full extension thick-skinned (like rind). On the inner surface one finds a number of closely-massed bulbs, ranging in size up to that of a walnut, with a mulberry-like surface which consists of a jelly-like tumorous tissue, white on the side cut. When cut, this tissue secretes a ropy fluid. Beside the tumor tissue, one can see some sinewy plates as on the right. The tumor tissue does not penetrate the base any deeper, and most of all, does not penetrate the lung tissue. Only in the region of the above-mentioned skin nodes on the left side of the chest does one find tumor nodes in the rib musculature. The left lung is strongly atelectatic and is attached to the chest wall only by a rope-shaped concretion. The lung tissue is of a tough-firm consistency, grey-reddish color and shows on scision and surface a black, net-like marking which is somewhat thicker than that on the right side. There is no tumor anywhere in the lung tissue itself. Trachea, bronchia of both lungs are of appropriate width and are thin-walled. Tumor itself is nowhere provable. Hilus lymph nodes on both sides are black in color and of soft consistency. The heart is hardly as large as the corpse's fist. Pericardia smooth and shiny. Subepicardial fatty tissue is present in moderate abundance. The left ventricle is small, the right one a bit

enlarged. The wall of the left one is 5 mm, that of the right one 2 to 3 mm thick. All heart valves delicate and capable of closing. Coronary arteries of medium width and thin-walled. The myocardium is evenly brown-red in all cuts. Over its full length, the aorta is delicate and elastic.

Microscopic findings:

Right lung. In places the lung structure shows minor emphysematous changes. Nodule-shaped deposits of a fine-grained black pigment are found in several places in the peribronchial tissue. In this region, the peribronchial tissue shows a distinct hyalin transformation and fibrosis. Yet beside the deposits of the anthracotic pigment, one also sees partly fresh, and also partly degrading, typical asbestosis corpuscles. These are always found together in larger quantities with the anthracosis pigment. However, they are also found independent, lying alone in the lung alveoli and in the interstitial tissue. Likewise, there are abundant coal dust deposits and asbestos particles found under the pleura. The large bronchia contain pasty mucus and partly-sloughed epithelium. The bronchioles are often enlarged, but they are coated with a single-layered ciliated epithelium. Epithelial metaplasis are nowhere provable. The lung tissue immediately under the pleura shows a slight collapse of the alveoli. Here the alveolar epithelium shows often a glandular, but nowhere atypical character. Other than that, nowhere pneumonic changes in the lung tissue.

Left lung. The tissue of the left lung reveals collapse induration with desquamative alveolar catarrh and fibrosis of the interstices. In the peribronchial tissue--just as on the right--there are

plenty of anthracosis deposits with a hyalinosis of the surrounding tissue. More abundantly than on the right side, one finds in this lung typical asbestosis corpuscles, and in fact in both synthesis and disintegration. Much less frequently one also comes across free asbestos needles. The coating of these particles gives (in typical fashion) a positive reaction to iron. In the left lung one finds further widespread bleeding and the resulting necrosis of tissue. These are nearly all of more recent date, as demarcations are completely absent. Asbestosis corpuscles are found everywhere in these necrotic areas and are easily seen in the necroses of the remaining tissue as well. In this lung there are also the same changes in the bronchia that are in the right one. There is also no sign of epithelial metaplasis in this lung.

Diagnosis: Numerous asbestosis corpuscles in both lungs with little localized fibrosis (limited asbestosis of the lungs). Compression atelektasis and collapse induration of the left lung. Bleeding necrosis and limited bronchopneumonia in the left lung.

Pleural tumor on the left side. The tumor changes in its structure. In some spots one finds solid cones and cords surrounded by signs of myxomatous connective tissue with delicate fibers. Nearly all tumor cells have large mucous vacuoles; one sees numerous signet ring shapes. There are isolated cells with burst vacuoles, where the mucous has oozed out into the surrounding connective tissue. On other places the tumor appears to contain closely-packed cavities, which are covered with a smooth single layer epithelium. Also these epithelial cells contain a lot of mucous and have rearranged themselves in a signet ring form. But also in the interstices one finds well-distributed mucous-producing tumor cells

throughout. In only a few places does one find solid epithelial formations without mucous formation in the manner of a carcinoma solidum. The tumor is everywhere in the pleura parietalis and visceralis on the left side and in places is slightly grown into the subpleural layers of lung tissue. The tumor is found particularly in the septa and in isolated spots in the lymph tract.

Diagnosis: Primary muciferous lymph cell carcinoma of the pleura, predominantly of adenomatos character.

The questionable glassy nodules from the abdominal side of the left subphrenic space and from the serosa of the small pelvis, seen microscopically, are metastases of the same structure of the primary tumor.

At this point one comes to the end of those cases of lung and pleural cancer with asbestosis which to this point have been observed and publicized in the world literature.

To date, only Nordmann and Sorge have undertaken the attempt to explore the connection between lung cancer and inhalation of asbestos dust--experimentally, on white mice. They took 150 mice for their purposes and exposed them to dust for between one and one-half and three months, comparable to the average human life- and workspans. Over half of the animals died before the end of the experiment. None survived the inhalation by longer than nine months. Twenty percent of the surviving animals demonstrated a horny, multicentric plate epithelial carcinoma and 42-57% showed epithelial changes of various stages. This is thought to support the causal role of asbestos dust in primary lung carcinoma of asbestos workers. The number of the animals which were run through the

experiments and out of which the above statistics were calculated is very small. Only two animals had new growths which were believed to be cancer. The authors themselves pointed out the difficulty of separating out simple metaplases. It remains for an experienced morphologist and expert to decide how far the conclusions of the experimenters are valid and how far the rules for uniformity and usability of the animal subjects were followed and to what extend spontaneous tumors in the area in question must be drawn into consideration. Nordmann and Sorge dealt with these issues in a brief fashion.

It is striking to note that similar results have not been obtained in subsequent experiments with animals exposed to asbestos dust. There were also no similar observations made during autopsies performed on the various animals (dogs, rats) that used to live in asbestos factories.

If one wishes to speak in terms of an occupational cancer in a certain group of workers, one must first establish statistical proof that the particular cancer occurs in that group with greater frequency than in other occupational and population groups. In this process it will be difficult to satisfy the requirement that the figures for comparison come from a group of nearly comparable age makeup. The statistical procedure in the area of asbestosis presents yet another unmistakable difficulty. This rare disease occurs in small absolute numbers, and therefore a single coincidental occurrence can create huge percentage shifts. Furthermore, one must agree with Nordmann that particularly in recent years the turnover of workers in asbestos factories will negatively influence the results, since the cancer occurs only after a long dust exposure, and perhaps a longer dust-free interval. Today, only a few workers are

staying that long in the dangerous plants. Furthermore, the fight against dust most desirably counteracts the dust damage to the lung. Nevertheless, concerning severe asbestoses, today we are still dealing mostly with workers who have carried their dust damage over from earlier times when work conditions were considerably less favorable.

As a second matter, important for the question of a link between cancer and asbestosis, one ought to elucidate what special conditions were encountered with regard to dust damage and the findings at the area of the disease which make the cancer intelligible and distinguish it from other lung cancers.

As keystone of the proof, laboratory experiments ought to document that the cancer can be induced in animals.

Let us first turn to the statistical method. Here we can use as really reliable only the autopsies with a detailed anatomical examination of the lung because error is possible with purely clinical diagnoses. Furthermore, there are no purely clinical works available concerning this question.

Thirty asbestos workers have hitherto been dissected in Germany. The accompanying table No. 1 (p. 197) shows the cases according to age, sex, length of work, stage of asbestosis and cause of death--the latter in cases where the cause was something other than asbestosis, the cardiac insufficiency caused by it, or anagonal pneumonia. The first eighteen deaths have already been published. I have collected the remaining twelve. We can disregard the young girl listed as No. 29, since she had only a short exposure to dust and, anatomically, had not yet developed asbestosis. Of the remaining twenty-nine dissected, four had

bronchial cancer and two others a malignant pleura tumor. From, this data, one sees that approximately 20% of those asbestosis sufferers dissected showed malignant tumors of the lung. Other malignant growths were found a total of only three times, one each of the stomach, the esophagus and the prostate. Even if lung cancer has statistically increased considerably in the past three decades, it is still far outstripped by the cancers of the digestive tract, according to major autopsy statistics. Otherwise, depending on the different authors, its frequency puts it in the fourth to second place in the statistics of organ cancers. In Germany lung cancer with asbestosis is far in the foreground, as the above figures demonstrate. The average age of the lung tumor vector at the time of death is also considerably lower than that of vestors of other carcinomata (approximately 51 to 66 years).

