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From the Pathological Institute of the Municipal Hospitals, Dortmund

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Pulmonary carcinoma in pulmonary asbestosis

By Fr. Boemke

with 3 illustrations

While, in the case of numerous other kinds of dust, the macroscopic morphological substratum of the dust does not have to be, by any means, immediately and unequivocally characteristic of a certain type of dust, the finding of asbestosis (!) corpuscles in the sputum or, post mortem, in the lungs, generally justifies a diagnosis of pulmonary asbestosis. It is true, that there are certain exceptions from that rule, inasmuch as the formations designated as asbestosis corpuscles occasionally - even though rarely - are found in the lungs of subjects who demonstrably have never been exposed to asbestos dust. Nordmann reported such findings and spoke, in such cases, of pseudo-asbestosis corpuscles. Recently, Langer reported the presence of asbestosis corpuscles in a worker who was employed in the glass wool industry. Doerr also mentioned recently, in an oral discussion, the case of a woman in whose lungs asbestosis corpuscles were found, and in whom, without any doubt, no occupational activity entailing any action of asbestos doubt had been present. But, despite those reservations, it may, indeed, be stated in a general way that, as a rule, the demonstration of asbestosis corpuscles makes for a diagnosis of asbestos pneumo-coniosis (pulmonary asbestosis), and that the afore-mentioned unusual observations of occurrence of asbestosis corpuscles without any action of asbestos dust are rare, isolated cases.

It is well known that pneumoconiosis caused by asbestos dust, when there is a considerable amount and when the action of the dust continues over a considerable period of time, may lead to fibrosis of pulmonary tissue; that fibrosis is a disease for which indemnity is established legally. Recently, Behrens demonstrated by means of animal experiments that this asbestos-fibrosis is to be considered a partial phenomenon of a connective-tissue encapsulation of foreign bodies, and that asbestosis corpuscles as such have no specific significance in the fibrosis of pulmonary tissue. According to his investigations, that fibrosis rather appears to be the reaction of the tissue to foreign bodies containing long fibers.

In this connection, we may point out, on the basis of our activities as medical expert, that not every pulmonary asbestosis as such is a disease legally to be indemnified. The proof of the presence of asbestosis corpuscles in the sputum alone is not sufficient for granting a disability pension, but the afore-mentioned connective-tissue-like changes, the fibrosis of extensive parts of the pulmonary tissue with loss of their function for respiration and circulation are required. We do not intend here to go into any further details about the propagation of the asbestos dusts in pulmonary tissue and on the type and spread of fibrosis in asbestos lung. We make reference to the pertinent communications in the literature - Nordmann and others. Beger recently characterized the mineralogical and chemical nature of asbestosis corpuscles in detail in several papers - lately in a lecture presented at the Meeting of the German Association of Pathology at Kiel in 1949.

Pneumoconiosis due to asbestos dust entails, however, not only a

fibrosis of the pulmonary tissue; under certain conditions a pulmonary carcinoma may also develop, in connection with asbestosis. This fact makes pneumoconiosis due to asbestos stand out among the group of pneumoconioses. It is well known that only a few conioses are associated with frequent development of lung cancer; among them, the so-called Schneeberg miners' disease, is probably best known. For the sake of completeness, we want to point out here that, according to more recent investigations, lung cancer is found also in workers handling chromium. At this point, a general statement is required. Pulmonary cancer associated with silicosis are not, by any means, frequent. Rather, it has been determined by means of statistical surveys that, percentage-wise, the number of lung cancers in workers suffering from silicosis does not exceed the number of lung cancers without silicosis (W. Fischer, Spörlein, and many others). When giving an expert opinion on a pulmonary carcinoma, one will be able to assume a connection only in the very rare cases, in which it can be demonstrated that it originated in a decay cavity within a silicotic nodule (di Biasi).

Things are different, inasmuch as lung cancer associated with asbestosis is concerned. The connection between the pathogenesis of this type of cancer and the action of that particular type of dust has been confirmed by animal experiments (Nordmann) and has been recognized legally for the purpose of insurance claims. Pertinent observations, partly with reviews of communications published up to the time of those observations, have been reported, among others, by Normann, Wedler and Linzbach, Gloyne, and Boemke. In any case, lung cancer associated with

asbestos is rare when related to the number of cases published. Up to the time of a first pertinent case, which I reported in 1943, I was able to find only 17 cases in the literature; for that reason, a comprehensive discussion of three observations of my own appears to be justified.

> Inasmuch as the facts of my first case are concerned, I can be brief since I have discussed it in this journal, in 1947. It was the case of a man of 71 years who had been employed as comber in an asbestos plant over a period of 11 years, and in whom grave pulmonary asbestosis had been diagnosed 6 years before his death. Shortly before his death, a pulmonary carcinoma was found during a hospital stay. The autopsy showed asbestos fibres of the pulmonary tissue and diffuse cancerous penetration of the lower right lobe of the lungs. In other lobes of the lungs too, cancerous proliferations were found. In addition, an extensive carcinomatosis existed in the right pleura. Cancer metastases were found in the intra-thoracic and intra-abdominal lymph nodes, in the spleen, in both kidneys, in the left adrenal gland, in the liver, in the wall of the large intestines, in the ribs, in the vertebral column,in the left femur, and in the skin of the head. Inasmuch as the proliferation of cancerous growths in the right lower lobe of the lungs and the chronological and spatial connections of asbestosis and pulmonary carcinoma are concerned, I make reference to the following over-all discussion of the three cases.

The two additional observations have not yet been reported by me in any detail. They have to do with a woman who died at the age of 57 years, and with a man of 53 years.

The woman of 57 years was admitted to the Medical Clinic of the St. Johannes Hospital at Dortmund in October 1950. She suffered from considerable breathing difficulties and bloody sputum, high temperature and nocturnal perspiration. Before admission, she had lost 6.5 Kg in a short period of time. The history of earlier illnesses is of no importance in the contest of this discussion. At the time of admission, her strength and nutritional state were at a very low ebb. There was an area of dullness with humid rattles sounding like small or medium-sized vesicles above the right lobe of the lungs. The erythrocyte sedimentation rate was 51/78 mm. During her stay at the clinic, continuous temperatures around 38°C were measured at first. The patient suffered from sputum that was lumpy, light red, partially similar to raspberry jelly. No tubercle becilli could be demonstrated at any time. The X-ray picture showed a striped-spotty shadow in the lower part of the left lobe of the lungs with formation of transverse strands. The shadow filled the left sinus phrenico-costalis. In October 1950, the sputum of the patient was sent to me to be tested for the presence of tumor cells (Test # 7,191/50). In the sputum, numerous typical asbestosis corpuscles were found (see Fig. 1).

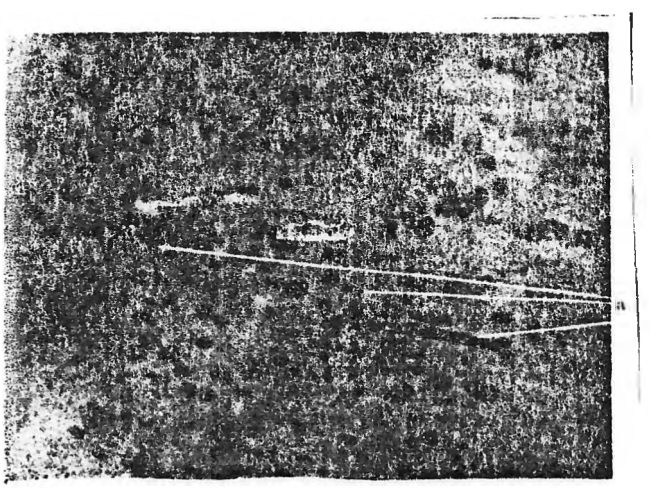

Fig. 1. Asbestosis corpuscles in sputum (Test # 7,191/50, 57 years old female)

During the further course of her hospital stay, the patient gradually became fever-free, but at the same time, an increasing dyspnea developed. The dullness in the region of the lower right lobe of the lungs persisted, as did the copious sputum which amounted to 50 to 250 cm^3 per day. Associated with increasing cachexia, increasing cardiac insufficiency developed. Death occurred in March 1951.

From the report on the autopsy (Autopsy #109/51), only those findings shall be mentioned here that are most essential in the context of this presentation. Both lungs, and in particular the lower part of the left lobe, showed accretions to their environment. The left lung was voluminous and heavier than normal. The lower lobe presented, on the cutting surfaces of the over-all densified tissue, regularly distributed, whitish, partly rough, partly pulpy areas with small black spots and stripes. In the rough, whitish, thickened pleura of the lower left lobe of the lungs, too, pulpy-grey strands and foci could be demonstrated. The consistency of the left upper lobe contained excessive air in the marginal areas. In part, central sections proved to be extensively densified and tough. Here,too, rough grey-whitish segments could be found, but they did not contain any pulpy foci. The marginal regions were coarsely meshed and collapsed when an incision was made. The right lung was also voluminous, but lighter in weight. The pleura showed rests of accretions,

in the form of grey-whitish, thickened shreds. In regions free of accretion, the pleura was light grey-red, with interspersed black spots and stripes. The marginal regions of the lung were partly inflated like air-cushions. In other regions, the consistency of the right lung was uneven, characterised partly by dense foci, partly rather by doughy densifications. On the cutting surfaces, the marginal regions corresponded to those of the upper part of the left lobe, while all the other pulmonary tissue was partly whitish, partly greyish-red to dark red, altogether unevenly spotted and interspersed with small black spots and stripes. . The bronchi in both lungs could be cut open up to the immediate vicinity of the pleura. No circumscribed tumor as origin of the pulpy, greyish-white regions which were described above and which appeared to us macroscopically to be neoplastic growths, could be found. The lymph nodes of the radix pulmonis which were somewhat larger than peas, were also partly tough-elastic, greyish-red with black inclusions. The pericardium adhered to the thickened pleura of the lower part of the left lobe on the one hand and to the heart on the other hand. Upon incision, the tissue in that region was found to be partly tough, greyish-white, partly pulpy-grey. After cutting the accretions on the rear wall of the left chamber, we found here that pulpy, greyish-white areas rested firmly on the epicardium and extended into the superficial muscle segments of the wall of the left chamber

of the heart. All cardiac cavities were enlarged. The left half of the diaphragm was also comprised within the pleural accretions and had degenerated into tough, greyish-white tissue with smaller pulpy, greyish-white areas. Those pulpy, greyish-white areas extended beyond the diaphragm into the left lobe of the liver, the upper pole of the spleen, the left adrenal gland, and the serosa of the stomach wall. The other findings of the autopsy are of no interest in connection with this discussion.

