FILE NAME: German Articles - Some with English Translation (GER)

DATE: 1960

DOC#: GER026

DOCUMENT DESCRIPTION: Medical Journal Article - Asbestosis

Archiv fur Gewerbepatholcgie und Gewerbehygiene, volume 18, pages 159-204, 1960

ASBESTOSIS*

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*Dedicated to Professor Heine in gratitude and respect on the occasion of his 65th birthday.

INTRODUCTION

In 1951, König presented a report at a meeting of North-West German pathologists concerning the histogenesis of asbestosis and asbestosis carcinoma of the lung, based on 16 cases of the Pathological Institute of the St. Georg Hospital in Hamburg. The investigation was aided by the fact that most of the cases were subjected to autopsy, mainly for diseases other than asbestosis. In many of them, the asbestosis was discovered in the course of the pathological and anatomical examination. The available material of this type has now increased to 36 cases, which demonstrate some of the problems discussed in the clinic from the standpoint of the pathologist. Through a more profound knowledge of the histogenetic problems, they may be brought nearer to a solution. For this reason, the author feels that publication is necessary.

ASBESTOSIS IS A DISEASE OF CIVILIZATION

In view of the rarity of asbestosis, it appears to be desirable to present briefly certain data concerning its importance as a disease of civilization, the conditions of its development and asbestos itself.

The date of the initial appearance of asbestosis is not known. Asbestos as a refractory and spinnable material, has been used and described in antiquity (Cooke, 1924; a detailed presentation by Frank, 1952), but on an industrial scale, it has been processed only since the middle of the past century. Its most important products are It-plates, asbestos cardborad, asbestos concrete plates and tubes, brake linings and

bands, gaskets, seals, filter- and gasket materials for acids. Modern technology is unthinkable without asbestos.

The disease of asbestosis was observed initially in England (Montague Murray 1900), then in Canada (1912, Wedler) and in Germany (Fahr and Feigl, 1914). The literature of asbestosis itself began in England in 1924 (Cooke). In 1927, numerous English and South-African papers were published; in 1930, asbestosis was recognized as an occupational disease in England. In 1951, Gloyne reviewed 121 autopsy cases of the period from 1920-1949. No such numbers were available in Germany, where papers on asbestosis did not appear until 1931 (Büttner-Wobst and Trillitsch, Kurger, Rostoski and Saupe). By 1943, Wedler had collected 29 autopsy cases, of which 18 were published. A few other cases were added in the meantime (Welz, Boemke, Werber, Weiss). According to Wedler, there must have been approximately 500 asbestosis patients in Germany, to which about 200 doubtful cases should be added. In 1939, Baader counted approximately 8,600 employees in the asbestos processing industry. Jacob and Bohlig estimated that there are about 4,000 asbestos workers in Germany at the present time, but this figure must be too low, because in the area of Dresden alone there are at least 2,000 asbestos workers. In Finland, Wegelius found 126 cases of asbestosis by radiological examinations of 476 asbestos workers.

Since 1936, severe cases of asbestos pneumoconiosis are being recognized as occupational diseases eligible for disability benefits. In 1952, the restricting qualification of "severity" was eliminated (M. Bauer). Since 1938, lung carcinoma qualifies for workman's compensation even in cases of slight asbestosis. The severity of the clinical

syndrome is evaluated differently in Canada than in Europe and South Africa (Cartier 1949). The prognosis of European and South African asbestosis is much less favorable than that of the Canadian disease. This is due perhaps to the type of asbestos. Different exposure conditions must also be considered. Not only the type and form of the asbestos, which differ widely, but also--as determined by experimental investigations (Vorwald, Durban and Pratt), the factors of dust density, exposure period and particle size are important.

ASBESTOS

The fibrous mineral, major deposits of which are located in the Urals, in Canada, in South Africa, and Northern Italy --lays in veins, crystallizes mostly transversely to the axis and consists of magnesium silicates and nonuniform components of lime, mica, various ores, quartz, clay-like substances, rutile (TiO_2) and talcum. Two principal types are distinguished: serpentine asbestos, mainly in the form of chrysotile asbestos which is primarily mined and processed in Canada and amphibole, which originates in South Africa and is added to the European asbestos. Both types are highly heat-resistant, but are very different chemically and physically. The monograph of Frank presents an excellent and encompassing review. Table 1 summarizes some of the most important data.

ASBESTOS DUST

The dust is generated during the opening up of the mulled (crushed) raw material, the mixing with binders (e.g. cotton), carding (combing) and during spinning, threading and weaving. The thickness of the dust

particles is 0.05-3 μ (Gardner and Cummings, Sundius and Bygden), the length of the particles inhaled 85-200 μ maximum (Beger, Beintker, Gardner and Cummings, Noro) or only up to 26 μ according to Knox and Beatties. In addition, irregular particles of other minerals with diameters of 0.5-10 μ may be found in the lungs.

ASBESTOS PARTICLES

Asbestos needles inhaled by humans are usually converted to particles in a few months. Only isolated needles remain permanently unchanged. The asbestos particles are generated by the formation of a so-called gel envelope around the needles; the envelope is brownish in color and contains much iron (Prussian blue reaction). The variety of shapes is great; piniform, claviform and dumbbell forms are found with segmental constrictions. Highly detailed investigations were performed of the genesis, the physical and chemical properties, and the fate of these formations, in the hope that the knowledge of the histogenesis and thus the cause of the progression of asbestosis can be emphasized (Beger, Sundius and Bygden, Holzapfel). According to more recent investigations by Holzapfel, the gel envelopes are created by the primary adsorption of carbohydrates, to which proteins are added. The primary bonding of OH-containing components, but not of amino groups, takes place with the release of the cations magnesium and iron from the lattice of silicon oxide chains, so that this cation exchange creates high-molecular organic silicon compounds, which are highly resistant to dissolution. It has been ascertained that the asbestos particles of amphibole survive decades in the lungs. Sundius and Bygden, also Ruska, found only amphibole

in the lungs but not chrysotile asbestos, which belongs to the serpentine type. In an investigation of the cause of carcinoma developing on a foundation of asbestosis, these are the particles that must be considered.

TABLE 1. Summary of the components and properties of important asbestos types (K. Frank, "Asbestos," Hamburg, Becker and Haag 1952).