Yet, to be sure, the small numbers do not at this time allow any particular conclusions. According to a breakdown by sex, for every four men there are two women with lung tumors. Otherwise, as for the proportion of sexes concerning lung cancers among men and women, the ratio of 3-4:1 is indicated. As to sex, the ratio of asbestos workers diseased with lung cancer also naturally depends on the number of women and men working in the plants. In Germany the former far outnumber the latter. With regard to the two above-mentioned women, the relatively young ages of 35 to 40 years at time of death is striking. All cancer vectors had a marked to severe asbestosis. Only the man with the pleura carcinoma (No. 20) had a moderate asbestosis with a very long, yet probably only slight, dust exposure. Nordmann has pointed out that a longer dust exposure is a contributing factor in all cases. According to the table

above, this applies without exception to all cancer vectors. The time period of exposure is seven years (two cases), ten years (two cases) and once each 18 and 42 years. The dust-free interval prior to diagnosable cancer, and during which the asbestos dust-depot continues to work away, varied in length from six months to twelve years. In one case it was not precisely known (No. 30 in the table).

These figures show unequivocally that lung cancer is the most frequent complication with asbestosis, if one disregards agonal pneumonia and cardiac unsufficiency. Even tuberculosis, whose frequency usually far surpasses that of cancer, in this case trails that of lung cancer. This is decisive proof of a closer connection between asbestosis and lung cancer. It is amazing that today's percentages from the larger volume of cases match exactly the figures which Nordmann had earlier reached from a smaller observed sample.

As of now the situation abroad, relating to this matter, is as follows:

The British are the most experienced in this field. However, it is impossible to separate out individual observations from the mass of English medical literature, and to discuss them as has been done above, because the individual cases are sometimes published several times, making it impossible to separate them. One has to be content, for the time being, with Gloyne's figures. In fifty dissections of asbestosis cases (according to Baader) he came across six cases of lung cancer (probably including one pleura tumor). From this follows a lung cancer with asbestosis frequency of 12%.

The figures reported from the USA are similar. From there I collected thirteen autopsy cases from medical literature in 1939. This figure may not be quite complete since some reports were not accessible to me. Among these dissected asbestoses I encountered two bronchial cancers, which were mentioned above. This would correspond to a percentage of approximately 15%. Other organ cancers were not specified there. Pneumonia has been reported relatively often (four times) as cause of death.

Oddly, there are no reports at all from France that are pertinent to our discussion. Similarly, very little has been published in other countries. In Italy, where asbestosis is very well known, no case of lunch cancer has been seen to date (Vigliani, etc.).

Thus in the medical world literature, to this point we see fourteen malignant lung-pleura tumors of epithelial origin which derived from 92 autopsies. This translates to approximately 16% cancer cases with dissected asbestosis. Of these fourteen only eleven have been described in particulars to the extent that additional statistical results can be derived from them (see table No. 2).

As to sex proportion, the result is seven (men) to four (women). The ages are from 35 to 71 years. Of these, four are in the relatively young age range of 35 to 41 years.

The time span from the start of work to the development of cancer is always comparatively long (from 12 to 42 years). After a short time of dust exposure, there usually comes a longer, dust-free interval, which seems to prove that the effect of the dust leads only very gradually--or at all--to the development of a cancer.

The majority of the afflicted patients suffered from very severe asbestosis, although it was not necessarily in that form. There were nine times lung and twice pleura tumors present. All lung cancers--as far as this can be determined after the fact--seem to have originated from a bronchial epithelium. Observations indicative of an alveolar cancer were not found.

According to histological character, horny plate epithelium carcinomata predominate. Of eight histologically more closely denoted lung cancers, five were horny plate epitheliums, a further plate epithelium cancer was not horny. Another cancer belonged to the group of undifferentiated tumors, and the last one was acinous.

The three pleura tumors were described as "pseudo-alveolar mesothelioma" as "adenomatous pleura carcinoma" and as "squamous carcinoma."

Four of the lung tumors--in a narrower sense--had no metastases established.

The localization of primary lung cancers took place seven times on lower lobes, where asbestosis is always most strongly developed. Four times the tumor was located in the left lower lobe and three times in the right one. In contrast, the right middle and upper lobe are represented but once each with a tumor.

This conformity of tumor localization with the strongest asbestosic tissue changes in the lower parts of the lungs is striking.

The abundance of lung cancer in dissected asbestosis vectors is the first clear evidence of a closer causal connection of these two diseases. The percentage of 16% lung and pleura cancers far exceeds the

frequency that would otherwise be expected statistically from other autopsies. Although the frequency of lung cancer has certainly increased considerably in the past decades, it does not amount to more than two to six percent on the average, according to general autopsy statistics. If the absolute figures for the asbestosis--as we were able to show--are still quite small, they nevertheless appear convincing insofar as they were found with approximately equal frequency in entirely different places (Germany, England, USA).

To these purely arithmetical relationships, one may add additional aspects drawn from conclusions, to which Nordmann already referred, based on smaller figures.

At first, we mention here the age of the cancer vectors. Four of them were still at the relatively young age of 35 to 41 years. Although lung cancer does occur in juveniles, it is found most frequently between the ages of 50 and 60 years. According to our material, 6 patients belong to this age group.

The distribution by sex, as in comparison with other numerical proportions, has here shifted in disfavor of the women. Among eleven cases, we encounter four women. General statistics usually show a ratio for lung cancer of 3-4:1 of men to women. Yet, one must keep in mind that in Germany and England women employees outnumber the men in asbestos plants, in contrast to the USA.

As was mentioned above, the frequent conformity between the location of the tumor and the severest asbestosic changes in the lower parts of the lungs seems to be very noteworthy.

Furthermore, the histological character of the lung tumors is striking. The mostly horny plate epithelium carcinoma is numerically predominant. We counted six of them among eight more closely denoted bronchial cancers alone. The usual proportion of various forms of tumors in lung cancer has been radically shifted in favor of the plate epithelium carcinoma. When one divides lung cancers histologically into three major groups--(a) undifferentiated cells, and (b) plate and (c) cylinder epithelium carcinomata--the former account for approximately 2/3 of all cases in the general statistical records. Since the plate epithelial cancers are the least inclined to metastasize, it may be understandable that in four of the above-mentioned cases no metastases were found. It is precisely the histological nature of lung cancer, with the predominance of plate epithelium cancers, which accounts for its independent status among lung cancers.

Cancer was always observed only after a relatively long period of dust influence. It may be that the time of working in the asbestos dust was very long or that after a short work time (usually with considerable exposure), there was a long interval during which the dust damage could further take effect. A series of irreproachable observations, some made by this author himself, teach us that with asbestosis the dust damage often appears precisely during such an interval and leads to an increasing fibrosis. Among all cases of lung cancer with asbestosis, not one single one is found where there was not this long period of asbestos dust influence. This is certainly consistent with experiences with other occupational cancers.

The other histological findings in the asbestos lung make a further understanding of the above connections possible. In the asbestos dust lung one mostly finds extended epithelium metaplasia at the minor bronchia which can be seen as pre-cancerous stages. The carcinomatous new formations most probably emerge in the main from them. In one case, Nordmann even made the observation that with a large carcinoma of the left lower lobe an emerging small cancer occurred on the other side which had to be regarded not as a metastasis, but as a cancer autochthonously springing from the metaplastic bronchial epithelium. He, therefore, regards the multiocular cancer origin with asbestosis as especially characteristic. Here we see parallels to Schneeberger lung cancer.

It appears that besides these metaplases, other histological changes in the lung also have a part in the cancer origin. In the first place, they have in common a strongly increased growth tendency. Here, the abundant epithelium desquamations are to be mentioned, along with changes in the shape of the cover cells, the formation of numerous macrophagia and foreign body-giant cells as well as the connective tissue proliferation. As a result (as noted by Linzbach), the individual tissues are disengaged from their normal relations without such a considerable damage to the tissue as to incur cell destruction. In this increased growth tendency and disturbance of the normal tissular relations, one can most probably see contributing forces for cancer origin.

These observations also apply to the pleura tumors. The pulmonary pleura is included in these rebuilding processes. There one finds epithelium desquamations, fibroid formation, development of

connective tissue, callosity and the depositing of asbestos crystals and asbestos particles (Gloyne, et al.)

All the above-mentioned observations agree with the conclusions of statistical studies and support the arguments for a close connection between asbestosis and lung cancer.