During histological examination, very large alveolar spaces with thin, elongated or torn septa were found in the marginal regions of the lungs. At other locations, all lobes presented rather extensive, hyaline, connective-tissue containing regions with irregular boundaries. Part of the alveolar septa are widened considerably by connective tissue formation. Every where, in the alveoli as well as in the connective tissue, asbestosis corpuscles of typical structure were found - partly shaped like dumbbells, partly in the form of rolls of coins, partly in spear-shaped or splinter-shaped formations that look as if they were broken off and are of a brownish-shiny color; in the Prussian-blue test, they reacted positively. In sections from the lower part of the left lobe of the lungs, epithelial cells of the type of plate epithelium could be shown every where they grew in irregularly infiltrating formations, and it was possible to observe numerous atypical

mitoses. Typical asbestosis corpuscles of the structure as described above lay also between those epithelial formations (see Fig. 2).

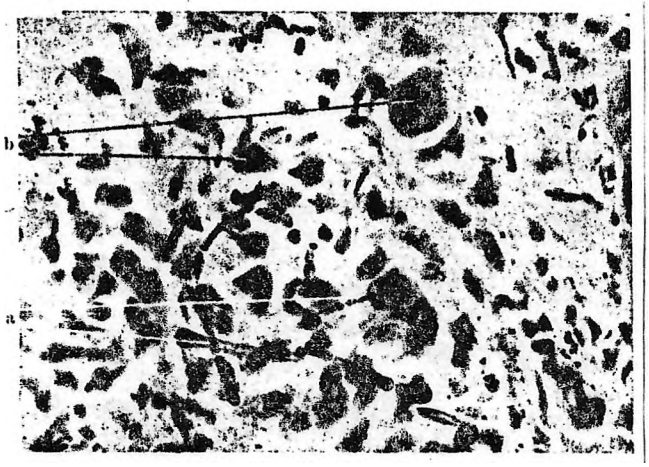

Fig. 2: Asbestosis corpuscles within the plate-epithelial carcinomatous growths in the lower part of the left lobe (Serial # 109/51, 57 years old female).

Asbestosis corpuscles = a. Cancer cells with mitoses = b

The histological examination of the other organs had the following important results: epithelial growth in the left chamber of the heart also, they spread to the muscle and are found also in the region of the left lobe of the liver, of the left adrenal gland, of the upper tip of the spleen, of the serosa of the stomach, of the left pleura, and of the left diaphragm.

Consequently, on the basis of the pathological-anatomical findings which agree with the clinical ones, we have to do with a typical asbestos fibrosis of the pulmonary tissue with extensive growths of plate-epithelial carcinoma in the lower left lobe of the liver, without any circumscribed point of origin, and with a carcinosis of the left pleura with invasion of the cancerous growth into the pericardium, the heart, the left half of the diaphragm with penetration of that half and further spread of the cancerous neoplasms to the liver,

the spleen, and the serosa of the stomach wall.

Lastly, we want to mention that, in this case, connective tissue areas that were poor in nuclei and included some asbestosis corpuscles could be found, a finding that is observed but rarely, because the asbestosis corpuscles - very likely because of their size - do not pass through the lymphatic pathways of the lungs as easily as other kinds of dust (see Fig. 3).

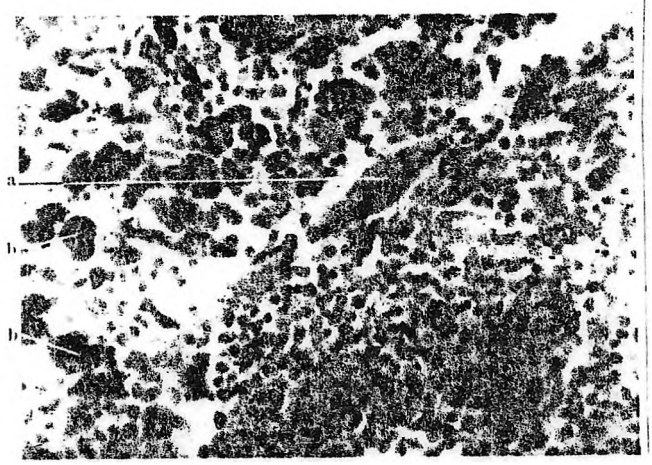

Fig. 3: Asbestosis corpuscles in a lymph node from the hilus of a lung (Serial # 109/51. 57 years old female) Asbestosis corpuscles = a. Anthracotic pigment = b.

The occupational history showed that the patient worked from her 17th to her 20th year in an asbestos factory on a pull-test machine. The raw material which arrived in the form of bales, was pulled apart there, and that caused the development of much dust which was eliminated by the fans that were available in the work room, only in a very unsatisfactory manner.

As we have mentioned before, the third case is that of a foreman who, at the time of his death, was 53 years old. He was gravely ill hen he was admitted to the 1st Medical Clinic of the Municipal Hospital at Dortmund, in August 1951. He said that he had felt ill only during the last 3 weeks before his admission to the Clinic.

His illness began with increasing dyspnea and swelling of the feet as well as with pain in the upper part of the right arm.

At the time of admission, we found a considerable cyanosis of the lips associated with severe dyspnea and frequent coughing. Both lungs presented the picture of congestion. The borders of the heart were broader than normal on both sides. The liver could be palpated, in a width of two fingers' breadth above the right lower costal arch. The abdomen was tympanous. Both lower legs showed edematous swellings. The patient made the impression of a gravely ill person, so that it was necessary to do without any additional clinical examinations. He died during the night after his admission to the clinic, and the obduction took place at the Pathological Institute of the Municipal Hospitals Dortmund on the following day (Protocol #305/51). We shall, once more, present only the findings that are most important in the present context.

Both lungs presented extensive accretions to the thoracic wall and and to the diaphragm. They were partly superimposed on the pericardium and were very voluminous and heavy. Their free margins were blunt or rounded. The pleura had extensive whitish-grey vestiges of accretions and rough-whitish, thickened areas, in particular in the region of the base and of parts of the tip. The interlobar fissures had also coalesced. The consistency of both lungs was rough, elastic, partly inflated, within circumscribed marginal areas only, in the manner of air-cushions. On the cutting surfaces, the lung tissue presented, on both sides, diffuse yellow-brown-reddish,

spots and isolated small, soft, black spots and stripes which, altogether, were not very extensive. Particularly, in the lower lobes, the cutting surfaces presented an extensive, grey-whitish net. Circumscribed formations of nodes could not be demonstrated. The bronchi appeared to have thick walls and/more or less compressed to be by the surrounding rough-elastic pulmonary tissue. But, it was possible to cut them open up to the immediate vicinity of the pleura, reaching into their more delicate ramifications. Their mucosa was greyish-red to darkened, covered by a greasy reddish-grey, tough-slimy fluid. The vessels of the lungs were empty, the lymph nodes of the hilus of the lungs had the size of two beans; they were soft, partly black, partly whitish-grey and spotty.

Since the findings in the lungs in combination with earlier observations appeared to me to justify a suspicion of asbestosis, native preparations were made during the autopsy. In the press-juice from the cutting surfaces of the lungs, numerous typical asbestosis corpuscles could be demonstrated microscopically.

In addition, pulpy whitish-grey regions were found in both adrenal glands; next to them, only scanty vestiges of adrenal parenchyma were present. The heart was enlarged and expanded; in particular, the wall of the right ventricle was thickened, and the clearance of the right ventricle was enlarged considerably.

The weight of the heart was 465 g. Lastly, there was an abundance of blood of the inner organs, due to congestion, with an ascites of 300 cm^3.

We want to mention one additional finding that is of lesser importance in this connection, but is important as a contributing cause of death, viz., an arteriosclerosis of the coronary arteries of the heart, associated with the formation of small callosities in the muscles of the heart.

In the histological examination, we found, once more, alveolar septa thickened by connective tissue and partly infiltrated by asbestosis corpuscles, in all lobes of the lungs. Likewise, we found in many alveolar clearances groups of asbestosis corpuscles of widely varying shapes, partly of the type of the coin-roll or dumb-bell shapes, partly of the type of spear-or splinter-shaped formations; they were of a brownish-brilliant hue. In the lower lobes, irregularly bordered, extensive areas of connective tissue were present. Between those stretches of connective tissue, especially in the lower lobes and less extensively in the other lobes of the lungs, there were irregularly arranged epithelial cell groups and skeins which, in part, filled the alveoli completely and, in many cases showed cells with atypical mitoses and polymorphous nuclei. A circumscribed point of orgin of those epithelial formations could not be demonstrated. Between those epithelial groups of cells, there were likewise a great many asbestosis corpuscles to be found. Lastly, very wide alveoli with thinly elongated or torn septa could be domonstrated in sections from marginal areas of the lungs.

The lymph nodes of the hilus of the lungs also presented, besides vestiges of lymphatic tissue, an irregular and diffuse infiltration of

epithelial cell groups of the described structure; among connective tissue areas, again, we were able here, too, to find asbestosis corpuscles. The adrenal gland presented, likewise, a diffuse infiltration of epithelial growths with many atypical mitoses.
Accordingly, we had to do in this case, too, with asbestosis complicated by fibrosis of pulmonary tissue and extensive cancerous growths in the lungs. The latter ones had caused metastasization into the lymph nodes of the hilus of the lungs and into both adrenal glands.

Later, an attempt was made, on the basis of the observations made, to look into the history of the subject's occupation. But, since he was a refugee, it was not possible to get any exact information as to his past activities. It could be ascertained only that he was supposed to have worked a long time in an asbestos plant. But, the duration and nature of his employment could not be determined.

Especially in the diagnosis of cancer in an asbestos-dust lung, the collection of data concerning former employment is of essential importance. Nordmann has pointed out certain laws governing the occurrence of cancers in asbestosis. In some of those who died of asbestosis complicated by carcinoma, the pulmonary carcinoma appeared when they were relatively young. It is true that in the cases which I have observed, that statement does not apply, particularly inasmuch as bronchial or lung cancers occuring without the presence of asbestosis are now observed in younger people more frequently. But, another finding seems to me to be of particular interest. In the majority of subjects suffering from lung cancer complicating asbestosis,

a certain rather identical period of time passes between the beginnings of their employment in an asbestos establishment and the time of their deaths due to lung cancer. That period of time amounts, according to Nordmann, to 18 years, and unequivocally applies to my first case, too. It is true that, in the 2nd case, a time period of no fewer than 37 years elapsed between the beginning of occupation in an asbestos plant and death due to lung cancer associated with an asbestos-dust lung, while in my third case the period cannot be calculated, for the reasons given above. Of course, the figure calculated by Nordmann is to be considered an average period only. As in my second case, upward and downward variations occur. Bauer gives the period elapsed between the onset of the action of the asbestos dust and the appearance of the carcinoma as ranging from 12 to 42 years. It does not matter whether the exposure to the dust was continuous up to the time of the development of the cancer, or whether a dust-free interval occurred between the exposure and the development of the cancer. But, it is a matter that, besides the cancer, an infiltration of the pulmonary tissue by asbestosis corpuscles must be present if lung cancer associated with asbestosis is to be the diagnosis.