	Chrysotile asbestos (Canada, Russia, Rhodesia, Cyprus)	Amphibole asbestos			
		Blue Asbestos (Cape)	Amosit (Transvaal)	Tremolite (Finland, Italy)	Antho-phylite (USA)
Components: silica	39.0-43%	51.1%	50.24%	55.1-62.02%	57.6%
Magnesia	35.1-42.6%	2.3%	--	27.2-29.5%	31.2%
Ferrous oxide	--	35.8%	32.0%	3.54-4.6%	5.8%
Iron oxides	0-4.9%	--	.7.8%	--	--
Alumina	0-3.5%	--	--	2.08-3.4%	0.9%
Water	14.0-16.5%	3.9%	3.0%	5.0-5.04%	4.5%
Alkalis	--	6.9%	2.12%	0.71-2.4% CaO	--
Acid resist-ance	soluble to 57%	good resistant	favorable resistant	good resistant	good resistant
Heat resist-ance	good brittle	good-low melting	good brittle	favorable to good	very good
Properties: Texture	soft to rough, mostly silky	soft to rough, rather rough	rough, but somewhat yielding	mainly rough, sometimes soft	rough, hard
Flexi-bility	very flexible	favorable flexible	poor com-pared to chrysotile	flexible to varying degrees	brittle, not flexible
Spinn-ability	very good	favorable	favorable	poor	poor
Impurities	Fe, Cr, Ni	Fe	Fe	lime	Fe

FINDINGS

1. Material.

Our report is based on 36 cases(*). In 20 of these, the occupational history was known. For the sake of clarity, these have been compiled in Table 2, while the remaining cases, where the history is incomplete, have been listed in Table 2.

2. Autoptic Findings.

The lungs. In summary, the picture that emerged was the following: most lungs were voluminous, heavy, of a more or less solid consistency that offered a noticeable resistance to the knife. The parenchyma appeared diffusely dense, tough, inelastic, especially subpleurally, and peribronchially. The reddish-brown section showed a fine, greyish-white to greyish-green net-like pattern and often felt rough, almost like fine sand or foam rubber. These changes were more marked in the apico-basal direction. In milder cases, they were slight and frequently limited to the lower lobes.

Besides these diffuse changes, there were also focal ones in a number of cases. There were areas containing air and compacted or callous ones, the latter especially basal, dorsal, and subpleural. Frequently observed were callous greyish-green to black nodules the size of peppercorns with star-shaped contours increasing in density in the apico-basal direction.

(*) My thanks for making the clinical data available go to Professors Bansi, Diebold, Hesse, Holthusen (General Hospital St. Georg , Hamburg), Dr. Belicke (General Hospital Wandsbeck, Hamburg), Professor Budelmann (General Hospital Rissen, Hamburg) and Professor Engelmann, Hamburg. Dr. Selberg (Path. Inst. of the General Hospital Barnbeck, Hamburg) made two cases available, for which I wish to express my gratitude. For the collection of cases since 1952, I wish to thank Dres. H. Hüsselmann, E. Kühl, J. Schlosshauer (Pathological Institute of the General Hospital St. Georg , Hamburg.

The bronchi, in particular the small ones, were frequently more or less dilated. Catarrhal and putrefacient bronchitides were often seen. The large branches of the pulmonary artery showed a smooth intima in most cases.

The lymph nodes at the hilus and at the bifurcation were in most cases slightly enlarged and brownish-grey.

The pleural membranes had in many instances grown together, often with callouses.

The most important autoptic findings in these cases have been compiled in Table 4, with special consideration of the morphological degree of severity of the asbestosis.

A classification of the morphological pulmonary changes according to their severity is possible only with reservations. We have largely forgone an evaluation of the histological sections, since they could not always be identified with both of the whole lungs, as can be seen from the description of the macroscopic pulmonary findings. The histological preparations represent a selected material, the finding being in most cases too severe rather than too mild in comparison to the macroscopic total finding. Diagnosis during autopsy was always the task of one person only (Professor Heine).

Thus, a classificaton was made on the basis of the macroscopic finding. Cases which were macroscopically inconspicuous and which were diagnosed only during histological examination, were called mild (= 1). Severe (= 3) were those cases, where the autoptic diagnosis permitted the conclusion that extensive and marked changes were present. All other

cases were evaluated as being moderately severe (= 2). In the few cases, where the autoptic diagnosis did not permit a classification, but where unambiguous radiological findings were available, the latter were considered in the sense of raising or lowering the grade (= 2-3). The findings from four cases were sent to us so that the histological findings had to be used as a basis for evaluation.

3. Histological Findings.

a) Lungs. Slight magnification revealed at first four structural characteristics: 1) deposits of small heaps of asbestos particles in the walls of the bronchioles and of a few asbestos particles in the alveolar end-sacs, 2) peribronchiolar and peribronchial and subpleural calloused areas, in part, radiating into the parenchyma or reaching it with finger-like formations, 3) a diffuse or focal dystelectasis and fibrosis of the alveolar skeleton, and 4) focal, substantial emphysema and bronchiectasis.

The asbestos particles, which attracted attention by their bright yellow to dark brown coloration when subjected to the customary staining methods, have already been described in the introduction.

A detailed examination is required by the deposits of asbestos needles and asbestos particles. A stronger magnification revealed, even in cases where years without symptoms had passed, asbestos particles and asbestos needles in small numbers. The tissue in which they buried themselves, was entirely without reaction. It was noteworthy that an occasional asbestos particle was found in a giant cell with its end protruding from the cell as a naked needle. The heaps of asbestos

particles were scattered in the alveoli of the respiratory bronchioles (Figure 1) and the alveolar ducts (Figure 2), or they were found in peribronchiolar callouses of calloused tissue (Figure 3). Appropriate cutting sometimes showed that the asbestos particles completely filled the alveoli. They were lying topsy-turvy, in most cases densely packed. Penetrated among them were macrophages and giant cells, or a granulation tissue had formed that surrounded and penetrated the cumulation of asbestos particles, forming a fine network of fibers (Figure 4). Sometimes, the asbestos particles were arranged radially--especially in the callosities--with the button-shaped, thicker end pointing toward the periphery (Figure 5). Despite not inconsiderable cumulations, the alveolar walls were still found to have remained quite fine, almost all had thickened and had become infiltrated with microcells.