In addition to the increased number of cancer vectors with asbestosis, one must await further support in the nature of reproducible animal studies. One cannot yet regard this conclusion as definitively proved. However, it is not that experiments have yielded contrary results, but rather that the matter has not yet been looked into on a large scale. The first experiments by Nordmann and Sorge reached strikingly similar results. We have already discussed it above. Out of caution, however, one will have to wait for further confirmations by other experts and acknowledgment of these complicated relationships.

At any rate, all hitherto known facts indicate with great likelihood that Nordmann's opinion of the occupational cancer of asbestos workers is justified. The other authors, such as Gloyne, Lynch and Smith, Egbert and Geiger, as well as Linzbach, evidence the tendency to divine here a closer causal connection. The attempt to refute this assumption has, as of now, not been undertaken by anyone.

If we now consider where to look for carcinogenic effects of asbestos dust, we have to separate the general and particular disposing factors. It is generally assumed that where a cancer has occurred, a disposition toward cancer was present. It is hard to say, though, where such a disposition could be found. From general human and experimental pathology, it is known that the tendency to cancer depends on factors of

disposition. This expresses itself in such a manner that under the same experimental conditions and with nearly equal exposure to carcinogens, only a fraction of those persons exposed actually develops cancer. The experiential data available to us regarding asbestosis does not allow a sufficient analysis of familial disposition to cancer.

We cannot say to what extent and in what manner asbestos dust damage is creating such a general disposition to cancer. Its assumption remains a hypothesis. Yet, it does not seem that this general disposition is so strongly effective that it could encourage cancer growth in other organs. The data presented do not suggest that. Of decisive importance seems to be, most of all, the localized change. Its morphological expression in the altered lung tissue reactions was more closely discussed above. As the cause of same, one must first consider chemical and mechanical factors. Since asbestos can be simply defined chemically, the conditions here are moderately surveyable. One can indeed say from the outset that substances from the group of the known carcinogenic agents are out of the question. The influence of asbestos dust on the lung is probably carried out by means of chemical and mechanical damage. We seek the chemical effect in silicic acid which ought to be separable from the more vulnerable serpentine asbestos. According to human pathology and abundant animal experiments, it is very improbable that silicic acid could have a carcinogenic effect, and this has been very nearly refuted. Yet one must keep in mind that the conditions are much different in the tissue changes in cases of asbestosis as compared to those present in cases of silicosis. This dissimilar arrangement and shape of new tissue formation could unleash different biological modes of reaction in the tissue. But

beyond that, one will have to consider the mechanical effects of the many pointed asbestos needles and particles which are particularly characteristic of hornblende asbestos, which is stiff and insoluble. The needles and particles are very significant, given the peculiar tissue reaction caused by their constant mechanical irritation.

Finally, one must remember that severe asbestosis inflammations (partly with formations of bronchiectases) occur at the bronchia--inflamations which, for their part, may promote the formation of cancer.

According to the current state of knowledge, we must look to asbestosis for the explanation of the origin of cancer. Many of the types of damage, by their own terms, do not exceed the effect of chronic irritation. Having said that, we are still very far from having a full understanding of the more complex relationships here--a problem common to both asbestosis and cancer origin.

Let us now turn to the clinical diagnosis of cancer in the asbestos lung:

Fundamentally, all the usual diagnostic tools can be used here that are normally used in the detection of cancer in the lungs and pleura. However, since in these cases cancer is based upon a foundational illness, we must reckon with certain peculiarities of the presentation and must master certain information of the symptomatology of asbestosis.

When taking the patient's medical history, it is important to record an exact listing of work experience and to remember that lung cancer presents itself first after yearlong exposure to dust, and that the duration of the exposure may be counterbalanced to an extent by the

severity of the exposure. We know of only one observation where the dust exposure lasted only one and one-half years; otherwise, the exposure time was seven years or more. However, where there is a short, intensive dust exposure, a long dust-free interval seems to be necessary to the development of cancer. To date, there has been no recorded case in which the time between the beginning of the dust-exposed work and the provable existence of cancer was less than twelve years. One will also typically expect that cancer will appear only in cases where there is pronounced asbestosis (if not necessarily the more severe forms of that disease). The above-discussed examples support this.

The first symptoms of a developing lung cancer (which does not offer anything characteristic or pathognomonic) will not be as pronounced as they would be in a previously healthy person, since shortness of breath, coughing, sputum and a certain uneasiness in the chest cavity of asbestosis sufferers are already typical complaints. Also, a certain general decline (which may not even appear at first with lung cancer)--loss of weight and appetite--are very common occurrences in severe forms of asbestosis. Even acute decline in a patient's general well-being, including localized lung complaints, occurs often as a result of infections, which are more difficult for the asbestosis sufferer to overcome than for a healthy person. In general, one will find that the process of asbestosis creates a general worsening of the patient over the years, even decades. If, in the course of this development, there are suddenly episodes of notable localized and general worsening of condition, one must consider, among other things, the possibility of cancer. Next to cancer, the other most common conditions are infections with bronchitis,

pneumonia or abscess. In our experience, the complication of tuberculosis plays only a very minor role and is often erroneously diagnosed. Of course, tuberculosis is always within the realm of possibility. Nothing is known of possible accompanying pulmonary syphilis or fungal infections.

As for general symptoms, sudden weight loss is indicative, but not definitive. The same is true, as mentioned, for loss of appetite, poor coloring in the face, and night sweats. If these symptoms are due solely to the progress of asbestosis, they will typically be accompanied by an increased shortage of breath, cyanosis, clubbed fingers, and other lung complaints--but one must recall that a lung tumor may also cause the increase of such symptoms. All in all, the situation cannot be clarified solely from the case history.

The situation is similar for most other localized complaints. Since severe asbestosis usually causes considerable coughing, this symptom is of little diagnostic use. The same is true for shortness of breath. To me, the appearance of the sputum is of greater importance.

With uncomplicated asbestosis, it is mostly scant, tough and mucous; in cases of bronchitis and bronchiectases, it is more ample and purulent. Blood is very rare. Frequent blood in the sputum, even if scant, requires a special explanation. I, personally, have seen blood in the sputum in form of the raspberry-colored sputum only once with a complicating lung tumor. There are only isolated, scant statements of this sort existing in medical literature. Tumor cells in the sputum ought to be very rare. Hornig claims to have seen abundant epithelium cells in the sputum in his case of tumor with asbestosis. If a disintegration of the lung tissue sets in, it will be easily recognizable by the change in

the sputum. This was very impressive in the case of my observation. The patient suddenly brought up large amounts of granular agglomerated necrotic masses. Perhaps it would be possible to find on one of such occasions the symptom noted by the British, namely the "asbestos bodies in clumps." It is a question of rosette-shaped piles of asbestos particles which may appear in the sputum when lung tissue disintegrates (through abscess, tuberculosis, tumor). Diagnostically, they are equivalent to the elastic fibers in the sputum. The significance of the shortness of breath has already been discussed above. It cannot be attributed to cancer until there is a great expansion of the tumor, bronchial occlusion or the like. On the other hand, it seems to me that chest pains are of greater significance. With asbestosis alone, they are usually trifling and undefined. In our case, they came fully to the fore with the advancing of the tumor; they took on a typical neuralgiform character. There are similar references in the medical literature. The cause of the pains can probably be attributed to the spreading of the tumor to the parietal pleura and, eventually, to the intercostal nerves, and perhaps even to metastases.

These references to the general and local complaints, which can be mostly deduced from the previous history, will suffice.

As to the other objective findings, the following may be noted: Asbestosis attacks both sides of the lungs. Strongly unilateral processes (as are present in most tumor cases) do not occur. Usually, there is also an extensive symmetry of the changes. One must know, however, that the right side of the lung can also normally be assailed more strongly by fibrosis. We never find any grosser dullness over the

upper lung region. The sound of respiration is here mostly harsh, only seldom muted. The dependent lung parts present mostly a moderate to medium strong weakening of sound which is, if not fully symmetrical, so almost always bilateral. Only thicker callosities or specific and unspecific complications can account for exceptions. The sound of respiration is weaker at the bottom than at the top. Secondary murmurs are more numerous and more frequent at the bottom than at the top; differences between the sides matter little. If unilateral unequivocal signs of an atelectasis are found, this is extremely indicative of a tumor. Yet, of course, this symptom of lung tumor is not obligatory. Effusions, especially those of a hemorrhagic nature, for all practical purposes do not occur with common asbestosis.

The tumor can have signs of liquefaction in common with the abscess and the tuberculosis. Bronchiectases in form of cylindrical dilations of the trachea are not rare in cases of severe asbestosis. Occasionally, they are difficult to clinically distinguish from liquefactions.