Data concerning the calculated percentage of lung cancer complicating asbestosis vary. In 50 autopsies of asbestosis cases, Gloyne observed lung cancers in 6 cases, i.e., 12%. In a smaller number of asbestosis deaths, Nordmann arrives at 17% of lung cancers. On the basis of my cases, I can confirm also additional regular phenomena as shown by Nordmann, i.e., the preference of the primary carcinoma for a

lower lobe of the lungs. We may assume that, in accordance with the kind of spread in the male of 71 years, the cancer started in the lower right lobe of the lungs. In the case of the female of 57 years, the cancer growths also had their primary location in the lower left lobe of the lungs. In the last case described, extensive carcinoma growths in both lower lobes could be demonstrated. It is true that, in that case, no preferred involvement of one or the other lower lobe could be shown. Lastly, it is a notable fact that, in the majority of all cases, plate-epithelial carcinomas are present - as is true of my two first cases while, in the third case, the cancerous growths were less differentiated even though they contained giant cells.

It is of special significance and downright typical of pulmonary carcinoma complicating asbestosis and as a sequel of asbestosis, that the cancerous growths in the lungs have a multi-centric pathogenesis. In such cases, it is never possible to demonstrate a circumscribed point of origin, as is the case, e.g., in bronchial carcinoma. The cancerous formations are rather present in the form of a completely irregular distribution within the affected regions of the lungs, so that multiple metaplastic carcinoma has to be called characteristic of asbestosis.

In view of the undoubted connection of asbestosis and lung cancer, there arises - as a matter of course - the question which factors are of decisive importance for the pathogenesis of the carcinoma. We have to think of the fact that a coarse-mechanical trauma of the relatively large asbestos dust structures must be considered; when that effect is

continuous, it may lead, in the end, to a precipitate regeneration and to epithelial metaplasias with subsequent cancerous degeneration. There is no doubt that that explanation alone does not solve the problem, inasmuch as it is likely that chemical processes have a determining influence in this type of cancer also.

Summary

On the basis of the author's observations, the connection between pulmonary asbestos fibrosis and lung cancer is discussed. The particular laws that are characteristic of this special form of cancer - in particular, the preferred location in the lower lobes and the multicentric origin of plate-epithelial cancerous growths in the lungs - are stressed.

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ei eindringen können. Man hat nun auch versucht verschiedene Formen der männlichen Sterilität, die auf einen Hyaluronidasemangel zurückzuführen sind, durch Substitutionstherapie anzugehen. *Kurzrock*[55] und Mitarbeiter wiesen schon 1946 nach, daß ein Teil der unfruchtbaren Ehen auf einen Hyaluronidasemangel im Sperma zurückzuführen ist. Sie konnten durch Beigabe von Hyaluronidase zum Sperma eine Gravidität erzielen. Das Medikament wird hierbei frischem Sperma beigefügt und in den Zervikalkanal — oder einige Zeit ante cohabitationem in denselben — injiziert. Spielt die Hyaluronidase beim Befruchtungsvorgang zumindest eine nicht unerhebliche ätiologische Rolle[56], so war es naheliegend auch das Gegenstück hierzu, eine Hyaluronidasehemmung als Antikonzipiens zu untersuchen. *Martin* und *Beiler*[57] fanden, daß Hesperidin als Hyaluronidaseinhibitor wirkt. Im Tierexperiment konnten sie durch diese Hyaluronidaseblockierung eine vorübergehende Sterilität erzielen. Inwieweit diese Methoden ohne eine gesundheitsschädigende Wirkung auch beim Menschen anwendbar sind, ist augenblicklich noch eine offene Frage.

An dieser Stelle konnten aus Raummangel nur die wichtigsten Ergebnisse aufgezeigt werden. Sicher bestehen bei vielen Krankheiten engere Beziehungen ätiologischer und pathogenetischer Art zum Hyaluronsäure-Hyaluronidase-System, als man bisher angenommen hat. Damit eröffnen sich auch neue therapeutische Möglichkeiten. Weitere Literaturangaben über das Hyaluronsäure-Hyaluronidase-System finden sich in den Medizinischen Mitteilungen von Schering sowie in den ausgezeichneten Arbeiten von *Gibian*[4] und *Billerbeck*[5].

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ORIGINALIEN

Aus dem Pathologischen Institut der Städt. Krankenanstalten Dortmund (Direktor: Prof. Dr. Fr. Boemke)

Das Lungenkarzinom in der Asbeststaublunge

Von Fr. Boemke

Mit 3 Textabbildungen

Während bei zahlreichen anderen Staubarten das grobe morphologische Substrat des Staubes zunächst keineswegs eindeutig typisch für eine bestimmte Staubart sein muß, gestattet die Feststellung von Asbestosiskörperchen im Sputum oder nach dem Tode in der Lunge in der Regel die Diagnose einer Asbeststaublunge. Allerdings gelten auch für diese Regel gewisse Ausnahmen, da die als Asbestosiskörperchen bezeichneten Gebilde gelegentlich, wenn auch selten in den Lungen von Menschen zur Beobachtung gelangen, die nachweisbar nicht mit Asbeststaub in Berührung gekommen sind. *Nordmann* hat entsprechende Befunde mitgeteilt und in solchen Fällen von Pseudoasbestosiskörperchen gesprochen. *Langer* berichtete kürzlich über das Vorkommen von Asbestosiskörperchen bei einem Arbeiter, der in der Glaswollindustrie tätig war. Auch *Doerr* hat letzthin in einer mündlichen Diskussionsbemerkung einen Fall mit Beobachtung von Asbestosiskörperchen in den Lungen einer Frau erwähnt, bei der mit Sicherheit keine Berufstätigkeit mit Asbeststaubeinwirkung vorgelegen hatte. Man kann aber trotz dieser Einschränkungen insgesamt wohl die Feststellung treffen, daß in der Regel der Nachweis von Asbestosiskörperchen auch die Diagnose einer Asbeststaublunge gestattet und daß die erwähnten ungewöhnlichen Beobachtungen des Vorkommens von Asbestosis-

körperchen ohne Asbeststaubeinwirkung seltene Einzelfälle darstellen.

Bekanntlich kann die Verstaubung des Lungengewebes mit Asbeststaub bei entsprechender Menge und Dauer zu einer Fibrose des Lungengewebes führen, die auch unter die entschädigungspflichtigen Lungenerkrankungen aufgenommen ist. *Behrens* hat kürzlich auf Grund von Tierversuchen nachgewiesen, daß diese Asbestfibrose als Teilerscheinung einer bindegewebigen Abkapselung von Fremdkörpern anzusehen ist und daß den Asbestosiskörperchen an sich keine spezifische Bedeutung für die Fibrose des Lungengewebes zukommt. Diese Fibrose stellt nach seinen Untersuchungen vielmehr die Reaktion des Gewebes auf langfaserige Fremdkörper dar.

Es sei in diesem Zusammenhang der sich aus der Gutachterpraxis ergebende Hinweis gestattet, daß nicht etwa jede Asbeststaublunge an sich eine entschädigungspflichtige Erkrankung darstellt. Für die Gewährung einer Rente genügt nicht allein der Nachweis von Asbestosiskörperchen im Sputum, vielmehr ist dazu die erwähnte bindegewebige Umwandlung, die Fibrose ausgedehnterer Lungengewebsanteile mit Ausfall ihrer Funktion für Atmung und Kreislauf erforderlich. Über die Ausbreitung des Asbeststaubes im Lungengewebe und über Art und Ausdehnung einer Fibrose in einer Asbeststaublunge sollen hier keine weiteren Ausführungen gemacht werden. Es wird auf die einschlägigen Mitteilungen im Schrifttum — *Nordmann* u. a. — verwiesen. Die mineralogische und chemische Natur der Asbestosiskörperchen hat *Beger* in mehreren Arbeiten und zuletzt ausführlich in einem Referat auf der Tagung der Deutschen Gesellschaft für Pathologie 1949 in Kiel gekennzeichnet.

Die Verstaubung des Lungengewebes mit Asbeststaub hat nun aber unter Umständen nicht nur eine Fibrose des Lungengewebes zur Folge. Im Zusammenhang mit einer Asbestosis kann sich auch ein Lungenkarzinom entwickeln. Diese Tatsache hebt die Asbeststaublunge aus dem Kreise der Staublungenerkrankungen besonders hervor. Bekanntlich sind nur einzelne bestimmte Staublungenerkrankungen mit der gehäuften Entstehung von Lungenkarzinomen verbunden, unter denen der sogenannte Schneeberger Lungenkrebs, der bei Arbeitern im Schneeberger Revier auftreten kann, wohl der bekannteste ist. Der Vollständigkeit halber sei hier darauf hingewiesen, daß nach neueren Untersuchungen auch Lungenkrebse bei Chromatarbeitern vorkommen können. Hier ist eine generelle Feststellung erforderlich. Lungenkarzinome in Verbindung mit einer Silikose treten keineswegs gehäuft auf. Durch statistische Feststellungen ist vielmehr erwiesen, daß Lungenkarzinome bei Arbeitern, die an einer Silikose erkrankt sind, die Zahl der Lungenkrebse ohne Silikose prozentual nicht übertrifft *(W. Fischer, Spörlein* u.v.a*)*. Man wird bei der Begutachtung eines Lungenkarzinoms bei einer Silikose sich nur in den sehr seltenen Fällen zu der Annahme eines Zusammenhanges entschließen dürfen, bei denen das Karzinom nachweisbar in einer Zerfallshöhle innerhalb einer silikotischen Schwiele entstanden ist *(di Biasi)*.

Anders liegen die Verhältnisse bei den Lungenkarzinomen bei einer Asbestosis. Der Zusammenhang der Entstehung dieser Karzinomformen mit der Einwirkung der besonderen Staubart ist durch Tierversuche erhärtet *(Nordmann)* und auch versicherungsrechtlich anerkannt. Entsprechende Beobachtungen, z. T. mit Übersichten über die bisher erfolgten Veröffentlichungen sind unter anderem von *Nordmann, Wedler* und *Linzbach*, *Gloyne* und von *Boemke* mitgeteilt. Immerhin sind Lungenkarzinome bei Asbestosis im Verhältnis zur Zahl der im Schrifttum veröffentlichten Fälle offenbar selten. Bis zu einem ersten von mir mitgeteilten einschlägigen Fall im Jahre 1943 konnte ich im Schrifttum insgesamt nur 17 Fälle feststellen, so daß eine zusammenfassende Besprechung von drei eigenen Beobachtungen berechtigt erscheint.