The bronchiole and alveolus duct were often barely recognizable where a granulation tissue with microcell infiltrations had developed in the mucosa and become fibrous. This narrowed the lumen and cut the filled alveolus off from the lumen so that compact cumulations of asbestos particles lay completely isolated in a callosity-transformed alveolar wall (Figure 3). The lumen, as far as it still existed in these sections, was stripped of mucous membrane and contained a few asbestos particles and ample quantities of desquamated macrophages. The granulation tissue penetrated into the cell-filled lumen. The resulting picture was that of bronchiolitis obliterans (Figure 4). Both in the bronchioli and, especially clearly, in the alveolar ducts, the smooth muscles had coarsened considerably (Figures 1 and 2). These areas were still visible even in the calloused tissue.

TABLE 2. Survey of the cases with a known occupational previous history.

No.	Serial No.	Age	Sex	Period of expos. Date	Duration (yrs.)	Free interval yrs.	First symptoms Date	Years before death	Clinical diagnosis	Radiological finding
3	1016/39	63	♀	1916—1933	17	6	Disabled with asthma in 1933	6	Suspicion 1939	Negative
4	1999/39	41	♀	1918—1930	12	9	Bronchitis 1930	9	1933	Probably positive
6	G 2053/41	59	♂	?	15	?	?	—	yes	positive
9	491/48	53	♂	1924—1948	24	0	1930	18	70% disabled 1938	Probable 1938
10	835/48	47	♂	1922—1937	15	11	1935	13	30% reduction of ability to work	positive
11	993/48	49	♀	1927—1933	6	15	Before 194?	?	1947	positive 1948
12	436/50	75	♂	?	30	?	?	—	No	positive but no diagnosis
13	823/50	39	♀	1926—1937	11	13	935: asthma after a cold	15	to 1949:no 1950: suspicion	1959: negative 1950: suspicion
14	227/51	61	♀	1907—1912 1927—1930	5 3 } 8	15 21	938:Bronch. (asbestos particles in expectorate)	13	Confirmed since 1938	?
15	276/51	55	♀	1925—1930	5	21	1950	1—2	No	positive, but no diagnosis

TABLE 2. (Continued)

16	567/51	45	♀	1928—1931	2½
17	630/51	44	♀	1928—1935, 1941—1949	7, 8 } 15
20	851/52	60	♀	1910—1917	7
22	923/52	59	♀	1946—1952(?)	6
23	198/53	41	♂	1929—1939	10
24	967/54	45	♂	1928—1936	8
29	1318/55	55	♂	1937—1955	18
30	1428/55	54	♂	1937—1946	9
31	1493/56	72	♀	?	25
34	393/57	47	♀	1928—1932, 1947	4, 1 } 5

20	1950	1	No, although occupational anamnesis was known	. Probably negative
2	?	—	suspicion because of occup.histo	Probably negative
35	1951	1	No	?
0	Prob. none	—	No	—
14	from 1939 med. superv for Tbc	14	No	Presumably negative
18	none	—	No	No
0	1952	2—3	1955 ability to work reduced by 30%	1944, 1951, 1953: negative, 1955 positive
9	1952	2—3	1955 susp. because of previous occupational history	negative
7	1956	10 weeks	suspicion, hospitaliz. for "dust lung"	1956: suspicion
15 9	1950	7	1950	Presumably positive

TABLE 3. Survey of cases with incomplete previous histories

No.	Serial No.	Age	Sex	First symptom	Years before death	Clinical diagnosis	Radio-logical findings
1	G 209/39	46	♀	1935 "lung disease"	4	2 wks. before death	positive
2	G 2110/39	55	♀	?	—	?	?
5	2076/39	52	♀	None	—	Probably no	—
7	G 1665/48	48	♀	?	—	Yes	—
8	109/48	67	♂	1928(?): Dry Pleuritis	20(?)	No	Asbestosis negative
18	15/52	46	♀	1928 treatment 1940: Pleuritis	24 12	No No	Since 1928 "callosi-ties"
19	248/52	62	♂	None	—	No	No
21	852/52	70	♀	Presumably None	—	No	—
23	1051/54	60	♂	Asthma, date?.	?	No	Presumably negative
26	1122/54	56	♀	None	—	No	negative
27	558/55	52	♀	?	—	No	?
28	879/55	63	♀	1955	10 weeks	No	—
32	15/57	61	♀	No	—	No	negative
33	296/57	57	♀	No	—	No	negative
35	1063/57	65	♂	?	—	No	negative
36	1039/57	77	♂	1953: "emphy-sematous" bronchitis allegedly before 46 yrs. ago	4 (46?)	No	positive, but no diagnosis

TABLE 4. Listing of the most important autoptic findings.

Degree of asbestosis: 1 = slight, 2 = moderate, 3 = severe (for details, cf. text); degree of anthracosis: – = not mentioned in autoptic diagnosis; moderate: = all cases which were not expressly termed severe, serious, etc., in the diagnosis.

No.	Main disease cause of death	Degree of asbestosis	Pulmonary carcinoma	Pulmonary tuberculosis	Degree of anthracosis
1	Material sent in (probably asbestosis)	Probably 3	--	--	?
2	Material sent in (probably asbestosis)	Probably 3	--	--	?
3	Tuberculosis, right cardiac insufficiency	2	--	Severe scarification of the upper lobes, middle lobe and of apical sections of the lower lobes. Frenher caseation in right lower lobe, pleuritis right	--
4	Asbestosis, right cardiac insufficiency	3	--	--	--
5	Sepsis	1	--	--	--
6	Pulm. carcinoma (material sent in)	2-3	Left lower lobe	--	?
7	Material sent in (probably asbestosis)	2-3	--	--	?

TABLE 4. (Continued)

No.	Main disease cause of death	Degree of asbestosis	Pulmonary carcinoma	Pulmonary tuberculosis	Degree of Anthracosis
8	Tuberculosis, pulmonary embolism	2	--	Indurating tuberculosis of the right upper lobe with some exudative foci empyema 1000 cm^3, cavern and chronic pneumonia in right lower lobe	--
9	Pulmonary carcinoma	3	Left lower lobe with diffuse infiltration, nodular metastases in right lower lobe	--	Moderate
10	Pulmonary carcinoma	3	Right lower lobe, invasion of mediastinum	--	Severe
11	Stomach carcinoma	3	--	--	Severe
12	Hydronephrotic atrophic kidney, uremia	2-3	--	Slate-like induration of right upper lobe	--
13	Pleural endothelioma	3	Over right lower lobe, also in right lower lobe	--	Severe
14	Asbestosis	2	--	--	Moderate
15	Glomerulonephritis uremia	3	--	--	Moderate
16	Pleural endothelioma	2	Over left lung, extensive invasion subpleural and in the hilus	--	--