Grosser asymmetries of the thorax, distortions of the pleura organs and diaphragm must be independently explained.

The X-ray finding may be the most important method of examination in the diagnosis of a tumor. In this connection, one must consider that contrary to what one might conclude from the literature, severe asbestosis does not always lead only to fine symmetrical concretions of the lung tissue. In addition to certain asymmetries, there also appear flattened localized areas of cloudiness in the lower fields, particularly in the medial aspects. These thicker shadows are, however,

not usually so compact and tumorlike and, inside, are more striated in marking and less sharply contrasted than a tumor. Hard photographs or tomograms will show the bronchial system open, even expanded. Inflammation-caused bronchostenosis have not been seen in cases of asbestosis to date. Compact, unilateral, localized shadows in the lung, possibly with bronchial occlusion, are typically proof of a tumor. So are displacements of the mediastinum (either constant or changing with breathing), paralysis of the diaphragm, or Horner's Syndrome. Localized thickening in the higher levels is never characteristic of asbestosis. Here, the conditions are must clearer and simpler than is the case with silicosis. Large shadows in cases of asbestosis are otherwise usually created by unspecific inflammations. Tuberculosis is nowhere near as common as is generally thought. Its first appearance in the lower fields is very rare, according to the observations to date. In the interest of completeness, it should be added that tomo- and bronchography can be of great assistance in the detection of lung tumors and as for them, the usual rules of interpretation apply. This is also the case for bronchoscopy. There is no experience with diagnostic lung punctures except for a few attempts in which asbestos particles were found in lung fluid. In cases of pleural tumors or metastases, the presence of tumor cells in the punctate may clarify the situation tremendously. This was the case in Alwens' observation.

Metastases always hasten the diagnosis.

The fact that tumors of long duration may cause fever is unimportant for the diagnosis, since infections may have the same results.

On the subject of hemograms and the acceleration of erythrocyte sedimentation, one must note that anemia is not part of asbestosis; rather, there have been cases of high pigment and cell counts as compensation phenomena. Accompanying infections may cause exceptions. In the absence of the numerous other possible causes, increasing anemia may be an indication of the presence of a tumor. One cannot expect help from a hemogram in the diagnosis of a tumor. In uncomplicated asbestosis, sedimentation is not accelerated. However, in serial tests on numerous asbestosis sufferers, one often finds that the sedimentation rate is modestly elevated, probably due to increased infections in the bronchial system. Strong and increasing acceleration of sedimentation is always to be noted and should be evaluated according to the usual clinical rules.

This concludes the most important clinical aspects for the diagnosis of a lung tumor with asbestosis. The correct interpretation is always the product of a careful clinical view of the whole and critical consideration of the individual signs. In this connection, it is important to know the general outline of the asbestosis syndrome and to be aware of the possibility of complication with a tumor, which appears to occur almost as frequently in the asbestosis lung as does tuberculosis. In Germany, to date only ten cases of active tuberculosis with asbestosis have been diagnosed, as against six cases with tumors.

If the occurrence of cancer in the asbestosis lung is as common as indicated above, and if there are other good reasons to believe that a closer causal connection exists between the two diseases, then even without taking animal experiments into consideration, one must today conclude that insurance protection should be extended to cover this

complication. In the few compensation cases decided to date, the employers' liability insurance associations have already recognized the connection, based on the unanimous opinions of the experts questioned. In the documents which I have examined on the subject, no medical expert[2] in Germany has taken a contrary stand.

SUMMARY

This has been a report on the hitherto known and expanded case reports appearing in world medical literature relating to malignant lung and pleural tumors in cases of asbestosis. The reasons that suggest a causal connection between the two illnesses have been set forth. The clinical picture of lung tumors in asbestosis was discussed and the extension of insurance protection to this complication was found to be appropriate.

LITERATURE

[Not translated.][3]

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2 May also mean "expert" as in "expert witness." See fn. 1, supra. [Translator's Note.]

3 Footnote 1 to the "Literature" section reads, "The original work was not available to the author." [Translator's Note.]

TABLE 1

The column headings are as follows:

a. Reference Number

b. Age, Sex

c. Years of Dust Exposure at Work

d. Dust-Free Interval (Years)

e. Stage of Asbestosis

f. Cause of Death

g. Publicized By

Text Omitted as Self-Explanatory Except As Below:

Ref. No.	Cause of Death
13	Stomach cancer
14	Bronchial cancer
15	Bronchial cancer
16	Lung abcess, empyem
17	Bronchial cancer
18	Bronchial cancer
19	Esophageal cancer
20	Pleural cancer
25	Prostate cancer
26	Lung abcess, amyloidosis
27	Kidney failure
28	Pulmonary tuberculosis
29	Pulmonary tuberculosis
30	Pleural tumor

TABLE 2

The column headings are as follows:

a. Reference Number

b. Age, Sex

c. Years of Dust Exposure

d. Dust-Free Interval (Years)

e. Stage of Asbestosis

f. Type of Tumor

g. Site of Tumor

h. Metastases

i. Author

Text of columns (a) through (e) omitted as self-explanatory:

Ref. No.	Type of Tumor	Site	Metastases	Author
1	horny plate epithelial carcinoma	right upper lobe	none	Gloyne
2	Same	right lower lobe	none	Gloyne
3	plate epithelial carcinoma	same	none	Lynch & Smith
4	acinous cancer	left lower lobe	widespread	Egbert & Geiger
5	horny plate epithelial carcinoma	same	liver, kidney	Nordmann
6	same	same	widespread also small cancer in right lower lobe	Nordmann

TABLE 2, cont'd

Ref. No.	Type of Tumor	Site	Metastases	Author
7	?	right middle lobe	yes	Bohne/ Wedler
8	horny plate epithelial carcinoma	right lower lobe	none	Wedler/ Linzbach
9	pseudoalveolar mesothelioma	right pleura	peritoneum	Teutschlaende
10	adenomatous pleura carcinoma	left pleura	widespread	Alwens-Fischer-Wasels
11	dedifferentiated carcinoma	left lower lobe	?	Gloyne

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[Aus der Ludolf Krehl-Klinik Heidelberg (Medizinische Universitätsklinik).
Direktor: Professor Dr. R. Siebeck.]

Über den Lungenkrebs bei Asbestose.

Von
Dozent Dr. H. W. Wedler,
Oberarzt der Klinik.

(Eingegangen am 20. März 1943.)

In den letzten 12—15 Jahren ist im deutschen und ausländischen Schrifttum eine so umfangreiche Erfahrung über die Asbestose niedergelegt worden, daß wir die Gefährdung der Asbestarbeiter und das klinische Krankheitsbild ihrer Berufskrankheit sowie deren Verlauf weitgehend kennen. Immerhin stehen bezüglich ihrer Pathogenese noch eine Reihe von Fragen offen, die vor allem von tierexperimenteller und chemisch-physikalischer Bearbeitung her weitere Aufklärungen erwarten lassen. Auf weniger breiter und gesicherter Grundlage sind dagegen unsere Kenntnisse von ihren Komplikationen und Begleitkrankheiten aufgebaut. Hier konnte in jüngster Zeit vom Verfasser ein umfangreicher Beitrag zum Verhalten der Lungentuberkulose bei dieser Koniose geliefert werden. Ebenso aufschlußreich wie wichtig ist die Frage nach den Beziehungen zum Lungenkrebs, auf dessen Häufung bei Asbestose in den letzten Jahren wiederholt aufmerksam gemacht wurde. Das Interesse hieran liegt nicht nur auf sozialmedizinischem und versicherungsrechtlichem Gebiet, sondern greift darüber weit ins Allgemeinmedizinische hinaus, weil damit ein neues Beispiel einer exogenen Krebsentstehung beigebracht werden würde. Die Zahl der hierher gehörenden Beobachtungen ist zwar absolut gesehen klein, aber doch im Verhältnis zu der Seltenheit dieses Leidens so beachtlich, daß eine zusammenfassende Darstellung erlaubt erscheint. Sie ist auch deswegen erwünscht, weil bisher von klinischer Seite eine solche Arbeit im Schrifttum überhaupt noch nicht vorliegt.

Wir schicken zunächst eine Wiedergabe der bisher bekannt gewordenen Beobachtungen von Lungenkrebs bei Asbestose im Weltschrifttum voraus, schließen dann die neuesten Erfahrungen hierzu an und beleuchten die Besonderheiten dieses Krankheitsbildes sowie dessen klinische Diagnostik.