Hinsichtlich der Angaben über meinen ersten Fall kann ich mich kurz fassen, da ich denselben in dieser Zeitschrift im Jahre 1947 bereits besprochen habe. Es handelt sich dabei um einen bei seinem Tode 71 Jahre alten Mann, der 11 Jahre in einer Asbestfabrik als Krempler tätig war und bei dem 6 Jahre vor dem Tode eine schwere Asbeststaublunge festgestellt wurde. Kurz vor seinem Ableben wurde während eines Krankenhausaufenthaltes ein Lungenkarzinom diagnostiziert. Bei der Obduktion bestand eine Asbestfibrose des Lungengewebes und eine diffuse karzinomatöse Durchsetzung des rechten Lungenunterlappens. Auch in den übrigen Lungenlappen waren Karzinomwucherungen vorhanden. Weiterhin fand sich eine ausgedehnte rechtsseitige Pleurakarzinose. In den intrathorakalen und intraabdominellen Lymphknoten, in der Milz, in beiden Nieren, in der linken Nebenniere, in der Leber, in der Dickdarmwand, in den Rippen, in der Wirbelsäule, im li. Femur und in der Kopfschwarte fanden sich Karzinommetastasen. Zur Frage der Ausbreitung der Karzinomwucherungen im rechten Lungenunterlappen und des zeitlichen und örtlichen Zusammenhanges zwischen Asbestosis und Lungenkarzinom verweise ich auf die nachfolgende gemeinsame Besprechung der drei Fälle.

Die beiden weiteren Beobachtungen wurden von mir noch nicht ausführlicher mitgeteilt. Es handelt sich dabei einmal um eine bei ihrem Tode 57 Jahre alte Frau, zum anderen um einen 53 Jahre alten Mann.

Die 57 Jahre alte Frau wurde in der Medizinischen Klinik des St.-Johannes-Hospitals in Dortmund im Oktober 1950 aufgenommen*. Sie litt an erheblicher Atemnot, blutigem Auswurf, Temperaturerhöhungen und Nachtschweiß. Vor der Klinikaufnahme hatte sie in kurzer Zeit 6,5 kg an Gewicht abgenommen. Die Anamnese über frühere Erkrankungen ist im Zusammenhang dieser Ausführungen unwesentlich. Bei der Aufnahme waren der Kräfte- und Ernährungszustand sehr stark herabgesetzt. Über der re. Lunge lag basal eine Dämpfung mit feuchten klein- bis mittelblasigen klingenden Rasselgeräuschen vor. Die Blutkörperchensenkungsgeschwindigkeit betrug 51/78 mm. Während des Klinikaufenthaltes bestanden zunächst dauernd Temperaturen um 38° C. Dabei litt die Patientin an Auswurf, der geballt, hellrot, z. T. leicht himbeergeleeartig war. Tuberkelbazillen ließen sich nie nachweisen. Röntgenologisch lag eine streifig-fleckige Verschattung im Untergeschoß der linken Lunge mit Ausfüllung des linken Sinus phrenico-costalis und mit queren Strangbildungen vor. Im Oktober 1950 wurde mir Sputum der Patientin zur Untersuchung auf Tumorzellen übersandt (E. Nr. 7 191/50). Darin fanden sich zahlreiche typische Asbestosiskörperchen (s. Abb. 1).

Im weiteren Verlauf des Klinikaufenthaltes wurde die Patientin allmählich fieberfrei. Dabei entwickelte sich jedoch eine zunehmende Dyspnoe. Die Dämpfung im Bereich des rechten Lungenunterlappens blieb bestehen, weiterhin auch der reichliche Auswurf in einer Menge von 50—250 ccm pro die. Unter zunehmender Kachexie entwickelten sich steigende Beschwerden im Sinne einer Herzinsuffizienz. Im März 1951 trat der Exitus ein.

Aus dem Befundbericht über die am Todestag durchgeführte Obduktion (S. Nr. 109/51) sollen hier nur die

* Herrn Chefarzt Dr. med. habil. *Nagel* danke ich für die freundliche Überlassung ausführlicher klinischer Angaben.

n Zusammenhang dieser Ausführung wesentlichsten Befunde genannt werden. Beide Lungen zeigten flächenhafte Verwachsungen mit ihrer Umgebung, besonders der linke Lungenunterlappen. Die linke Lunge war voluminös und schwerer als normal. Der Unterlappen zeigte auf den Schnittflächen des insgesamt verdichteten Gewebes regellos verteilte weißliche, z. T. derbe, z. T. auch markige Herde mit schwarzen Fleckchen und Streifen. Auch in der derben weißlich verdickten Pleura des linken Lungenunterlappens ließen sich markig-grau-weiße Stränge und Herde nachweisen. Die Konsistenz des linken Oberlappens war in den Randbezirken vermehrt lufthaltig. Zentrale Abschnitte erschienen z. T. ziemlich ausgedehnt zäh verdichtet. Auf den Schnittflächen ließen sich auch hier derbe grau-weißliche Abschnitte, jedoch ohne markige Herde nachweisen. Die Randbezirke waren grobmaschig und sanken bei Einschnitt zusammen. — Die rechte Lunge war gleichfalls voluminös, dabei aber leichter. Die Pleura zeigte Verwachsungsreste in Form grauweißlicher fetziger Verdickungen. In von Verwachsungen freien Bezirken erschien die Pleura hellgraurot, von schwarzen Flecken und Streifen durchsetzt. Die Randbezirke der rechten Lunge waren z. T. luftkissenartig gebläht. Im übrigen war die Konsistenz der rechten Lunge ungleichmäßig, z. T. herdförmig dicht bis derb, z. T. auch eher teigig verdichtet. Auf den Schnittflächen entsprachen die Randbezirke denen des linken Lungenoberlappens, während das übrige Lungengewebe z. T. weißlich, z. T. graurot bis dunkelrot, insgesamt ungleichmäßig fleckig erschien und von schwarzen Fleckchen und Streifen durchsetzt wurde. Die Bronchien waren in beiden Lungen bis dicht unter die Pleura aufschneidbar. Ein umschriebener Tumor als Ursprungsort der beschriebenen markig-grauweißen makroskopisch als Tumorwucherungen imponierenden Bezirke im linken Lungenunterlappen ließ sich nicht feststellen. Die übererbsgroßen Lungenwurzellymphknoten waren z. T. auch derb-elastisch, graurot mit schwarzen Einlagerungen. Der Herzbeutel war mit der verdickten Pleura des linken Lungenunterlappens einerseits und mit dem Herzen andererseits verwachsen. Bei Einschnitt war das Gewebe in diesem Bereich z. T. derbe, grau-weißlich, z. T. auch markig-grau. Nach Lösung der Verwachsungen an der Hinterwand der linken Kammer saßen hier dem Epikard markig-grauweißliche Bezirke fest auf, die auf die oberflächlichen Muskelabschnitte der linken Herzkammerwand übergriffen. Die Herzhöhlen waren insgesamt erweitert. Auch die linke Zwerchfellhälfte war in die Pleuraverwachsungen einbezogen und in ein derbes, grau-weißliches Gewebe mit kleineren markig-grauweißlichen Nestern umgewandelt. Diese markig-grauweißlichen Bezirke griffen über das Zwerchfell hinaus auf den linken Leberlappen, den oberen Milzpol, die linke Nebenniere und die Serosa der Magenwand über. Die übrigen bei der Obduktion erhobenen Befunde sind im Zusammenhang dieser Ausführungen ohne Interesse.

Bei den feingeweblichen Untersuchungen ließen sich in den Lungen in Randbezirken sehr weite Alveolarräume mit dünn ausgezogenen oder eingerissenen Septen nachweisen. An anderen Stellen fanden sich in allen Lappen ausgedehntere unregelmäßig begrenzte hyalin bindegewebige Bezirke. Zum Teil waren die Alveolarsepten stark bindegewebig verbreitert. Sowohl in den Alveolen wie auch im Bindegewebe lagen überall Asbestosiskörperchen vom charakteristischen Aufbau, z. T. von hantelähnlichen Formen, z. T. von Geldrollenform, z. T. in wie abgebrochen erscheinenden spieß- oder splitterförmigen Gebilden von bräunlich glänzender Farbe vor, die bei der Berliner Blaureaktion positiv reagierten. In Schnitten aus dem linken Lungenunterlappen ließen sich in regelloser Anordnung überall epitheliale Zellen vom Plattenepitheltyp nachweisen, die in unregelmäßig infiltrierenden Verbänden wuchsen und zahlreiche atypische Mitosen erkennen ließen. Auch zwischen diesen epithelialen Formationen lagen typische Asbestosiskörperchen des beschriebenen Aufbaues vor (s. Abb. 2).

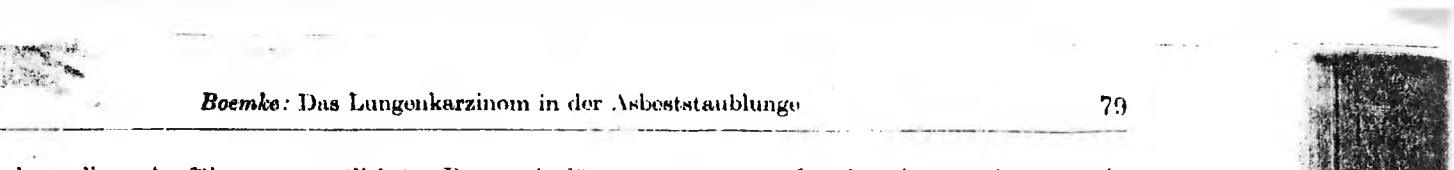

Abb. 1. Asbestosiskörperchen im Sputum (a). (E. Nr. 7191/50, 57 J. ♀)

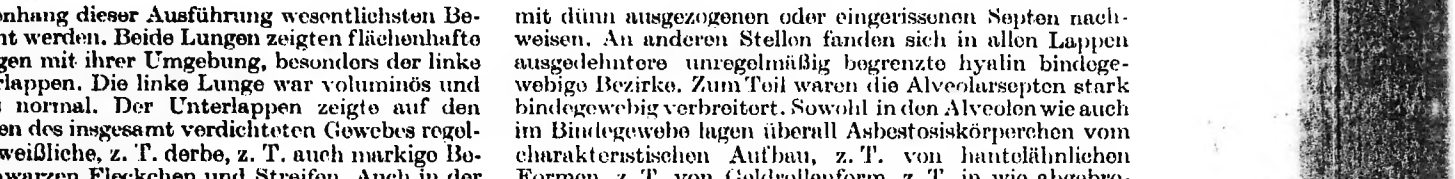

Abb. 2. Asbestosiskörperchen innerhalb von Plattenepithelkarzinomwucherungen im linken Lungenunterlappen (S. Nr. 109/51 57 J. ♀). Asbestosiskörperchen = a, Karzinomzellen mit Mitosen = b

Die histologische Untersuchung der übrigen Organe ergab an wesentlichen Befunden in der linken Herzkammer gleichfalls epitheliale Wucherungen, die vom Epikard auf die Muskulatur übergriffen, ebenso im Bereich des linken Leberlappens, der linken Nebenniere, des oberen Milzpoles, der Serosa des Magens, der linksseitigen Pleura und der linken Zwerchfellhälfte.

Es handelt sich also nach den pathologisch-anatomischen Erhebungen in Übereinstimmung mit dem klinischen Befund um eine typische Asbestfibrose des Lungengewebes mit ausgedehnten Plattenepithelkarzinomwucherungen im linken Lungenunterlappen ohne umschriebenen Ausgangspunkt und um eine linksseitige Pleurakarzinose mit Übergreifen der Karzinomwucherungen auf den Herzbeutel, das Herz, die linke Zwerchfellhälfte mit Durchbruch derselben und weiterem Übergreifen der karzinomatösen Formationen auf Leber, Milz, linke Nebenniere und auf die Serosa der Magenwand.