TABLE 4. (Continued)

No.	Main disease cause of death	Degree of asbestosis	Pulmonary carcinoma	Pulmonary tuberculosis	Degree of Anthracosis
17	Peritoneal carcinoma	2-3	--	--	Moderate
18	Peritoneal carcinoma	2-3	--	--	Severe
19	Ca. of the urinary bladder, uremia	1	--	--	Moderate
20	Stomach carcinoma, cardiac infarct	1	--	Carnifying and scarifying tuberculosis of both upper lobes w/ chalky foci.	Moderate
21	Cardia carcinoma	1	--	--	Severe
22	Esophageal carcinoma	1	--	Chalky focus in right upper lobe	Moderate
23	Pulmonary ca.	1	Right lower lobe	Chronic-cirrhotic tuberculosis of both tips w/ minimal caverns	Severe
24	Pulmonary embolism after urethral injury	3	--	Bilateral slate-like scars in tips	Severe
25	Bronchial asthma, insufficiency of right heart	1	--	Scars in tips of both upper lobes	--
26	Pulmonary carcinoma	1	Left upper lobe in tuberculous induration	Indurated Tbc of tip w/ fresh caseation	Moderate
27	Pleural endothelioma	Presumably 1	Over right lung	--	Moderate

TABLE 4. (Continued)

No.	Main disease cause of death	Degree of asbestosis	Pulmonary carcinoma	Pulmonary tuberculosis	Degree of Anthracosis
28	Peritoneal ca. Tbc, cardiac infarct	Probably 3	--	Chron. cavernous Tbc of both lungs carnifying pneumonia in left lower lobe, fresh scattering	Moderate
29	Pancreas ca.	2-3	--	--	Severe
30	Pulmonary ca.	2	Left lower lobe	--	Severe
31	Asbestosis	3	--	Old indurating Tbc with fresh activity	Moderate
32	Pleural endothelioma	2	Bilat., especially right lower lobe	--	Severe
33	Ca. of sigmoidal colon	2	--	--	Moderate
34	Dermoid of left ovary stomach ca.	3	--	--	Moderate
35	Pulmonary ca.	1	Left lower lobe, spread into both pleural cavities	Slatey focus in right tip	Severe
36	Asbestosis	3	--	--	Severe

Figure 1. Respiratory bronchiolus with cumulations of asbestos particles in the alveoli (case 4, hematoxylin-eosin, oc. 10, lens 10).

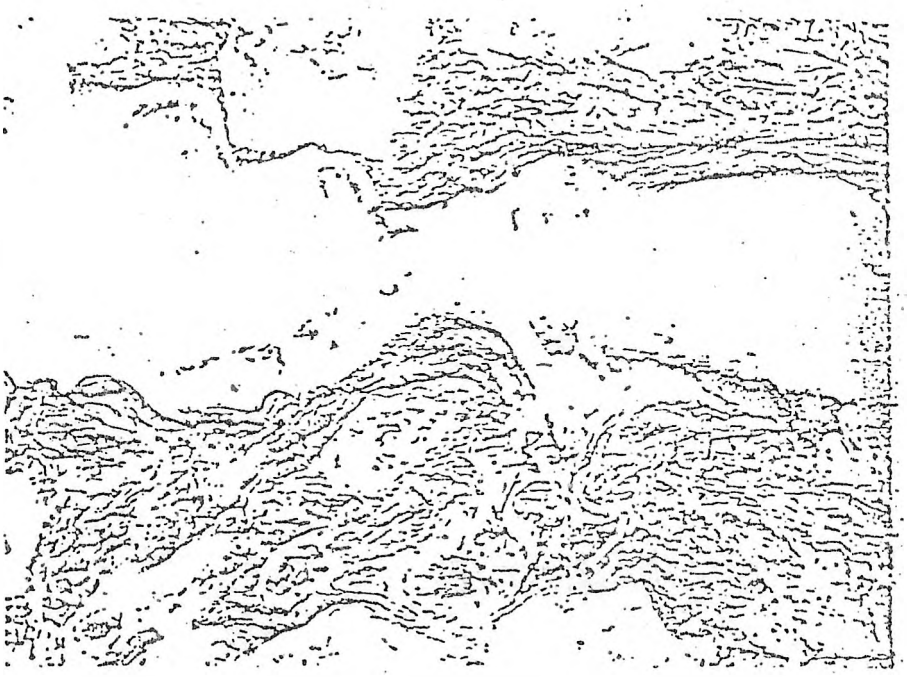


Figure 2. Alveolar duct with cumulations of asbestos particles in the alveoli (case 5, hematoxylin-eosin, oc. 10, lens 10).

Figure 3. Peribronchiolar indurated tissue with cumulations of asbestos particles (case 6, hematoxylin-eosin, oc. 10, lens 10).