Die erste Erwähnung einer Krebsgeschwulst in der Asbeststaublunge treffen wir 1933 bei Gloyne in einer Arbeit, die sich mit der pathologischen Anatomie und Histologie der Asbestose beschäftigt. Er spricht dort von Komplikationen der Asbestose, die in ursächlichem Zusammenhang mit ihr stehen sollen (eitrige Bronchitis, Bronchopneumonie, Tuberkulose, Emphysem, Bronchiektasen) und von Begleitkrankheiten, die nach dem damaligen Stande des Wissens nichts mit der Staubeinwirkung zu tun hätten. Unter den letzteren erwähnt er eine Beobachtung.

Prozeß anmutete, aber als Tumor erkannt werden konnte, weil Metastasen im Becken und der Wirbelsäule vorhanden waren. Bei der Sektion wurde neben der Asbestose ein 5 : 5 : 4 cm messender acinöser Krebs im linken Lungenunterlappen festgestellt, der in den Lungen, den linksseitigen Hilus- und Aortendrüsen, in der rechten Nebenniere, der Bauchmuskulatur, dem Becken, der Wirbelsäule und dem Schädel Metastasen gesetzt hatte. Den Ausgangspunkt der Geschwulst bildete ein großer Nebenast des linken Unterlappenbronchus. Ein ätiologischer Zusammenhang zwischen beiden Erkrankungen schien ihnen sehr naheliegend: „That the irritating effects of the inhaled asbestos particles may in this case have been a significant factor concerned in the developement of the primary lung cancer seems sufficiently plausible to be worthy of consideration."

Gloyne konnte 1936 zu seinen 3 Beobachtungen eine weitere hinzufügen. Er fand ein entdifferenziertes Carcinom des linken Unterlappens bei einer Asbestose, dessen Träger 59 Jahre alt war und 21 Jahre im Asbestberuf gearbeitet hatte.

1938 machte Sparks ohne nähere Einzelheiten die Mitteilung, daß Gloyne bei seinen Sektionen 6 Fälle von Lungenkrebs bei Asbestose angetroffen habe. Baader erfuhr brieflich von Gloyne, daß sich diese 6 Krebse auf 50 Autopsien bezögen.

Nordmann erweiterte im gleichen Jahr unsere Kenntnisse um 2 neue Krebsfälle bei Asbestose, die er kurz hintereinander in Hannover sezieren konnte. Die erste Patientin war 35 Jahre alt. Sie hatte von ihrem 17.—26. Lebensjahr, genau 7 Jahre, in der Krempelei, Spinnerei und Weberei einer Asbestfabrik gearbeitet. 4—5 Jahre vor dem Tode bekam sie Husten und Atemnot. ¾ Jahr vor dem Tode trat sie unter dem Verdacht einer Tuberkulose in ärztliche Behandlung. Hornig stellte die Wahrscheinlichkeitsdiagnose auf Krebs im linken Unterlappen bei ausgeprägter Asbestose, weil klinisch die Zeichen einer Atelektase bestanden und tomographisch der Hauptbronchus verlegt war. Anatomisch handelte es sich um ein verhornendes Plattenepithelcarcinom mit walnußgroßer Zerfallshöhle, die Anschluß an den Unterlappenbronchus hatte, Pleuraverschwielung und Metastasen in Leber und Nieren.

Die zweite Beobachtung betraf einen 55jährigen Mann, der vom 36. bis 43. Lebensjahr in der Vorbereitung einer Asbestfabrik 7 Jahre tätig gewesen war. 13 Monate vor seinem Tode magerte er stark ab und bekam blutigen Auswurf. Er stand anfangs unter dem Verdacht einer Tuberkulose. Über der linken Lunge unten fand sich Dämpfung und abgeschwächtes Atmen. Röntgenologisch war das linke Unterfeld verschattet. Die behandelnden Ärzte diagnostizierten eine Asbestose mit Lungenkrebs. Die Sektion bestätigte dies. Der Krebs war im linken Unterlappen in Zusammenhang mit dem Hauptbronchus auf Walnußgröße zerfallen und hatte Beziehungen zum Herzbeutel, der linken Kammerwand, dem Zwerchfell, dem Peritoneum des linken Oberbauches, dem retroperitonealen Gewebe hinter der Milz, den dortigen Lymphknoten und der unteren Brust- und oberen Lendenwirbelsäule. Histologisch handelte es sich wieder um ein verhornendes Plattenepithelcarcinom. Auch im rechten Lungenunterlappen fand sich ein beginnendes Bronchialcarcinom.

Nordmann schloß an diese Beobachtungen eine eingehende Würdigung der Gesichtspunkte an, die ihm einen Berufskrebs zu beweisen schienen. Er sprach als erster klar von einem Berufskrebs der Asbestarbeiter.

1939 machte Wedler auf eine weitere Beobachtung in Deutschland aufmerksam, die von Bohne stammte, aber nicht mitgeteilt worden war. Der 58jährige Mann hatte von 1925—1935 10 Jahre zum Teil als Meister in einer Asbestfabrik gearbeitet. Wenige Jahre nach der Staubexposition bekam er schon Beschwerden von seiten der Atmungsorgane. 1928 war er 2 Monate verschickt. Später machte er öfter Heilstättenkuren, ohne daß Tuberkelbacillen bei ihm gefunden wurden. Wegen

Im Peritoneum bestand eine ausgedehnte Tumoraussaat mit Ascites. Der linke Pleuraraum enthielt einen Erguß von 50 ccm. Kompensatorisches Emphysem der linken Lunge. Die kachektische Frau starb an Kreislaufschwäche infolge der Lungenerkrankung.

Die zweite Beobachtung stammt von Alwens. Die Sektion nahm Fischer-Wasels vor. Ich kam als Gutachter mit dem Fall in Berührung. Der 60jährige Mann (13. 8. 81 bis 19. 9. 41) hatte bis $^1/_2$ Jahr vor dem Tode 42 Jahre in einer Asbestkautschukabteilung gearbeitet. Er erkrankte im Januar 1941 unter zunehmender Atemnot und Gewichtsabnahme mit den Zeichen eines linksseitigen Pleuraergusses. Absolute Dämpfung, aufgehobenes Atemgeräusch und Rechtsverdrängung des Herzens. Der Auswurf enthielt reichlich Asbestkörperchen. In dem mehrfach durch Punktion abgelassenen, gallertigen, rötlichen Erguß wurden reichlich Tumorzellen gefunden. Über der rechten Lunge unten waren vereinzelt feinblasige Rasselgeräusche zu hören. Die Blutsenkung stieg schnell an. Im Auswurf keine Tuberkelbacillen. Röntgenologisch wurde eine Asbestose mittleren Grades festgestellt und im rechten Hilus evtl. der Primärtumor vermutet. Die Sektion deckte eine leichte Asbestose mit einem diffusen primären schleimbildenden Drüsenzellcarcinom der linken Pleura von größtenteils adenomatösem Charakter und Metastasen an der Bauchseite der linken Zwerchfellkuppe, der Serosa des kleinen Beckens und der Brustmuskulatur links auf. Das Sektionsprotokoll der Brustkorborgane sei im einzelnen angeführt, da bisher darüber nicht berichtet wurde.

Brustsektion. Panniculus adiposus mäßig entwickelt. Thorax ist mäßig gewölbt und elastisch. Rippenknorpel sind gut zu durchschneiden. Das Zwerchfell steht rechts in Höhe des 5. Intercostalraumes; auf der linken Seite ist es nach unten umgeklappt und ragt weit in die Bauchhöhle hinein. Sein unterer Pol steht hier tiefer als der Beckenkamm. Bei der Pneumothoraxprobe entweichen aus der linken Pleurahöhle fast 3000 ccm einer gelblich-braunen, fadenziehenden Flüssigkeit. Das ganze Mediastinum ist nach rechts verdrängt. Das Herz hängt tropfenförmig im Mediastinum; seine linke Kante liegt in der Mittellinie. Die rechte Lunge ist bis auf geringe strangförmige Verwachsungen frei in der Pleurahöhle. In der Pleura costalis finden sich bis handflächengroße, derbe, weiße, sehnige Platten mit einzelnen knollenförmigen ebenso derben, weißen Knötchen. In der Pleura des rechten Lungenoberlappens sieht man eine große strahlige Narbe. Auf der Pleura der rechten Lunge erkennt man einen feinen, mäßig fest haftenden grauen filzigen Belag. Die rechte Lunge selbst ist von gehöriger Größe und mittlerem Luft- und Flüssigkeitsgehalt. Die Pleura und die Schnittfläche zeigen eine mäßig starke, schwarze, netzförmige Zeichnung. Im übrigen ist das Lungengewebe von roter Farbe. Herderkrankungen sind nicht nachzuweisen. Im Unterlappenast der rechten Lungenarterie haftet auf der Intima ein kleiner braunroter Blutpfropf. Die Lungenarterien sind leer. — Die linke Pleura ist in ganzer Ausdehnung schwartig verdickt. Auf der Innenfläche findet man massenhaft dicht beieinander stehende, bis walnußgroße Knollen mit maulbeerartiger Oberfläche, bestehend aus einem gallertigen — auf der Schnittfläche weißen — Geschwulstgewebe. Dieses sondert beim Durchschneiden eine fadenziehende Flüssigkeit ab. Neben dem Tumorgewebe sieht man ebenfalls einige sehnige Platten wie rechts. Das Geschwulstgewebe dringt an keiner Stelle tiefer in die Unterlage ein, vor allem nicht in das Lungengewebe. Nur im Bereich der eingangs erwähnten Hautknoten an der linken Brustseite findet man Geschwulstknoten in der Zwischenrippenmuskulatur. Die linke Lunge ist stark atelektatisch und nur mit einer strangförmigen Verwachsung an der Brustwand adhärent. Das Lungengewebe ist von zäh-fester Konsistenz, graurötlicher Farbe und zeigt auf Schnitt- und Oberfläche eine schwarze, netzartige Zeichnung, die etwas dichter ist als die der rechten Seite. Im Lungengewebe selbst nirgends Tumor. Trachea, Bronchien beider Lungen sind von gehöriger Weite und