Es sei hier schließlich noch erwähnt, daß sich in diesem Falle auch in den Lungenwurzellymphknoten kernarme Bindegewebsbezirke mit einzelnen Asbestosiskörperchen nachweisen ließen, ein Befund, der seltener zur Beobachtung gelangt, da die Asbestosiskörperchen offenbar wegen ihrer Größe die Lymphbahnen der Lunge nicht so leicht passieren wie andere Staubarten (siehe Abb. 3).

Die Beschäftigungsanamnese ergab, daß die Patientin von ihrem 17.—20. Lebensjahr in einer Asbestfabrik an einer Zerreißmaschine gearbeitet hatte. Das

in Ballen eintreffende Rohmaterial wurde dort zerrissen, wobei es zu einer erheblichen Staubentwicklung kam, die durch die im Arbeitsraum vorhandenen Ventilatoren nur unzulänglich beseitigt wurde.

Der dritte Fall betrifft, wie oben bereits erwähnt, einen bei seinem Tode 53 Jahre alten Werkmeister, der in schwerkrankem Zustand im August 1951 in der I. Medizinischen Klinik der Städt. Krankenanstalten Dortmund aufgenommen wurde*. Er fühlte sich angeblich erst seit drei Wochen vor der Klinikaufnahme krank. Seine Erkrankung begann mit ständig zunehmender Atemnot und einer Schwellung der Füße sowie mit Schmerzen im rechten Oberbauch.

Bei der Aufnahme bestand eine erhebliche Lippenzyanose mit hochgradiger Dyspnoe und häufigen Hustenstößen. Beide Lungen zeigten das Bild einer Stauung. Die Herzgrenzen waren bds. verbreitert. Die Leber war zweifingerbreit über dem rechten unteren Rippenbogenrand tastbar. Das Abdomen war meteoristisch gebläht. Beide Unterschenkel waren ödematös geschwollen. Der Patient machte einen schwerkranken Eindruck, so daß

Abb. 3. Asbestosiskörperchen in einem Lymphknoten vom Lungenhilus. (S. Nr. 109/51. 57 J. ♂) Asbestosiskörperchen a. Anthrakotisches Pigment — b

von weiteren klinischen Erhebungen abgesehen werden mußte. Er starb in der Nacht nach der Klinikaufnahme und wurde am nächsten Tage im Pathologischen Institut der Städt. Krankenanstalten Dortmund obduziert (S. Nr. 305/51). Aus dem Leichenöffnungsbefundbericht sollen hier wiederum nur die im Zusammenhang dieser Ausführungen wichtigsten Befunde wiedergegeben werden.

Beide Lungen waren flächenhaft ausgedehnt mit der Brustwand und dem Zwerchfell verwachsen. Sie überlagerten den Herzbeutel zum Teil und waren sehr voluminös, dabei schwer. Ihre freien Ränder waren stumpf, bzw. abgerundet. Das Lungenfell zeigte ausgedehnte grauweißliche Verwachsungsreste und derbe grau-weißliche Verdickungen, besonders im Bereich der Basis und der Spitzenanteile. Auch die Interlobärspalten waren untereinander verwachsen. Die Konsistenz beider Lungen war derb elastisch, nur in umschriebenen Randbezirken luftkissenartig gebläht. Auf den Schnittflächen war das Lungengewebe bds. diffus fleckig graubraun-rötlich, mit vereinzelten kleinen, weichen, schwarzen Fleckchen und Streifen, die insgesamt nicht sehr ausgedehnt waren. Vor allem in den Unterlappen zeigten die Schnittflächen weiterhin ein ausgedehntes feines, grauweißliches Netz- und Maschenwerk. Umschriebene Knotenbildungen waren nicht nachweisbar. Die Bronchien erschienen derbwandig, vom umgebenden zäh-elastischen Lungengewebe wie eingeengt. Sie waren jedoch bis nahe unter die Pleura in ihre feineren Verzweigungen hinein aufschneidbar. Ihre Schleimhaut war graurot bis dunkelrot, von schmierig-graurötlicher, zäh-schleimiger Flüssigkeit bedeckt. Die Lungengefäße waren leer, die Lungenhiluslymphknoten doppelbohnengroß, weich, z. T. schwarz, z. T. fleckig grau-weißlich.

Da mir bereits bei der Obduktion auf Grund der früheren Beobachtungen der Lungenbefund für eine Asbestosis verdächtig erschien, wurden Nativpräparate bei der Sektion angefertigt. Im von den Schnittflächen der Lungen ausgepreßten Gewebesaft ließen sich mikroskopisch zahlreiche typische Asbestosiskörperchen nachweisen.

Weiterhin fanden sich in beiden Nebennieren markiggrauweißliche Bezirke, neben denen nur noch spärliche Reste von Nebennierenparenchym vorlagen. Das Herz war vergrößert und erweitert, besonders die rechte Herzkammerwand war verdickt und die Lichtung der rechten Herzkammer stark erweitert. Das Herzgewicht betrug 465 Gramm. Schließlich bestand eine Stauungsblutfülle der inneren Organe mit einem Aszites von 300 ccm.

An in diesem Zusammenhang weniger wichtigen, aber für den Eintritt des Todes wesentlichen Befunden, ist noch eine Arteriosklerose der Herzkranzarterien mit kleinen Schwielenbildungen in der Herzmuskulatur zu erwähnen.

Bei der feingeweblichen Untersuchung fanden sich wiederum in allen Lungenlappen bindegewebig verbreiterte Alveolarsepten, die z. T. von Asbestosiskörperchen durchsetzt waren. Ebenso lagen in zahlreichen Alveolarlichtungen Gruppen von Asbestosiskörperchen der verschiedensten Form vor, teils nach Art der schon oben erwähnten charakteristischen Hantel- oder Geldrollenform, teils auch in spieß- oder splitterförmigen bräunlich glänzenden Gebilden. In den Unterlappen waren regellos begrenzte ausgedehntere Bindegewebsbezirke vorhanden. Zwischen diesen Bindegewebszügen fanden sich vor allem in den Unterlappen, weniger ausgedehnt in den übrigen Lungenlappen regellos angeordnete epitheliale Zellnester und -stränge, die z. T. die Alveolen völlig ausfüllten und vielfach Zellen mit atypischen Mitosen und polymorphen Kernen erkennen ließen. Ein umschriebener Ausgangspunkt dieser epithelialen Formationen ließ sich nicht nachweisen. Zwischen diesen epithelialen Zellnestern waren gleichfalls massenhaft Asbestosiskörperchen vorhanden. In Schnitten aus den Randbezirken der Lungen ließen sich schließlich sehr weite Alveolen mit dünn ausgezogenen oder eingerissenen Septen nachweisen.

Die Lungenhiluslymphknoten zeigten gleichfalls neben Resten lymphatischen Gewebes eine regellose und diffuse Durchsetzung mit epithelialen Zellverbänden des beschriebenen Aufbaues zwischen Bindegewebsbezirken. Vereinzelt ließen sich auch hier wiederum Asbestosiskörperchen feststellen.

Auch die Nebennieren zeigten eine diffuse Durchsetzung mit epithelialen Wucherungen mit zahlreichen atypischen Mitosen.

Es handelt sich also auch in diesem Falle um eine Asbestosis mit Fibrose des Lungengewebes und ausgedehnten Karzinomwucherungen in den Lungen. Letztere hatten zur Metastasierung in den Lungenhiluslymphknoten und in beiden Nebennieren geführt.

Es wurde nachträglich auf Grund des erhobenen Befundes versucht, eine Anamnese über die berufliche Tätigkeit des Verstorbenen zu erheben. Da es sich um einen Flüchtling handelte, war es jedoch unmöglich, eine genaue Auskunft über seine frühere Tätigkeit zu erhalten. Es ließ sich lediglich feststellen, daß er früher angeblich lange Zeit in einem Asbestwerk gearbeitet hatte. Die Dauer und Art der Tätigkeit ließ sich jedoch nicht mehr in Erfahrung bringen.

Gerade bei der Diagnose eines Karzinoms in einer Asbeststaublunge ist die Erhebung einer Arbeitsanamnese von wesentlicher Bedeutung. *Nordmann* hat auf gewisse Gesetzmäßigkeiten bei dem Auftreten von Karzinomen bei einer Asbestosis hingewiesen. Bei einem Teil der an Asbestosis und Karzinom Verstorbenen trat das Lungenkarzinom in einem relativ jugendlichen Alter auf. In den von mir beobachteten Fällen ist allerdings eine solche Feststellung nicht zutreffend, zumal die ohne Asbestosis vorhandenen

* Herrn Chefarzt Professor Dr. *Wenckhaus* danke ich für die Überlassung der klinischen Angaben.

Bronchial- bzw. Lungenkarzinome jetzt auch häufiger schon bei jüngeren Menschen beobachtet werden. Dagegen erscheint mir eine andere Feststellung von besonderem Interesse. Bei der Mehrzahl der an einem Lungenkarzinom mit einer Asbestosis erkrankten Menschen liegt ein ziemlich gleichmäßiger Zeitraum vom Beginn ihrer Arbeit in einem Asbestbetrieb bis zum Eintritt des Todes an einem Lungenkarzinom vor. Dieser Zeitraum ist von *Nordmann* mit 18 Jahren angegeben und trifft auch bei meinem ersten Fall eindeutig zu. Im zweiten Fall ist allerdings ein Zeitraum von immerhin 37 Jahren zwischen dem Beginn der beruflichen Tätigkeit in einer Asbestfabrik und dem Tod als Folge eines Lungenkarzinoms bei einer Asbeststaublunge vergangen, während in meinem dritten Fall aus den obengenannten Gründen dieser Zeitraum sich nicht berechnen läßt. Natürlich ist die von *Nordmann* errechnete Zahl lediglich als Durchschnittszahl zu werten. Schwankungen nach oben und nach unten kommen, wie auch in meinem zweiten Fall, durchaus vor. Die Zeit zwischen dem Beginn der Einwirkung von Asbeststaub und der Krebsentwicklung wird von *Bauer* mit 12—42 Jahre angegeben. Dabei spielt es keine Rolle, ob die Staubexposition fortlaufend bis zur Entwicklung des Krebses vorhanden war, oder ob zwischen dieser und der Entwicklung des Lungenkrebses ein staubfreies Intervall vorlag. Selbstverständlich muß aber, wenn man einen Lungenkrebs in Zusammenhang mit einer Asbestosis annehmen will, histologisch auch neben dem Krebs eine Durchsetzung des Lungengewebes mit Asbestosiskörperchen vorhanden sein.

Die Angaben über die errechneten Prozentzahlen von Lungenkarzinomen bei Asbestosis schwanken. *Gloyne* hat bei 50 Obduktionen von Asbestosis in 6 Fällen, also in 12%, einen Lungenkrebs beobachtet. *Nordmann* errechnet bei einer geringeren Zahl von Asbestosistodesfällen 17%, bei denen gleichzeitig ein Lungenkarzinom bestand.