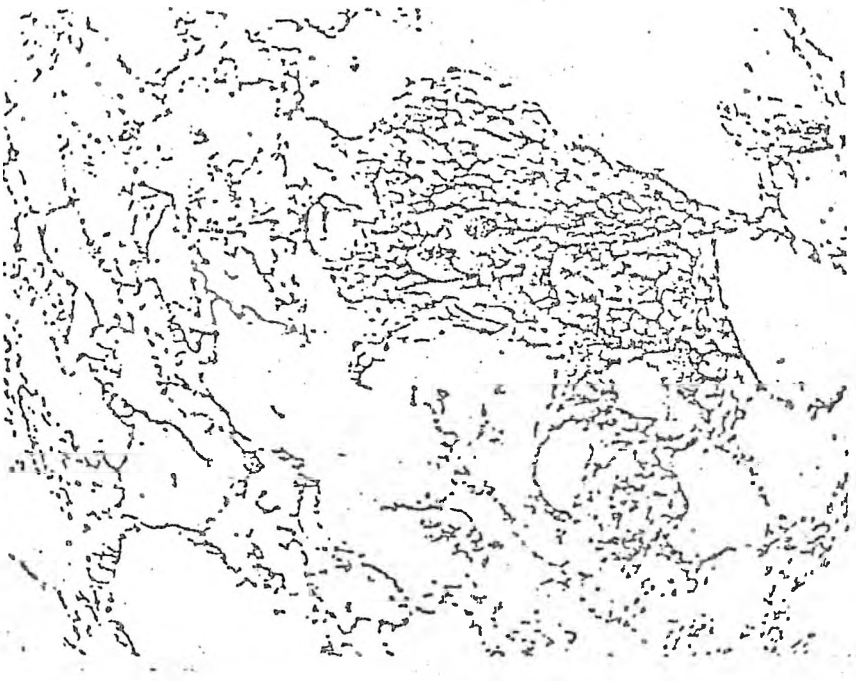
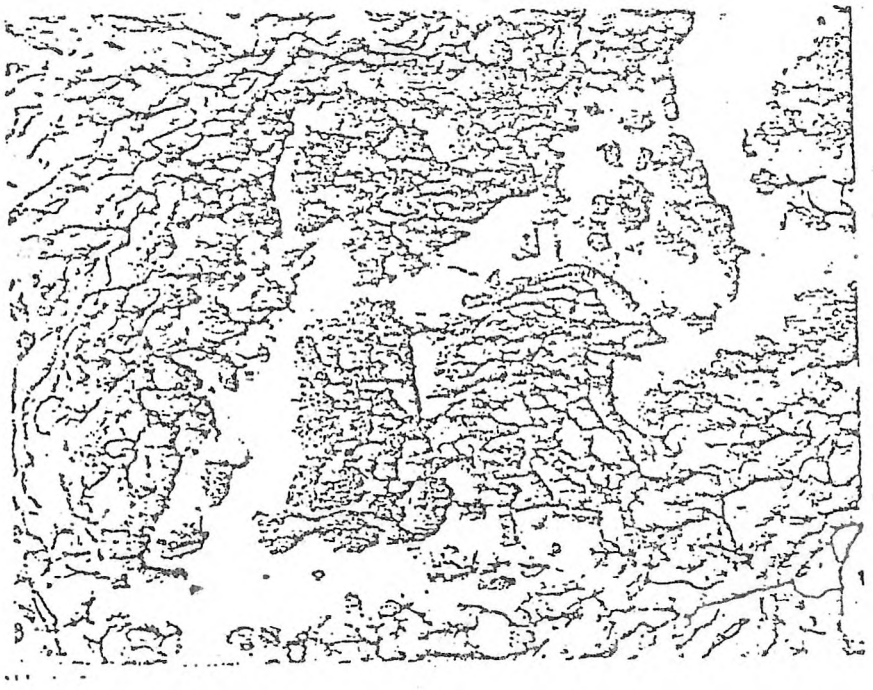


Figure 4. Bronchiolitis obliterans. Cumulations of asbestos particles in the lumen, partially enclosed by giant cells and partially infiltrated by a granulation tissue (case 7, Tibor-Pap, oc. 10, lens 40).

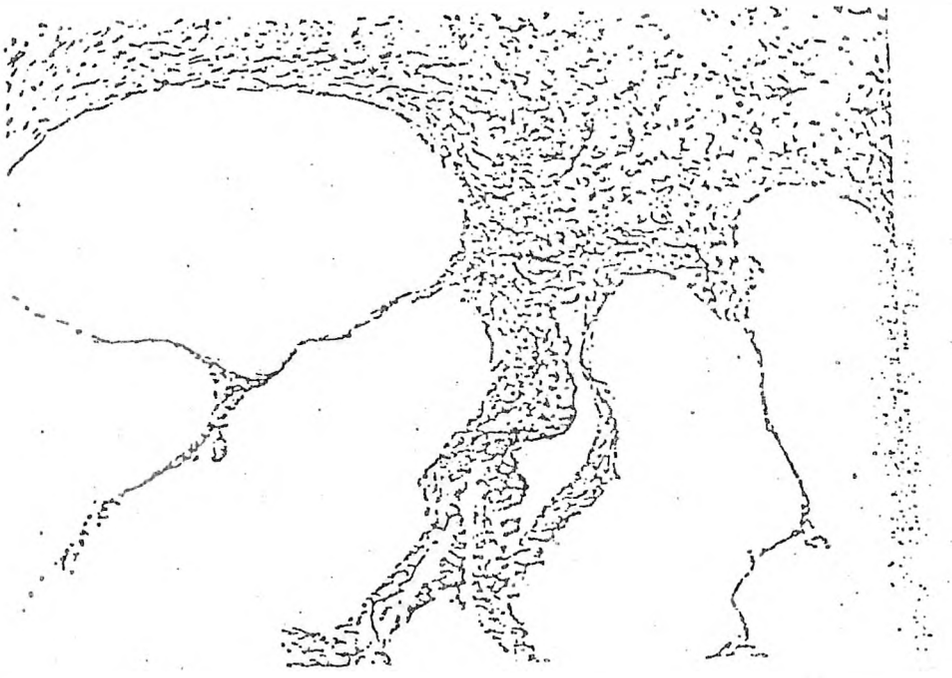


Because of the addition of fibrous-collagenous material tending toward hyalinization in the loose, peribronchial connective tissue layers, a structural definition of the bronchiolar wall as distinct from the adjoining parenchyma was no longer possible. The severely fibrous tissue radiated into the alveolar structure, which was itself more or less fibrous. The whole peribronchial tissue was infiltrated at varying degrees by small cells and showed some asbestos particles. In a few cases, dilated lymph paths were found within the peribronchial fibrotic areas, in which lay macrophages and short asbestos particles.

Figure 5. Radially arranged asbestos particles in a band-like callosity (case 5, hematoxylin-eosin, oc. 10, lens 40).

In advanced cases, the parenchyma contained scattered roundish and band-like callous areas (Figure 6). There were no structural indications as to the location where these foci had formed. Some showed a few characteristics of hyperplastic, smooth muscles and cumulations of asbestos

Figure 6. Marked emphysema, hand-shaped callosity and obliteration of the parenchyma (case 24, hematoxylin-eosin, oc. 10, lens 10).



particles strung up in a rosette shape, sometimes capped by large plasma-rich giant foreign body cells (Figure 5). In other layers of the callous tissue, some particles and frequently rows of dust cells.

Ying in the alveolar terminal sacs were short asbestos particles in small numbers. These alveoli showed desquamation of alveolar epithelium and also giant cells. While in the early stages, the parenchyma showed a mild emphysema, the advanced stages, where the bronchiolar and peribronchiolar processes of callous formation increased, were characterized by dystelectasis, sometimes of a very marked degree. Also present were an alveolar desquamative catarrh, small-celled infiltrates in the interstitial space and finally also a lattice fiber hyperplasia and extensive fibroses. The sclerosis of the alveolar septum sometimes reached a considerable degree of severity. Thus, there were pictures

pointing to a collapse induration. Instead of the desquamated alveolar epithelium, a granulation then blocked the remainder of the lumen. Finally, in a few cases, connective tissue obliterations of whole areas of the parenchyma were observed, combined with the wasting of the elastic fibers. These obliterations involved primarily the subpleural and peribronchial areas. The vessels that supplied such sections, showed swelling and hyalinization of their walls, loss of the tunica elastica int., intima proliferations and fibrous-hyaline densification of the adventitia.