übertreten. Aber auch im Interstitium findet man überall locker verstreut schleimbildende Geschwulstzellen. Nur an wenigen Stellen findet man solide Epithelformationen ohne Schleimbildung nach Art eines Carcinoma solidum. Die Geschwulst findet sich überall in der Pleura parietalis und visceralis links und ist stellenweise gering in die subpleuralen Schichten des Lungengewebes hineingewuchert. Hier findet man sie besonders in den Septen und vereinzelt auch in Lymphbahnen.

Diagnose: Primäres schleimbildendes Drüsenzellencarcinom der Pleura, größtenteils von adenomatösem Charakter.

Die fraglichen glasigen Knötchen von der Bauchseite der linken Zwerchfellkuppe und von der Serosa des kleinen Beckens erweisen sich mikroskopisch als Metastasen vom gleichen Bau wie der Primärtumor.

Damit sind die bisher beobachteten und in der Weltliteratur bekannt gewordenen Fälle von Lungen- und Brustfellkrebs bei Asbestose erschöpft.

Als einzige haben bisher Nordmann und Sorge den Versuch unternommen, tierexperimentell an weißen Mäusen die Zusammenhangsfrage zwischen Asbeststaubinhalation und Lungenkrebs zu bearbeiten. Sie setzten 150 Mäuse zu ihren Versuchen an und bestäubten sie entsprechend der durchschnittlichen Lebens- und Arbeitsdauer des Menschen zwischen $1^1/_2$ und 3 Monaten. Über die Hälfte der Tiere starb vorher. Keines überlebte die Inhalation länger als 9 Monate. 20% der überlebenden Tiere wiesen ein verhornendes multizentrisches Plattenepithelcarcinom und 42—57% epitheliale Neubildungen aller Stadien auf. Damit soll die ursächliche Bedeutung des Asbeststaubes für das primäre Lungencarcinom des Asbestarbeiters experimentell gestützt werden. Die Zahl der endgültig durch den Versuch gebrachten Tiere, aus denen die obigen Zahlen errechnet wurden, ist sehr klein. Nur 2 Tiere hatten Neubildungen, die als Krebs angesprochen wurden. Die Autoren wiesen selbst auf die Schwierigkeit der Abgrenzung von einfachen Metaplasien hin. Es muß einem erfahrenen Morphologen und Sachkenner überlassen bleiben zu entscheiden, wieweit die Schlüsse der Experimentatoren berechtigt sind und wieweit die erforderlichen Vorsichtsmaßregeln bezüglich Einheitlichkeit und Brauchbarkeit des Tiermaterials beobachtet wurden und wieweit in diesen Grenzen Spontantumoren in den Bereich der Erwägungen gezogen werden müssen. Nordmann und Sorge sind hierauf kurz eingegangen.

Auffällig ist, daß man sonst bisher bei den Tierexperimenten mit Asbeststaub, die allerdings unter anderen Gesichtspunkten angestellt wurden, offenbar ähnliche Beobachtungen nicht gemacht hat. Auch ist man bei verschiedenen Tiersektionen (Hunde, Ratten), die an Tieren vorgenommen wurden, die in Asbestfabriken lebten, auf solche Beobachtungen nicht gestoßen.

Wenn man von einem Berufskrebs in einer bestimmten Arbeitergruppe sprechen will, so wird man zunächst den statistischen Beweis erbringen müssen, daß der betreffende Krebs in größerer Häufigkeit als in anderen Berufs- und Bevölkerungsgruppen vorkommt, wobei die Forderung nach einer möglichst gleichartigen Alterszusammensetzung bei den Vergleichszahlen schwer zu erfüllen sein wird. Der statistische Weg hat auch für die Asbestose noch eine weitere unverkennbare Schwierigkeit. Es wird sich bei dieser an sich seltenen Krankheit immer nur um kleine absolute Zahlen handeln können. Eine einzige Beobachtung als Zufallsereignis kann dabei schon recht große prozentuale Verschiebungen herbeiführen. Weiter wird man mit Nordmann berücksichtigen müssen, daß besonders in den letzten Jahren der Arbeiterwechsel in den Asbestfabriken die Ergebnisse im negativen Sinne

Tabelle 1.

a	b	c	d	e	f	g
Lfd. Nr.	Alter, Geschlecht	Staub-arbeit Jahre	Freies Intervall Jahre	Stadium der Asbestose	Todesursache	Publiziert durch
1	35 J., ♀	?	?	III		Fahr 1914
2	47 J., ♂	26		III		Buresch/Loeschcke 1931
3	50 J., ♂	21		III		Beintker/di Biasi 1931/37
4	? ♂	20		III		Beintker/Path. Inst. Münster 1931
5	35 J., ♂	20		III		Stroebe/Beger 1933
6	31 J., ♀	8		II—III		Bohne 1936
7	54 J., ♀	11		III		Saupe/Letterer 1938
8	44 J., ♀	18		III		Saupe/Baniecki 1938
9	38 J., ♀	13		III		Wedler/Walkhoff 1939
10	45 J., ♂	15		III		Wedler 1939
11	63 J., ♂	12	6	III		Wedler/Koch 1939
12	69 J., ♀	10		III		Wedler 1939
13	61 J., ♂	10		II	Magen-Ca.	Wedler/Walkhoff 1939
14	35 J., ♀	7	9	II	Bronchial-Ca.	Nordmann 1938
15	55 J., ♀	7	12	III	Bronchial-Ca.	Nordmann 1938
16	38 J., ♀	12	7	III	Lungenabsceß, Empyem	Nordmann 1938
17	58 J., ♂	10	2	III	Bronchial-Ca.	Bohne/Wedler 1939
18	60 J., ♂	18	1	III	Bronchial-Ca.	Wedler/Linzbach 1940
19	70 J., ♂	16	1	III	Oesoph.-Ca.	di Biasi u. a.
20	60 J., ♂	42	½	I—II	Pleura-Ca.	Alwens/Fischer-Wasels
21	38 J., ♀	4	1	III		Bohne
22	54 J., ♂	27		III		Koopmann
23	59 J., ♀	4	6	III		Bohne
24	52 J., ♂	3,25	2	III		Holm u. a.
25	66 J., ♂	22	2	III	Prostata-Ca.	
26	42 J., ♀	6	10	I	Lungenabsceß, Amyloidose	Wedler/Poczka
27	50 J., ♀	12	2	III	Niereninsuff.	Wedler u. a.
28	35 J., ♂	5,5	6	I?	Lungentbk.	Wedler u. a.
29	18 J., ♀	1,75		0	Lungentbk.	di Biasi u. a.
30	40 J., ♀	10	?	III	Pleuragewächs	Teutschlaender

kleinen Zahlen erlauben allerdings hieraus zunächst noch keine besonderen Schlüsse. Nach der Geschlechtsverteilung kommen auf 4 Männer 2 Frauen mit Lungengewächsen. Für die Geschlechtsverteilung der Krebse der Lunge unter Männern und Frauen werden sonst Zahlen von 3—4 : 1 angegeben. Die Quote der lungenkrebskranken Asbestarbeiter nach dem Geschlecht ist natürlich auch abhängig von der Zahl der in den Betrieben arbeitenden Frauen und Männer. In Deutschland überwiegen die ersten bei weitem. Bei den beiden obengenannten Frauen

In der Weltliteratur übersehen wir also bisher 14 maligne Lungen-Rippenfellgewächse epithelialer Herkunft, die auf 92 Sektionen entfallen. Das sind rund 16% Krebsfälle bei sezierten Asbestosen.