Weitere von *Nordmann* aufgezeigte Gesetzmäßigkeiten über die Bevorzugung des primären Karzinomeintritts in einem Lungenunterlappen kann ich auf Grund meiner Fälle auch bestätigen. Man kann wohl annehmen, daß nach der Art der Ausbreitung bei dem 71 Jahre alten Mann das Karzinom vom rechten Lungenunterlappen seinen Ausgang genommen hat. Auch bei der 57 Jahre alten Frau hatten die Karzinomwucherungen ihren Sitz primär im linken Lungenunterlappen. Im letzten Falle ließen sich ausgedehnte Karzinomwucherungen in beiden Unterlappen nachweisen. Allerdings war dabei keine bevorzugte Beteiligung des einen oder anderen Unterlappens vorhanden. Bemerkenswert ist schließlich die Tatsache, daß es sich bei der Mehrzahl aller Beobachtungen um Plattenepithelkarzinome handelt, so auch in meinen beiden ersten Fällen, während in dem dritten Fall die Karzinomwucherungen undifferenzierter, wenn auch großzellig waren.

Von besonderer Bedeutung und geradezu typisch für das Lungenkarzinom bei einer Asbestosis und als Folge einer solchen ist vor allem die multizentrische Entstehung der Karzinomwucherungen in den Lungen. Man kann in solchen Fällen nie einen umschriebenen Ausgangspunkt etwa wie bei einem Bronchialkarzinom nachweisen. Die krebsigen Formationen sind vielmehr in völlig unregelmäßiger Verteilung in den betroffenen Lungenbezirken vorhanden, so daß man das multiple metaplastische Karzinom als charakteristisch für eine Asbestosis bezeichnen muß.

Bei der sicheren Kenntnis des Zusammenhanges von Asbestosis und Lungenkarzinom erhebt sich natürlich die Frage, welche Faktoren für die Karzinomentstehung von maßgeblicher Bedeutung sind. Man muß daran denken, daß durch die relativ großen Asbeststaubgebilde eine grob-mechanische Schädigung der Alveolardeckzellen in Frage kommt, die bei ständiger Einwirkung schließlich zu einer überstürzten Regeneration und zu Epithelmetaplasien mit nachfolgender krebsiger Entartung führen kann. Sicher wird eine solche Erklärung dem Problem der Karzinomentstehung jedoch nicht allein gerecht, da auch bei dieser Karzinomform wohl chemische Prozesse von maßgeblicher Bedeutung sind.

Zusammenfassung

Auf Grund von drei eigenen Beobachtungen wird der Zusammenhang von Asbestfibrosen der Lunge mit Lungenkarzinom besprochen. Die dieser besonderen Karzinomform eigentümlichen Gesetzmäßigkeiten — vor allem der bevorzugte Befall der Unterlappen und die multizentrische Entstehung von Plattenepithelkarzinomwucherungen in den Lungen — werden hervorgehoben.

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Weitere ausführliche Literaturangaben siehe auch bei *Beger* und *Nordmann*

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LUNG CARCINOMA IN PATIENTS SUFFERING FROM ASBESTOS PNEUMOCONIOSIS

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Although with other types of dust the main morphological substrate of the dust at first does not appear uniformly typical of any specific type of dust, the identification of asbestos particles in the sputum or in the lungs after death usually leads to a diagnosis of asbestos pneumoconiosis. However there are exceptions to this rule since the formations defined as asbestos particles are sometimes, though rarely, found in the lungs of persons never having come in contact with asbestos dust. Nordmann reported similar observations in which he spoke of pseudo-asbestos particles. Langer published a short report on the presence of asbestos particles in an employee of the glass wool industry. More recently during a verbal discussion, Doerr also mentioned one case where asbestos particles were observed in the lungs of a woman who had never been exposed to the effects of asbestos dust on an occupational basis. In spite of these exceptions, however, we can come to the conclusion that the detection of asbestos particles generally does warrant a diagnosis of asbestos pneumoconiosis and that these unusual observations of asbestos particles without previous exposure to asbestos dust are really exceptional.

As we know, the dusting of the lung tissue with a given quantity of asbestos dust for a given duration can lead to fibrosis of said lung tissue. This fibrosis also belongs to the lung diseases subject to compensation. Behrens recently determined through animal experimentation that asbestos fibrosis should be considered as a secondary symptom of a connective tissue encystment of foreign bodies and that the asbestos particles as such have no special significance as far as the lung tissue fibrosis is concerned. According to his studies, this type of fibrosis is much more a reaction of the tissue to long and fibrous foreign bodies.

On this point, expert experience has shown that not just any case of asbestos pneumoconiosis represents a disease subject to compensation. To qualify for a pension, it is not sufficient to determine the presence of asbestos particles in the sputum but also the previously mentioned connective tissue changes, fibrosis of distended lung tissue parts with functional respiratory and circulatory disorders. No additional information will be given here on the distribution of the asbestos dust in the lung tissue and on the type and extent of fibrosis in cases of asbestos pneumoconiosis. Please refer to the individual reports contained in the literature (Nordmann, etc.). The mineralogical and chemical nature of asbestos particles was defined by Beger in several of his works and more recently in a report on the meeting of the German Pathological Association in Kiel in 1949.

Under certain conditions, however, the dusting of the lung tissue with asbestos dust does not result exclusively in fibrosis of the lung tissue. Asbestosis can also be accompanied by carcinoma of the lungs. This fact is particularly emphasized by the inclusion of asbestos pneumoconiosis among pneumoconiosis diseases. As we know, only a few types of pneumoconiosis diseases are accompanied by the appearance of lung carcinoma. These include the so-called and best known Schneeberg lung cancer with a high incidence among workers of the Schneeberg region. For purposes of completeness, let us add that more recent studies have also indicated the high incidence of lung cancer among chromate workers. This requires a general specification. The incidence of lung carcinoma in

connection with silicosis is definitely low. Statistical studies have shown that the number of lung carcinoma cases among workers suffering from silicosis did not proportionally exceed the number of lung cancer cases in persons not suffering from silicosis (W. Fischer, Sporlein and many others). During the expert examination of lung carcinoma in persons suffering from silicosis, there are very few cases where a correlation can be drawn and where the carcinoma can be shown to have originated within the frame of a silicotic callosity (di Biasi).

The conditions are different as far as lung carcinoma with asbestosis is concerned. The correlation between the appearance of this type of cancer and the effects of the specific type of dust was demonstrated through animal experimentation (Nordmann) and recognized by legal insurance regulations. Related observations with partial reviews of previous publications were reported by Nordmann, Wedler and Linzbach, Gloyne and Berger among others. Still the number of lung carcinoma cases among patients suffering from asbestosis is evidently small as compared to the number of cases reported in the literature. With the exception of one isolated case which I personally reported in the year 1943, I was only able to find 17 such cases in the literature, and I feel that this justifies my discussing three additional observations of my own.

Information with regards to my first case was already published in the present journal in the year 1947. This was a case of a man who died at the age of 71. He had been employed as carder in an asbestos plant for a period of 11 years and had been found to be suffering from severe asbestos pneumoconiosis six years prior to his death. During a period of hospitali-

zation shortly prior to his death, a diagnosis of lung carcinoma was given. The autopsy revealed the presence of asbestos fibrosis of the lung tissue and diffuse carcinomatous infiltration of the right lung lower lobe. Carcinomatous growths were also present in the other lung lobe as well as extensive pleural carcinosis on the right. Cancerous metastases were found in the intrathoracic and intra-abdominal lymph nodes, the spleen, both kidneys, the left suprarenal gland, the liver, the large intestinal wall, the ribs, the vertebral column, the left femur and the scalp. Please see the following discussion of three of my own cases with regards to the distribution of the carcinomatous growth in the right lung lower lobe and the time/localization relationship between asbestosis and lung carcinoma.

I had not as yet reported on the two following cases. One of these concerns a woman who died at the age of 57, the other a man who died at the age of 53.

The 57-year-old female was hospitalized in the Medical Clinic of the St. Johannes Hospital in Dortmund in October of 1950.* She was complaining of extreme shortness of breath, bloody expectoration, high temperature and night-sweat. Prior to her admission, she had lost 6.5 kg within a very short period of time. Her medical history did not reveal

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*I wish to thank Dr. Nagel, head physician, for providing us with detailed clinical information on the case.

any significant information with regards to her disease. Upon her admission, she was in extremely bad physical and nutritional condition. Over the right lung towards the base was an area of suppression with small to moderately vesicular rattling sounds. The blood sedimentation rate was 51/78 mm. During her hospitalization, her temperature first remained around 38°C. During that time, the patient had expectorations which were round and light red in color and sometimes closely resembled raspberries. There were no tubercle bacilli to ever be detected. On the X-rays, there was a striped and spotty shadow in the under part of the left lung with filling of the left Sinus phrenico-costalis and the transversal formation of strands. In October of 1950, the patient's sputum was sent for analysis in the search for tumor cells (E. No. 7 191/50). The latter was found to contain numerous typical asbestos particles (Fig. 1).

The patient's fever gradually disappeared during the rest of her hospitalization, but she developed increasing dyspnea. The area of suppression in the right lung lower lobe persisted as well as abundant expectoration of 50-250 ccm per day. With increasing cachexia, her complaints increased and took the form of a cardiac insufficiency. The patient finally died in March of 1951.

As far as the report of the autopsy performed on the day of death is concerned (see No. 109/51), only the relevant points will be given here. Both lungs were found to have superficially grown together with the adjacent parts, particularly the left lower lobe. The left lung was larger and heavier than normal. On the surface cut of the entire thickened tissue, the lower lobe showed partly firm and partly marrowy irregularly distributed whitish areas with black spots and stripes. Marrowy gray and white strands

and nests could also be found in the thickened whitish pleura. The consistency of the left upper lobe in the peripheral areas contained large amounts of air. Parts of the central sections appeared extensively thickened. The edges were coarsely meshed and decomposed when cut. The right lung was equally large but lighter. The pleura showed growth rests in the form of grayish white particle thickening. In the areas free of any growths, the pleura appeared light grayish-red in color, covered with black spots and stripes. The peripheral areas of the right lung were partly inflated in the form of a cushion. The general consistency of the right lung was irregular with some dense to firm or even paste-like thickening. On the sections, the peripheral areas corresponded to those of the left lung upper lobe, but the remaining lung tissue was partly whitish and partly grayish-red to dark red in color, had an irregular spotty appearance and was covered with black spots and stripes. The bronchia could be dissected in both lungs up to right underneath the pleura. There was no evidence of a circumscribed tumor being at the origin of the described marrowy and grayish-white macroscopic areas having the appearance of tumor growths in the left lung lower lobe. The p-like pulmonary route lymph nodes were also partly viscous and elastic and grayish-red in color with black infiltrations. The pericardium had grown together with the thickened pleura of the left lung lower lobe on the one side and with the heart on the other side. Upon incision, the tissue within this area was partly firm, grayish-white in color and sometimes marrowy gray.