In cases where the changes were mild, only a portion of the bronchioli were involved in the above-described manner, while some appeared unchanged. No asbestos particles were seen in these cases. The irregular involvement was not bound to relatively large areas, such as perhaps a lobe, but was evidently circumscribed by one or several alveoli. These systems revealed a tendency toward the development of marked emphysema at an early stage. At advanced stages of the changes, such emphysematous foci were found between indurating, fibrous sections of the parenchyma (Figure 6). In extensive indurations, there were occasionally multi-chambered systems of spaces separated from each other only by trabecular structures of fibrous tissue. These contained air, mucus, expelled epithelial cells, leukocytic exudate or mushroom-shaped granulation tissue although generally speaking no asbestos particles. Frequently, they were lined with epithelium. This was in part flattened, such as in mucus-filled spaces, but partly also cubic or cylindrical so that this picture resembled that of a glandular structure, such as the prostate. The phenomenon was

Figure 7. Callosities and rearrangement; epithelial destruction and re-formation, mucus retention (case 7, hematoxylin-eosin, oc. 10, lens 10).

that of an adenomatous restructuring (Figure 7). The original structures of the airways were no longer recognizable.

The bronchial epithelium must be examined by itself. In the respiratory bronchioli, where asbestos particles and processes in the sense of bronchiolitis obliterans were found, there was frequently no epithelium. In the unchanged sections of the bronchioli, the epithelium was intact. Hyperplastic formations were found here in some cases, where cubic epithelium had become multi-layered or irregularly proliferating in bundles in the manner of a cylinder epithelium. Atypical developments of a few or several cellular characteristics were registered and there were some findings of a rich, intracanalicular epithelial proliferation, which could not be interpreted as carcinomatous only because of its sharply basal outlines. This applies in particular to formations

which recall squamous cell carcinomas. The nature of the atypical feature may differ greatly even in one and the same case. The described epithelial changes were most marked in the adenoma-like transformation areas that have already been described.

The picture of pulmonary asbestosis as described here must yet be supplemented by a summarizing description of the carcinomatous findings. These did not offer a uniform picture; small- to polymorphous large-celled carcinomas were just as frequent as uniform microcellular carcinomas. In case 35, squamous cell carcinoma appeared.

Locally, there were some formal relationships to the described adenomatous transformation process. In case 6, for example, there was a polymorphous large-celled carcinoma in callous areas of connective tissue adjoining bronchiectases, in which atypical epithelial proliferations were conspicuous. In two cases, a microcellular carcinoma showed transitional stages either to a large-celled carcinoma (case 10), or to formations resembling squamous cell carcinoma, enclosed by callosities (case 9). But, these callosities enclosed open areas lined with cylinder epithelium, which tended on the one hand to atypical intra-canalicular proliferations and marked invasions of the connective tissue wall, on the other hand, so that it was not possible to make a reliable distinction between carcinoma and the atypical, hyperplastic epithelium. While these open areas were generally free from asbestos particles, there were large numbers of them in the callous tissue. Similar relations between carcinoma, atypical hyperplastic epithelium and callous tissue were also discerned in other cases. They were observed, in particular, in cases of pleural endotheliomas.

Concerning the parallel existence of asbestosis and tuberculosis, no peculiarities were observed. Asbestos particles may occur in all tuberculous structures, be it in areas of cheesy degeneration, be it in unspecific, perifocal connective tissue. Giant foreign body cells containing asbestos particles were found lying next to giant Langerhans cells.

b) Lymph nodes. In regional lymph nodes of the hilus and the bifurcation, small asbestos particles were found. They were usually located in circumscribed areas of the peripheral sinus, but occasionally also in the central sinuses. Giant cells did occur. Other findings were a marked sinus catarrh and histiocytic proliferations. The proliferated endothelial cells of the sinuses give the Prussian blue reaction. Small callosities were seen in some cases. Besides asbestos particles, brownish or blackish clods and lumps were also found frequently, often phagocytized by giant cells. Judging by their shapes, these were evidently fragments of old segmented asbestos particles. These fractions also gave the Prussian blue reaction.

The tracheo-bronchial lymph nodes almost always contained asbestos particles and their fragment in relatively large numbers, sometimes also needles measuring up to about 70 µ in length. In some cases, a few such fragments were determined in the lymph nodes of the neck (Figure 8). The degree of involvement of the lymph nodes appeared to correspond to the degree of severity of the pulmonary asbestosis.

c) Paranasal Sinuses(*). In one case, the maxillary sinus, the frontal sinus, and the sphenoidal sinus were examined. All sections

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(*)These studies were performed by Dr. H. Hüsselmann and Dr. J. Schlosshauer.

Figure 8. Lymph nodes of the neck: sinus containing asbestos particles (case 4, hematoxylin-eosin, oc. 10, lens 10).

showed short asbestos particles up to a length of about 40 μ and also small to moderate numbers of fragments. But in addition to these, highly edematous, submucous tissue was found to contain ample amounts of coarse particles containing iron, which were obviously fragments of disintegrated asbestos particles. There was no tissual reaction apart from a slight microcellular infiltration.

Irregularly distributed asbestos particles lying singly or in groups were also determined in the tonsil and pharyngeal tonsil. Their lengths reached 70 to 90 μ. Likewise, there were fragments, some with giant foreign body cells, which appeared to have enclosed some of these particles. Close to some of the particles were the beginning of fibrous scarification.

d) Systemic Organs. In the livers, kidneys, and myocardiums of the nine cases that were examined in this respect, no asbestos particles were found. But, of 13 spleens that were dissected, nine showed asbestos particles of lengths of up to about 50 μ, or large fragments of such particles, still clearly recognizable as such. Most of them were isolated, only sometimes they were arranged in small groups, often in the peripheral sinuses at the trabeculae or otherwise sparsely distributed throughout the whole organ. In some cases, a very slight anthracosis of the spleen was diagnosed.