Von diesen 14 sind zunächst nur 11 soweit in Einzelheiten beschrieben worden, daß aus ihnen noch weitere statistische Ergebnisse gewonnen werden können (s. Tabelle 2).

Tabelle 2.

Lfd. Nr.	Alter, Geschlecht	Staub exp. Jahre	Freies Intervall Jahre	Stadium der Asbestose	Art des Gewächses	Lokalisation	Metastasen	Autor
1	35 J., ♀	8	9	I—II	verhorntes Platten-epithel-Ca.	rechter Ober-lappen	keine	Gloyne
2	71 J., ♀	1,5	15	II	verhorntes Platten-epithel-Ca.	rechter Unter-lappen	keine	Gloyne
3	57 J., ♂	21		III	Platten-epithel-Ca.	rechter Unter-lappen	keine	Lynch und Smith
4	41 J., ♂	18		III	acinöses Ca.	linker Unter-lappen	ausgedehnte Metastasierung	Egbert und Geiger
5	35 J., ♀	7	9	II	verhorntes Platten-epithel-Ca.	linker Unter-lappen	Leber, Niere	Nordmann
6	55 J., ♂	7	12	II	verhorntes Platten-epithel-Ca.	linker Unter-lappen	ausgedehnte Metastasierung	Nordmann. Kleiner Krebs, auch im rechten Unterlappen
7	58 J., ♂	10	2	III	?	rechter Mittel-lappen	ja	Bohne/Wedler
8	60 J., ♂	18		III	verhorntes Platten-epithel-Ca.	rechter Unter-lappen	keine	Wedler, Linzbach
9	40 J., ♀	10	?	III	pseudo-alveoläres Meso-theliom	rechte Pleura	Peri-toneum	Teutschlaender
10	60 J., ♂	42	½	I—II	adenomatöses Pleura-Ca.	linke Pleura	ausgedehnte Metastasierung	Alwens-Fischer-Wasels
11	59 J., ♂	21	?		entdifferenziertes Ca.	linker Unter-lappen	?	Gloyne

sind, so wirken sie doch dadurch überzeugend, daß sie an ganz verschiedenen Orten mit ungefähr gleichmäßiger Häufigkeit gefunden wurden (Deutschland, England, USA.).

Diesen rein zahlenmäßigen Verhältnissen lassen sich nun aus obigen Ableitungen noch weitere positive Gesichtspunkte anfügen, auf die Nordmann allerdings an kleineren Zahlen zum Teil schon hingewiesen hat.

Wir nennen hier zunächst das Lebensalter der Krebsträger. Allein 4 von ihnen befanden sich noch in dem relativ jugendlichen Alter von 35—41 Jahren. Wenn auch der Lungenkrebs schon bei Jugendlichen vorkommt, so liegt seine größte Häufigkeit sonst doch erst zwischen dem 50.—60. Lebensjahr. Dieser Stufe gehören unter unserem Material 6 Kranke an.

Die Verteilung nach dem Geschlecht ist gegen die sonstigen Zahlenverhältnisse hier zuungunsten der Frauen verschoben. Unter 11 Fällen treffen wir 4 Frauen an. Für den Lungenkrebs geben die großen Statistiken sonst eine Verteilung der Geschlechter von 3—4 : 1 zwischen Männern und Frauen an. Immerhin wird man im Auge behalten müssen, daß besonders in Deutschland und England im Gegensatz zu USA. in den Asbestfabriken die Frauen als Arbeitnehmer zahlenmäßig die Männer übertreffen.

Sehr beachtlich erscheint die häufige Übereinstimmung des Sitzes der Geschwulst mit den schwersten Veränderungen der Asbestose in den Untergeschossen der Lunge, wie wir es oben ausführten.

Weiter ist der histologische Charakter der Lungengewächse auffällig. Das meist verhornende Plattenepithelcarcinom steht zahlenmäßig ganz im Vordergrund. Wir zählten unter 8 näher bezeichneten Bronchialkrebsen allein 6 solche. Das bei den Lungenkrebsen sonst übliche Zahlenverhältnis unter den einzelnen Gewächsformen ist hier ganz zugunsten des Plattenepithelkrebses durchbrochen und einseitig verschoben. Wenn man die Lungenkrebse histologisch in die 3 großen Gruppen der undifferenzierten Zellen, der Platten- und Zylinderepithelcarcinome einteilt, so stellen die ersteren in den großen Statistiken das Hauptkontingent mit rund $^2/_3$ aller Fälle. Da die Plattenepithelkrebse an wenigsten zu Metastasierung neigen, mag es verständlich erscheinen, daß bei den obigen Beobachtungen in 4 Fällen keine Metastasen gesehen wurden. Gerade die histologische Beschaffenheit der Lungenkrebse mit dem eindeutigen Überwiegen des Plattenepithelkrebses spricht für seine selbständige Stellung unter den Lungenkrebsen.

Der Krebs wurde immer erst nach einer relativ langen Einwirkungszeit des Staubes gesehen. Sei es, daß die Arbeitszeit im Asbeststaub sehr lange war, oder daß sich bei kurzer Arbeitszeit mit gewöhnlich beträchtlicher Exposition ein längeres Intervall einschob, in dem der Staubschaden sich weiter auswirken konnte. Eine Reihe einwandfreier

barkeit dieser Verhältnisse gefordert werden. Dieser Punkt kann für die Asbestose bisher noch nicht als gesichert angesehen werden. Das liegt aber nicht an negativ ausgefallenen Versuchen, sondern einfach daran, daß diese Frage in größerem Umfange noch nicht in Angriff genommen worden ist. Die ersten Versuche haben Nordmann und Sorge mit einem frappant erscheinenden Übereinstimmungsergebnis unternommen. Wir kamen bereits oben darauf zu sprechen. Man wird allerdings vorsichtigerweise weitere Bestätigungen und Anerkennung dieser komplizierten Verhältnisse durch weitere Sachkenner abwarten müssen.

Jedenfalls sprechen alle bisher bekannt gewordenen Tatsachen doch mit großer Wahrscheinlichkeit dafür, daß die Nordmannsche Ansicht über den Berufskrebs der Asbestarbeiter berechtigt ist. Auch die anderen Autoren wie Gloyne, Lynch und Smith, Egbert und Geiger sowie Linzbach zeigen die Tendenz, hier engere ursächliche Beziehungen zu vermuten. Der Versuch einer Widerlegung dieser Annahme ist bisher von keiner Seite unternommen worden.

Wenn wir uns nun die Frage vorlegen, worin die cancerogene Wirkung des Asbeststaubes zu suchen ist, so müssen wir allgemeine und örtliche disponierende Faktoren trennen. Daß zum Zustandekommen eines Krebses eine allgemeine Krebsdisposition (Veranlagung) vorauszusetzen ist, wird allerorts angenommen. Worin sie zu suchen ist, läßt sich schwer sagen. Es ist aus der allgemeinen menschlichen und experimentellen Pathologie bekannt, daß die Bereitschaft zu Krebs von anlagemäßigen Faktoren abhängig ist. Das drückt sich darin aus, daß unter gleichen Experimentbedingungen und einigermaßen gleichmäßiger Exposition für cancerogene Schäden beim Menschen die Quote Krebskranker immer nur einen Teil der Gefährdeten ausmacht. Das uns für die Asbestose vorliegende Beobachtungsmaterial läßt eine Analyse nach familiärer Krebsbelastung nicht ausreichend zu.

Wieweit und in welcher Weise der Asbeststaubschaden eine solche allgemeine Krebsdisposition schafft, wissen wir nicht. Ihre Annahme bleibt eine Hypothese. Dabei scheint es nicht so zu sein, daß sich diese allgemeine Disposition so stark auswirkt, daß sie etwa auch die Entstehung von Krebsen an anderen Organen begünstigte. Dafür sprechen die vorgelegten Zahlen gar nicht. Von entscheidender Wichtigkeit scheint immer vor allem die örtliche Umstimmung zu sein. Ihren morphologischen Ausdruck in den abgeänderten Gewebsreaktionen der Lunge haben wir oben näher aufgeführt. Als deren Ursache kommen in erster Linie chemische und mechanische Faktoren in Betracht. Da der Asbest chemisch einfach definiert ist, liegen die Verhältnisse hier leidlich übersichtlich. Man kann wohl von vornherein sagen, daß Stoffe aus der Gruppe der bekannten cancerogenen Agentien nicht in

betrug, sonst erstreckte sie sich auf 7 Jahre und mehr. Bei kurzer intensiver Bestäubung scheint dennoch zur Krebsentstehung immer ein längeres staubfreies Intervall hinzukommen zu müssen. Es gibt bisher keinen Krankheitsfall, bei dem der Zeitraum vom Beginn der Staubarbeit bis zum Nachweisbarwerden des Krebses weniger als 12 Jahre betragen hätte. Man wird weiter gewöhnlich erwarten dürfen, daß der Krebs nur bei ausgesprochenen, wenn auch nicht immer schwersten Formen der Asbestose auftritt. Die obigen Beispiele belegen dies.