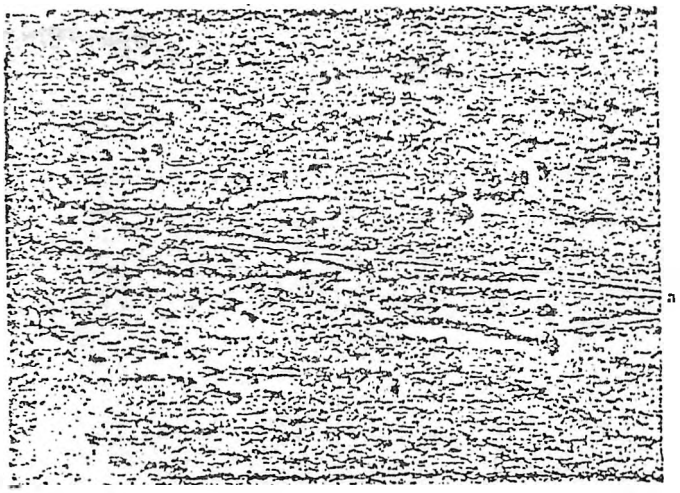

FIGURE 1. Asbestos particles in sputum (a). (see No.7191/50, 57-year-old female)

After releasing the growth on the inner wall of the left chamber, we found marrowy grayish-white areas which adhered to the epicardium and also attacked the superficial muscle sections of the left cardiac chamber wall. On the whole the cardiac cavities were all distended. The left half of the diaphragm was also involved in the pleural growth and had converted into a firm grayish-white tissue with small grayish-white marrowy nests. These grayish-white marrowy areas extended beyond the diaphragm onto the left lower lobe, the upper tip of the spleen, the left suprarenal gland and the stomach wall serosa. Additional findings during the autopsy are of no interest with regards to the question at hand.

Examination of the fine tissue showed the presence of wide alveolar spaces around the peripheral areas of the lung with thin continuous or torn septa. In other areas, all the lobes contained extensive irregularly-defined hyalin connective tissue areas. There was partial thickening of the connective tissue of the alveolar septa. In the alveoli as well as in the connective tissue, there were characteristic asbestos particles which were partly dumbbell-shaped, coin roll shaped and shiny brown spear or splinter shaped formations which reacted positively to the Berlin blue reaction.

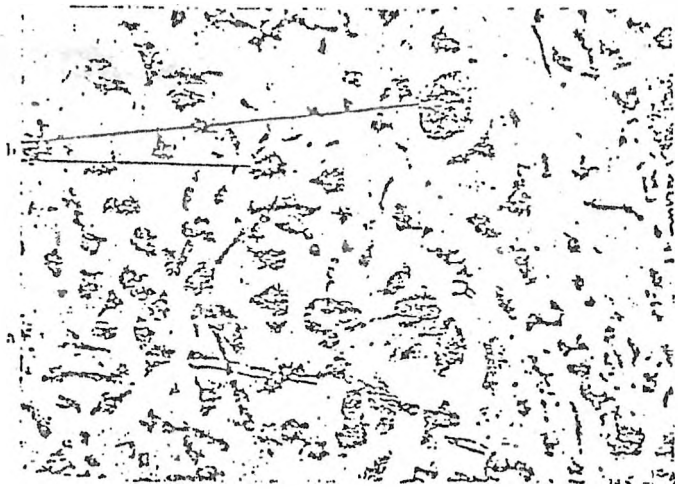

FIGURE 2. Asbestos particles inside squamous cell carcinomatous growth in the left lung lower lobe (see No. 109/51 57-year-old female). Asbestos particles = a, carcinomatous cells with mitoses = b.

Sections of the left lung lower lobe showed irregularly arranged pavement epithelial cells growing in irregularly infiltrating series and numerous atypical mitoses. Typical asbestos particles as described also grew between these epithelial formations (Fig. 2).

Other significant findings obtained during the histological examination of the remaining organs also showed epithelial growth in the left cardiac chamber which attacked the musculature from the epicardium and in the area of the left hepatic lobe, the left suprarenal gland, the upper tip of the spleen, the stomach serosa, the left pleura and the left half of the diaphragm.

Based on the pathological-anatomical findings which are in agreement with the clinical findings, this is a typical case of asbestos fibrosis of the lung tissue with extensive growth of the squamous cell carcinoma in the left lung lower lobe without a circumscribed point of origin accompanied by pleural carcinosis on the left with the carcinomatous growth affecting the pericardium, the heart, the left half of the diaphragm with

rupture of the latter and further attacks by carcinomatous formations on the liver, spleen, left suprarenal gland and stomach serosa.

Let us finally mention that in this case the pulmonary root lymph nodes also contains almost coreless connective tissue areas with individual asbestos particles; this is rarely observed since the size of the asbestos particles generally does not allow them to pass through the lymph tract of the lungs as easily as other types of dust (Fig. 3).

The occupational history showed that the patient had operated a tearing machine in an asbestos plant between the ages of 17 and 20. The raw material received in the form of balls was torn producing considerable amounts of dust, part of which remained in the working room due to the lack of ventilation.

FIGURE 3. Asbestos particles in lymph node of lung hilus (see No. 109/51, 57-year-old female). Asbestos particles = a, anthracotic pigment = b.

As mentioned above, the third case concerns a foreman who died at the age of 53. He was severely ill and died in August of 1951 in the First Medical Clinical of the Dortmund Municipal Hospital.*

*I wish to Dr. Woenckhaus, professor and head physician, for providing us with relevant clinical information.

He had apparently begun to feel ill only three weeks prior to his hospitalization. The disease began with constantly increasing shortness of breath and swelling of the foot as well as pain on the right side of the upper abdomen.

Upon his admission, he had a severe cyanosis of the lips with marked dyspnea and frequent coughing spells. Both lungs appeared congested. The cardiac edges were distended bilaterally. The liver was palpable approximately two fingers above the right lower side of the rib cage. The abdomen was meteorestically inflated. Both tibias were swollen by edemas. The patient was in such a poor condition that further clinical studies could not be made. He died during the night following his hospitalization and was autopsied shortly thereafter in the Pathological Institute of the Dortmund Municipal Hospital (see No. 305/51). Again, only the most important observations made during the autopsy will be reported here.

Both lungs were distended and had superficially grown together with the thoracic wall and the diaphragm. It thus overloaded the pericardium and had become very voluminous and thus heavy. Their free edges were flat or round. The visceral pleura showed large amounts of grayish-white growth residue and firm grayish-white thickening, particularly around the base and the tip. Even the intralobar spaces had grown together. The consistency of both lungs was firm and elastic and inflated in the circumscribed peripheral edges. On the cut surface, the lung tissue had diffuse grayish-brown-red spots with isolated small, soft, black spots and stripes which were not altogether extensive. In the lower lobes,

particularly, the cut surface also showed an extensive fine, grayish-white mesh or network. There were no circumscribed nodular formations to be seen. The walls of the bronchia appeared firm and somewhat compressed by the surrounding viscous and elastic lung tissue. These could however be removed by cutting their fine branching all the way underneath the pleura. Their mucous membrane was grayish-red to dark red in color and covered with a glutinous grayish-red tough slimy fluid. The lung vessels were empty and the pulmonary hilar lymph nodes were about the size of two beans, soft, partly black and partly with gray and white spots.

Since even during the autopsy I already suspected asbestosis due to earlier observations of lungs, an untreated specimen was prepared. The tissue fluid obtained from the cut surface of the lung was microscopically found to contain numerous typical asbestos particles.

The two suprarenal glands also contained grayish-white marrowy areas as well as some small rests of the suprarenal parenchyma. The heart was enlarged and distended and the right cardiac chamber wall was particularly thickened while the right cardiac chamber orifice was highly distended. The heart weighed 465 g. Finally, the inner organs were filled with congested blood with 300 ccm ascites.

One point of lesser importance with regards to this question but which played a significant role in promoting the patient's death was arteriosclerosis of the coronary arteries with small callosity formations in the cardiac musculature.

A study of the fine tissue again showed alveolar septa with distended connective tissue in all lung lobes, with said septa partly covered with asbestos particles. Several alveolar spaces also contained numerous groups of asbestos particles of various forms with some of them having the above-mentioned characteristic dumbbell or coin roll shape, others in the form of glossy brownish spear or splinter-shaped formations. Large, irregularly-defined connective tissue areas were present in the lower lobes. Between these connective tissue processes and more particularly in the lower lobe, there were smaller epithelial cell nests and strands irregularly distributed throughout the other lung lobes. These cell nests and strands sometimes totally filled the alveoles and often showed the presence of atypical mitoses and polymorphic cores. There was no circumscribed point of origin of these epithelial formations to be found. Numerous asbestos particles were also present between these epithelial cell nests. Finally, sections of the peripheral areas of the lung showed very large alveoles with thin continuous or torn septa.

In addition to residues of lymphatic tissue, the pulmonary hilar lymph nodes showed an irregular and diffuse infiltration of epithelial cells with the above structure between the connective tissue areas. There were also isolated asbestos particles to be found here.

The suprarenal glands also showed a diffuse infiltration of epithelial growth with numerous atypical mitoses.

This case is therefore also a case of asbestosis with fibrosis of the lung tissue and extensive carcinomatous growth in the lungs. This

led to the formation of metastases in the pulmonary hilar lymph nodes and in both suprarenal glands.

Based on these findings, we attempted to obtain an occupational history of the patient. This was unfortunately impossible since the patient was a refugee and no information was available on his previous occupations. We did find out that he had been employed in an asbestos plant for a long period of time but could not obtain any information with regards to the duration and nature of his work.

The occupational anamnesis is of great importance in diagnosing carcinoma in a patient suffering from asbestos pneumoconiosis. Nordmann pointed out some legal points which apply to the presence of carcinoma in a case of asbestosis. In a number of patients who died from asbestosis and carcinoma, lung carcinoma had originated at an early age. This, however, did not apply to my observations, especially since cases of bronchial or lung carcinoma without asbestosis are now more frequently seen among the lung population. On the other hand, one other point appears of significant interest. In the majority of cases of lung carcinoma with asbestosis, there seemed to be an equal period of time between the time of employment in an asbestos plant and the time of death due to lung carcinoma. Nordmann found this period of time to be 18 years; this also applies to my first case. In my second case, however, there was a period of 37 years between the time of employment in an asbestos plant and the time of death as a result of lung carcinoma in a case of asbestos pneumoconiosis; the latency period could not be determined in my third case due to the above-mentioned reasons.

Of course the figure quoted by Nordmann is merely an average and there can be increasing and decreasing variations. Twelve to 42-year periodswere quoted by Bauer between the initial exposure to asbestos dust and the development of cancer, regardless of whether there was constant exposure to the dust prior to the development of cancer or whether there was a dust-free interval in between. Of course if we are to speak of lung cancer in conjunction with asbestosis, histologically there must necessarily be an infiltration of the lung tissue with asbestos particles in addition to cancer.