DISCUSSION

First, we shall discuss the casuistic data reported above. They confirmed much of what is known today of asbestosis. A detailed screening, however, also uncovered a number of facts, which are still being discussed or which have not yet been sufficiently recognized. This raises questions that direct our attention to the histiogenesis of asbestosis. For this reason, the concepts presented at Lübeck (König) shall be presented in greater detail. These permit a discussion of the questions that have remained open with respect to these case histories. The result, in our opinion, leads to certain consequences in the fields of occupational hygiene and official medical evaluations. The discussion thus consists of four parts.

1. Case Histories.

a) Selection. Our patient material consisted of 13 men and 23 women. This ratio becomes understandable if it is realized that in this area, more women than men are employed in various manufacturing processes of the asbestos industry. In the material of Gloyne, the female sex also

predominated. The age at the time of death was 58.5 years for the men and 54.3 years for the women. These ages were thus much higher than those determined by Gloyne (men = 38.5 years, women = 33.5 years). These figures suggest that the severity and progressive nature of asbestosis were less in our cases than in those of Gloyne. Table 5 provides a survey of the cases classified by us as mild (= 1), moderately severe (= 2), or severe (= 3).

The Table shows that all degrees of the disease were rather equally present. There was no difference between the sexes in this respect. The distribution indicates already that in our material, asbestosis was often a secondary finding. Thus, our patient material was selected on a different basis than that of a group with pneumoconiosis. It appears necessary to emphasize this fact without proceeding further. Since the number of our cases is much higher than those in studies published so far in Germany, we feel justified in considering our collective as a representative one. It appears permissible to compare 25 of the 36 cases to cases from the general autoptic material at the St. Georg Hospital, from which they differed in only one respect: the presence of some degree of asbestosis. Whether all cases without exception that occurred since 1939 have actually been included remains questionable, however, since mild cases were recognized only when the lungs were subjected to histological examinations.

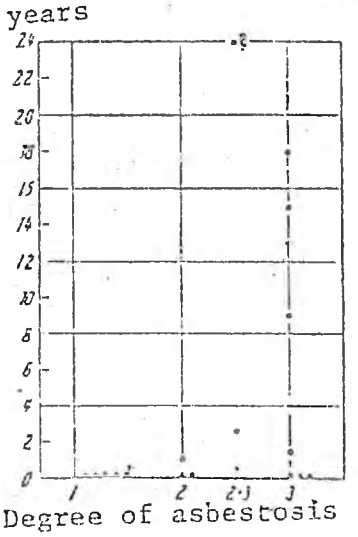
Table 5. Survey of the cases classified as mild (= 1), moderately severe (= 2), and severe (= 3).

Degree of severity	Men			Women		
	n	%		n	%	
1	5	38	46%	6	25	48%
2	1	8		5	22	
2—3	3	23	54%	3	13	52%
3	4	31		9	39	

uncharacteristic and gradual onset, a determination of dates is objectively difficult. The dates are, therefore, frequently, but not always, related to some remembered event, such as a medical treatment, a determination of disability, or a similar circumstance. It can be assumed that in many cases, the symptomatology goes back further in time than was reported. Those anamnestic data that could be related to a possibly existing pulmonary tuberculosis, were not considered. On the other hand, cases of pulmonary carcinoma were included, since the history, as far as it was dictated by the carcinoma, can only have been important for a short time. Logically included in this category were those cases, where another pathological condition led to shortness of breath a relatively short time before the death of the patient.

A study of the relationship between the duration of the complaints and the severity of the asbestosis shows that the cases where the pulmonary changes were minor (1) went back on the average for a period of 0.14 years, that moderately severe cases (2) had a history of 3.3 years and that in the severe cases (2-3 and 3), the corresponding period was 7.6 years on the average. Figure 9 shows that a positive correlation between the duration of the shortness of breath and the severity of the pulmonary finding exists only in some of the cases. In a considerable portion of the severe and moderately severe cases, no symptoms were reported

Figure 9. Relationship between the duration of the symptoms and the degree of asbestosis.



or only those of a relatively short duration. The morphological degree of severity is thus not simply identical with the duration of the subjective disorder of the respiratory function.

This and a symptomatology that lacks characteristic aspects explains that a clinical diagnosis was established in only some of these cases. Table 6 provides a survey of the extent to which these cases appeared to be clinically suspicious or were definitely recognized and to which category of severity they belonged. It becomes evident that of the 23 moderately severe and severe cases, ten were not diagnosed. Of these ten cases, four had a previous history with symptoms. In the group of the cases which were recognized only shortly before death or which were considered suspicion at that stage, there were four, whose previous history mentioned revealing symptoms. Only in one-fifth of the moderately severe and severe cases had the asbestosis been known to exist for several years.

These considerations lead us to one of the most important problems in connection with asbestosis, which is the discrepancy between the clinical and the morphological pictures. Using the autoptic experiences, we add yet another aspect to this problem. The morphological finding may be more severe than the clinical picture or the duration of the previous history would lead one to expect in regard to the symptomatology. From the viewpoint of the clinical experience, the opposite impression is in the foreground; the subjective condition is frequently much worse than is suggested by the objective physical signs of the disease (Sparks 1938, Baader 1939, Luton et al. 1953, Behrens 1956). A negative radiological finding was obtained by Wood and Gloyne in 9 of 53 cases, by Alvens in 13 of 38, although all other clinical signs of asbestosis were present.

The same experience was reported by Gerbis and Ucko. Cases which radiologically correspond to dust lung of the first and second degrees (Schulte), may reveal such severe functional disorders that they would, without hesitation, be evaluated as the most severe cases of dust lung (Di Biasi). Totally different--and evidently in agreement with our concepts developed in relations to the work at the autopsy table--are the experiences of Cartier, who described the clinical aspect in Canadian asbestos workers by saying that in uncomplicated and even in advanced asbestosis, the symptoms were more often missing than pressent.

TABLE 6. Number of clinically diagnosed cases arranged according to the degree of severity of the asbestosis (Cases 2, 6, and 7 could not be considered).