Die ersten Symptome eines sich entwickelnden Lungenkrebses, die an sich ja schon meist nichts Charakteristisches oder gar Pathognomonisches bieten, werden nicht so auffällig sein wie bei einem vorher gesunden Menschen, weil Kurzatmigkeit, Husten, Auswurf und gewisse Mißempfindungen im Brustraum dem Asbestosekranken sowieso geläufige Beschwerden sind. Auch ein gewisser Verfall der allgemeinen Kräfte, der einen Lungenkrebs sogar anfangs gar nicht zu begleiten braucht, Gewichtsabnahme und Appetitlosigkeit sind bei den schweren Formen der Asbestose recht häufige Erscheinungen. Auch akute Verschlechterungen im Allgemeinzustand, einschließlich der örtlichen Lungenbeschwerden, kommen oft als Ausdruck aufgepfropfter Infekte, die schwerer überwunden werden, vor. Im ganzen wird man es sich für die Vorgeschichte der reinen Asbestose aber doch zur Regel machen müssen, daß der Krankheitsprozeß eine nur ganz allmähliche über Jahre, ja Jahrzehnte sich hinziehende Verschlechterung erfährt. Wenn in dieser Entwicklung plötzlich Einbrüche sichtlicher örtlicher und allgemeiner Verschlechterungen vorkommen, wird unter anderem der Gedanke an eine Krebsentwicklung auftauchen müssen. Neben dem Krebs kommen sonst hierfür am häufigsten unspezifische Infekte mit Bronchitis, Pneumonie oder Abscess in Frage. Die komplizierende Tuberkulose spielt nach unseren Erfahrungen nur eine untergeordnete Rolle. Sie wird dabei viel zu häufig diagnostiziert. Daß sie natürlich im Bereich des Möglichen liegt, ist selbstverständlich. Über begleitende Lungenlues oder Pilzerkrankungen ist bisher nichts bekannt geworden.

Von den Allgemeinsymptomen ist schneller Gewichtsverlust beachtlich, aber nicht beweisend. Das gleiche gilt — wie gesagt — von der Appetitlosigkeit, schlechter Gesichtsfarbe und Nachtschweißen. Beruhen diese allein auf der Zunahme der Asbestose, so werden sie gewöhnlich auch von einer verstärkten Atemnot, Cyanose, evtl. Trommelschlegelfingern und sonstigen örtlichen Lungenbeschwerden begleitet sein, aber natürlich wird man sich vor Augen halten müssen, daß ein Lungentumor die Zunahme solcher Beschwerden auch bedingen kann. Im ganzen wird sich die Situation aus der Vorgeschichte allein nicht ausreichend klären lassen.

Nicht viel anders ist es mit den meisten örtlichen Beschwerden bestellt. Da die schwerere Asbestose meist erheblichen Reizhusten setzt,

ist. Nur gröbere Schwarten oder spezifische und unspezifische Komplikationen können Ausnahmen bedingen. Das Atemgeräusch pflegt unten schwächer als oben zu sein. Selten ist es umgekehrt. Nebengeräusche sind unten zahlreicher und häufiger als oben; Seitenunterschiede besagen nicht viel. Findet man einseitig eindeutige Zeichen einer Atelektase, so ist dies im höchsten Grade auf Tumor verdächtig. Daß dieses Symptom beim Lungentumor aber nicht obligat zu sein braucht, ist ja selbstverständlich. Ergüsse, besonders solche hämorrhagischer Art, kommen bei der gewöhnlichen Asbestose praktisch nicht vor. Einschmelzungszeichen kann der Tumor mit dem Abseeß und der Tuberkulose gemeinsam haben. Bronchiektasien in Gestalt von zylindrischen Luftröhrenerweiterungen sind bei schwerer Asbestose nicht selten. Sie werden gelegentlich bei der klinischen Untersuchung in ihrer Abgrenzung gegen Einschmelzungen Schwierigkeiten machen können.

Gröbere Asymmetrien des Brustkorbes, Verziehungen der Mittelfellorgane und Zwerchfelle bedürfen immer einer gesonderten Erklärung.

Der Röntgenbefund dürfte stets die wichtigste Untersuchungsmethode zur Erkennung einer Geschwulst sein. Dabei muß man beachten, daß die schwere Asbestose nicht immer — wie man nach dem Schrifttum glauben könnte — nur zu feinen symmetrischen Verdichtungen des Lungengewebes führt. Neben gewissen Asymmetrien kommen auch flächenhafte Trübungen umschriebener Art in den Unterfeldern, besonders medial vor. Diese dichteren Schatten sind aber doch gewöhnlich nicht so kompakt und tumorartig, sondern mehr streifig gezeichnet und unscharf abgesetzt. Harte oder tomographische Aufnahmen werden das Bronchialsystem offen, evtl. sogar erweitert erkennen lassen. Durch Entzündungen bedingte Bronchusstenosen sind bisher bei der Asbestose nicht bekannt geworden. Kompakte, einseitige, umschriebene Verschattungen in der Lunge, womöglich mit Bronchusverschluß, sind praktisch für einen Tumor beweisend. Dahin gehören auch ständige oder mit der Atmung wechselnde Verschiebungen des Mediastinums und Lähmungen des Zwerchfells, des Recurrens oder bei Oberlappenprozessen meist auch ein Hornerscher Symptomenkomplex. Umschriebene Verdichtungen in den Obergeschossen eignen niemals der Asbestose. Hier liegen die Verhältnisse viel klarer und einfacher als bei der Silicose. Grobe Schattenbildungen entstehen sonst bei der Asbestose vornehmlich durch unspezifische Entzündungen. Die Tuberkulose ist längst nicht so häufig wie gemeinhin angenommen wird. Ihr erstes Auftreten in den Unterfeldern ist nach den bisherigen Beobachtungen bei Asbestose sehr selten. Daß im Rahmen der üblichen diagnostischen Verwertbarkeit die Tomo- und Bronchographie für die Tumorerkennung in der Lunge von entscheidendem Wert sein kann und daß für sie die üblichen Regeln der Deutung gelten, sei der Vollständigkeit halber angeführt. Ähnlich

Zusammenfassung.

Es wird über die bisher bekannt gewordene und erweiterte Kasuistik von bösartigen Lungen- und Pleuragewächsen bei Asbestose aus dem Weltschrifttum berichtet. Die Gründe, welche einen ursächlichen Zusammenhang zwischen beiden Erkrankungen nahelegen, werden aufgezeigt. Das klinische Bild des Lungentumors bei Asbestose wird besprochen und die Ausdehnung des Versicherungsschutzes auf diese Komplikation für angebracht gehalten.

Schrifttum.

Baader, E. W.: Dtsch. med. Wschr. 1939 I, 407. — Egbert, D. S. and A. J. Geiger: Amer. Rev. Tbc. 34, 143 (1936). — Gloyne, S. R.: Tubercle 14, 550 (1933); 17, 5 (1935); 18, 100 (1936)[1]. — Hornig, F.: Z. Krebsforsch. 47, 281 (1938). — Linzbach, A. J. u. H. W. Wedler: Virchows Arch. 307, 387 (1941). — Lynch, K. M. and W. A. Smith: Amer. J. Canc. 24, 56 (1935). — Nordmann, M.: Z. Krebsforsch. 47, 288 (1938). — Ber. 8. internat. Kongr. Unfallmed. u. Berufskrkh. Frankfurt a. M., Bd. 2, S. 983. Leipzig: Georg Thieme 1939. — Nordmann, M. u. A. Sorge: Z. Krebsforsch. 51, 168 (1941). — Sparks, J. V.: Brit. J. Radiol. 11, 371 (1938). — Wedler, H. W.: Klinik der Lungenasbestose. Leipzig: Georg Thieme 1939.

[1] Die Originalarbeit lag dem Verfasser nicht vor.