The reports received on the calculated rate of lung carcinoma among asbestosis patients fluctuates. Out of 50 autopsies of asbestosis cases, Gloyne found six cases or 12% accompanied by lung cancer. In a small number of patients who died of asbestosis, Nordmann calculated an average of 17% in which lung carcinoma was present simultaneously.

Based on my own cases, I am also in a position to confirm additional legalities pointed out by Nordmann on the higher number of primary carcinomas originating in a lower lobe of the lung. Given the nature of the carcinomatous spread in the 71-year-old male, we can assume that the said carcinoma originated from the right lung lower lobe. The carcinomatous growth in the 57-year-old female also had its primary seat in the left lung lower lobe. In the last case there was extensive carcinomatous growth in both lower lobes. Finally, one interesting point is that the majority of observations concerns squamous cell carcinomas; this also applies to my first two cases whereas the third involved carcinomatous growths of non-differentiated large cells.

Particularly significant and typical of lung carcinoma in conjunction with asbestosis or as a result of the latter is the multicentric origin of the carcinomatous growth in the lungs. In such cases, there is never any circumscribed point of origin to be found as would be the case with bronchial carcinoma. The cancerous formations are very irregularly distributed in the affected areas of the lungs so that we can consider multiple metaplastic carcinoma as characteristic of asbestosis.

In view of the undisputable correlation between asbestosis and lung carcinoma, we can now question exactly which factors can be of any significance for the development of carcinoma. We must consider the fact that the relatively large asbestos dust formation could promote coarse mechanical injuries to the alveolar stigmata which, under continued effect, could finally lead to excessive regeneration and epithelial metaplasia followed by cancerous degeneration. Surely this simple explanation does not in itself solve the problem of carcinoma development since this type of carcinoma also involves important and significant chemical processes.

SUMMARY

This is a discussion of the correlation between asbestos fibrosis of the lungs and lung carcinoma based on three of my own observations. Legalities relevant to this particular type of carcinoma are given, primarily with regards to the origin in the lower lobes and the multicentric development of squamous cell carcinomatous growth in the lungs.

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reabsorption which are independent of filtered Na load. 35 references. Theresa McKee

Study of mast-cells in human subjects with relation to atheroma, heparin and cholesterol. D. P. Basu. *Indian Heart J.* 4, 65–71(1952).—Mast cells occur in the human aorta, coronary artery, and lungs. Fewer occur in atheromatus vessels and under these conditions rupture of the cells occurs. Few mast cells occur in the lung when there is pulmonary hypertension and the pulmonary artery has undergone atheromatous changes. A large no. of mast cells occur in lung tissue when there is pulmonary tuberculosis with no atheromatous changes in the pulmonary artery. These findings suggest a close connection between mast cells, atheromatous changes, and cholesterol. It is suggested that the stress on arterial walls, which is caused by generalized or pulmonary hypertension, damages the mast cells with a subsequent reduction in heparin production; the power to rupture the globulin lipide bond then decreases. This agrees with the view that an increase in the no. of mast cells produces extra heparin and thus produces a lowered plasma cholesterol concn. Theresa McKee

Lung carcinoma caused by asbestos inhalation. Fr. Boemke (Städt. Krankenanstalten, Dortmund, Ger.). *Med. Monatsschr.* 7, 77–81(1953).—The relation between fibrotic changes caused by asbestos deposits in the lung and carcinoma is discussed. The lower lobe is the site of predilection. Characteristic are the multicentered developments of flat epithelium carcinoma. A. E. Meyer

Determination of 17-ketosteroids in acne rosacea. Rodolfo Néstor Corti and Pedro H. Magnin. *Semana méd.* (Buenos Aires) 1953, I, 113–15.—The values found were normal in rosacea, higher in common acne, which difference is of diagnostic importance. A. E. Meyer

Altered liver function of chronic congestive heart failure. John M. Evans, Hyman J. Zimmerman, J. Grant Wilmer, Lawrence J. Thomas, and Clayton B. Etheridge (George Washington Univ., Washington D.C.). *Am. J. Med.* 13, 704–12(1952).—Impairment of the hepatic excretory capacity for Bromsulphalein was often marked, generally paralleling the severity of heart failure. Flocculation and turbidity tests were less frequently abnormal, the latter usually in assocn. with the hyperglobulinemia found in some of the patients. Serum bilirubin concns. were moderately increased in about 25% of the patients, particularly in those with higher levels of venous pressure. The serum albumin concn. was less than 3.5 g./100 ml. in 35 of 56 patients; the serum globulin was 3.59% or above in 15 of 56 patients. The impaired excretion of Bromsulphalein showed a pos. correlation with the height of the venous pressures; no significant correlation was observed with the degree of arterial O unsatn. 34 references. Barbara R. Murray

Autoimmune hemolytic disease and cryoglobulinemia associated with chronic lymphocytic leukemia. Hematologic and metabolic studies. Albert B. Craig, Christine Waterhouse, and Lawrence E. Young (Univ. of Rochester, Rochester, N.Y.). *Am. J. Med.* 13, 793–804(1952).—Reductions in the no. of circulating lymphocytes, in the size of the peripheral lymph nodes, and in the rate of red cell destruction were sustained for 9 months following administration of 1250 mg. adrenocorticotropic hormone (ACTH) in 15 days. A 2nd course of ACTH produced a less marked but still well-sustained response. The expected loss of N, P, and K occurred. 32 references. Barbara R. Murray

Observations upon the absorption of urinary constituents after ureterosigmoidostomy. The importance of renal damage. C. D. Creevy and M. P. Reiser (Univ. of Minnesota, Minneapolis). *Surg., Gynecol. Obstet.* 95, 589–96(1952).—Absorption of urinary chlorides through the mucosa of the colon after ureterosigmoidostomy can cause hyperchloremia and acidosis. Barbara R. Murray

Systemic lupus erythematosus. A review of the literature. S. William Ross and Benjamin B. Wells (Univ. of Arkansas, Little Rock). *Am. J. Clin. Pathol.* 23, 139–60 (1953).—The review includes changes in the blood chemistry and the "L.E." factor. 193 references. J. T. M.

Electrolyte equilibria in erythrocytes during diabetic acidosis. George Nichols, Jr., and Nancy Nichols (New England Deaconess Hosp., Boston, Mass.). *J. Clin. Invest.* 32, 1–5(1953).—Values for plasma and erythrocyte Na, K, and water during diabetic acidosis are compared with the values in 21 normal subjects. During acidosis the corpuscular and plasma water [illegible] while the water content was normal. Following therapy with insulin and 0.85% NaCl soln. the patients showed rapid clinical improvement and return of the plasma bicarbonate and water to normal. Undesirable side effects were occasional hypernatremia, const. transient hyperchloremia, and hypokalemia, which persisted several days. With treatment the erythrocytes lost no further K, but did lose water and Na. Na reaccumulated in the cells more rapidly than did K or water. In most patients, however, water and K were lower than normal at the time of discharge from the hospital. There is a parallelism between water and base shifts in the erythrocytes and in the total body mass during recovery from diabetic acidosis. 28 references. John T. M[illegible]

The cholate:cholesterol relationship in clinical and experimental nephrosis. Ray H. Rosenman, Meyer Friedman, and Sanford O. Byers (Mt. Zion Hosp., San Francisco, Calif.). *J. Clin. Invest.* 32, 121–4(1953).—An increased accumulation of bile acid (hypercholatemia) was found in the blood of human subjects with nephrosis and in the blood of rats in which exptl. nephrosis had been induced by injection of antirat-kidney serum when hypercholesterolemia was also present. The nephrotic rat also showed a diminished ability to rid his blood of excess injected cholate. Feeding of cholate to nephrotic rats appeared to prevent the decrease of plasma cholesterol, which usually occurred following the initial rise. John T. M[illegible]

Pulmonary hypertension. I. Pulmonary circulatory dynamics in patients with pulmonary emphysema at rest. Paul N. G. Yu, Frank Lovejoy, Jr., Howard A. [illegible], Robert E. Nye, Jr., William S. McCann, S. John Vitarelli, and Carol Gouverneur (Univ. of Rochester, Rochester, N.Y.). *J. Clin. Invest.* 32, 130–7(1953).—The degree of pulmonary hypertension varied directly with the severity of emphysema, hypercapnia, and anoxia. The O tension of arterial blood varied inversely with the mean pulmonary artery pressure, but did not parallel the other determinants. The O tension of arterial blood did not vary precisely with any of the determinants. The CO_2 tension of arterial blood correlated closely with mean pulmonary artery pressure, total pulmonary resistance, and arteriolar resistance but not with "pulmonary capillary" pressure. The ratio of residual vol. to total capacity varied directly with the pulmonary artery pressure and total pulmonary resistance. The role of anoxia in the pathogenesis of pulmonary hypertension is confirmed. CO_2 retention is probably important in raising pulmonary artery pressure and in increasing pulmonary vascular resistance. 33 references. J. T. M.

The effect of thyrotropic hormone on the metabolism of radioiodine in euthyroid, hyperthyroid and acromegalic individuals. David V. Becker, J. E. Rall, Wendell Peters, and Rulon W. Rawson (Sloan-Kettering Inst. and Memorial Center, New York, N.Y.). *J. Clin. Invest.* 32, 1–5 (1953).—The effect of a single intramuscular injection of thyroid-stimulating hormone (TSH) on the metabolism of a tracer dose of I^{131} was studied in 3 euthyroid, 3 hyperthyroid and 3 acromegalic patients. When administered 1 hr. after the tracer I^{131}, TSH increased the level of protein-bound I^{131} and I^{127} in the blood and of I^{131} in the urine. Methods are presented for the estn. of the total thyroid hormone discharged from the thyroid after TSH and for calcg. the total I content of the thyroid. Following a standard dose of TSH, euthyroid patients appeared to secrete more thyroid hormone than did hyperthyroid patients. The max. effect of TSH appeared in the first 24 hrs. in the hyperthyroid patients, and not until 48 hrs. in euthyroid patients. The hyperthyroid patients demonstrated an unusual ability in handling radio-I, which was characterized by a very rapid turnover rate of I by the thyroid with abnormally decreased serum protein-bound radio-I and urinary radio-I levels. 31 references. John T. M[illegible]

Histamine sensitivity and anaphylaxis in the pertussis vaccinated rat. Saul Malkiel and Betty J. Herpst (Northwestern Univ. Med. School, Chicago). *Proc. Soc. Exptl. Biol. Med.* 81, 689–91(1952).—Inoculation of rats with *Hemophilus pertussis* increased its sensitivity to histamine. Pertussis organism mixed with horse serum [illegible] enhanced the ability of the horse serum to induce anaphylactic sensitivity. Richard [illegible]

Electrophoretic studies of the serum [illegible] with experimental infectious anemia. [illegible] (Faculté de Médecine, Lyon, France). *C. R. Soc. Biol.* 146, 1[illegible].—Electrophoretic studies