	Degree of severity of the asbestosis			
	1	2	2 - 3	3
> Year preceding death		1		4
< Year preceding death			1	3
Suspicion shortly before death		1	1	2
No	10	4	3	3

The different experiences as far as our cases are concerned, can be explained by the selection of the material, depending on whether the clinical or the pathologico-anatomical observer supplies the comment. The contrast is only an apparent one, since the same principle is expressed by both kinds of experiences. From the pathological and anatomical viewpoint, we can confirm the clinically important experience, "that the roentgenological picture is more a yardstick for the intensity of the reaction on the part of the pulmonary tissue than for the severity

of the dust lung disease," as Baader emphasized. This raises the question as to which possibilities exist for understanding this discrepancy from the histological point of view.

c) Which conditions determine the degree of severity of the morphological finding in the light of our data? First, the exposure time must be examined. It is known in 20 cases. On the average, it amounted to 7.7 years in the cases where the pulmonary changes were mild (1), to 9.1 years in the cases with moderately severe changes (2), and in the severe cases (2-3 and 3), the exposure time averaged 14.5 years. Figure 10 shows that the increasing severity of the asbestosis was combined with increasingly longer exposure periods, although there was no positive correlation in a number of severe cases. Relatively short exposure times were reported for these. It can be assumed that added to the exposure period is the dust concentration as the second essential factor. In the individual case, this factor remained largely unknown. Some insight into this might be gained from examining the relationships between the sex of the patients and the degree of severity of the asbestosis. Severe asbestosis was not more frequent in men than in women, although the exposure period for the men was 16.1 years and for the women, 10 years. In six men and seven women suffering from severe asbestosis,

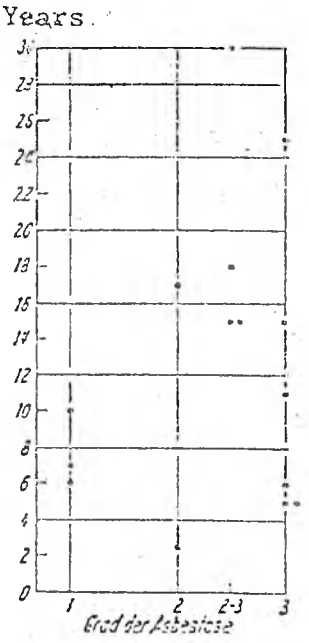


Figure 10. Relationship between exposure time and degree of severity of the asbestosis.

the average exposure time was calculated at 18.3 and at 11.3 years. This could be considered as the expression of a greater exposure of the women, but also that of a stronger disposition.

Besides the duration and the intensity of the exposure, another factor that must be taken into account is the time as a whole, i.e., the exposure period plus the free interval. Knox and Beattie have proven the importance of this fact or for the degree of the pulmonary changes in their quantitative studies. Such relationships did not become apparent in our material, since the time from the beginning of the exposure to the fatal outcome did not indicate any reliable differences for the moderatley severe and the severe cases. Again, the difficulty of evaluating this lies in the fact that we do not know the intensity of the exposure (time x absorbed dust quantity). If Knox and Beattie are right, we should have to assume that the patients whose exposure time was shorter, have absorbed more dust.

Let us examine the seven severe cases of asbestosis in Table 7. The time between the beginning of the exposure and death (the whole history) is approximately of the same order of magnitude. The exposure time varies. The results in the lungs of these patients were about the same. If the time from the beginning of the exposure to the appearance of the first symptoms is taken as a yardstick for the progress of the disease, case 4, 10, 13, and 29 permit the assumption that relatively more dust was absorbed in the cases where the exposure period was shorter. And in cases 11, 15, and 24, we must, on the contrary, assume that the amount of dust that was absorbed during the relatively brief exposure period, was not sufficient to cause symptoms soon thereafter, although it did affect a

TABLE 7. Comparison of exposure times to the time that passed between the start of the exposure and the appearance of the first symptoms in cases of severe asbestosis.

Case	Exposure time	1st symptom-years after beginning of exposure	Free interval	Duration of the total history
13	11	9	13	24
4	12	12	9	21
10	15	13	11	26
29	18	15	0	18
11	6	≈ 19	15	21
15	5	≈ 25	21	26
24	8	--	18	26

progression of a gradual character that reached far into the free interval, i.e., into the time between the end of the exposure and death. The importance of the time factor for the development of the pulmonary process is particularly well illustrated by these cases.

The differences of the reactions in the individual case, whether they be of a chronological or a quantitative nature, however, are certainly not attributable to differences of the exogenous factors, which are only partly known or estimated. This is also the conclusion of Knox and Beattie. There can be no doubt as to the participation of an individual disposition, although its importance has not yet been elucidated (Baader, Wedler). The anamnestic data are insufficient for an evaluation of this factor.

A more detailed investigation of the type and the development of the pulmonary process is, thus, in the final analysis restricted to the picture presented by the lungs and to its chronological arrangement, i.e., to the study of the histogenesis.

d) Which pulmonary findings of general importance were combined in our cases with the asbestosis? Mixed pneumoconioses in the strict sense of the term did not occur in our material. Only one case showed histologically small callosities or indurations that aroused the suspicion of silicosis. The distribution of anthracosis among our cases is shown in Table 8. Accordingly, the men showed a severe anthracosis more often than the women. The degree of severity of the asbestosis was not parallel to that of the anthracosis.

TABLE 8. Relationship between the degree of severity of the asbestosis and anthracosis.

Sex	Degree of severity of the asbestosis	Degree of severity of the anthracosis		
		Mild and moderate n cases	Severe n cases	not mentioned n cases
Male	1	1	2	2
	2		1	
	2 - 3		1	1
	3	1	3	
Female	1	4	1	1
	2	2	2	1
	2 - 3	2	1	1
	3	3	2	3

Tuberculous changes were determined in 12 cases. Seven of these were old processes that had largely healed and had involved, more or less, the apical segments of the upper lobes. In this group, the number of cases with mild asbestosis was disproportionally large (n = 5). In another three cases, there were fresh foci, twice (cases 8 and 31) in indurative tuberculosis of the upper lobes and once (case 28) in double cavernous tuberculosis. The remaining two cases presented a relatively new tuberculosis with cheese degeneration that involved both lungs in

case 26 and the right lower lobe in case 3, which showed marked induration in both upper lobes. In these five cases where the tuberculosis was still active, two (8 and 26) had a mild, one (case 3) a moderately severe and two (28 and 31) a severe asbestosis. In cases 3, 8, and 28, the tuberculosis was probably an important contributing factor in regard to the fatal outcome. The age of these patients at the time of death was 63, 63, and 67 years. In the remaining two cases, the cause of death was once the asbestosis (case 31) and once a scar (?) carcinoma of the lung (case 26). The ages at the time of death were 72 and 56 years. This compilation does in our opinion not permit a conclusion as to a mutual dependence of pulmonary tuberculosis and asbestosis. The dependence on general time factors is probably of some importance. Using comprehensive statistics, Wedler proved that tuberculosis of the lungs is not more frequent in asbestos workers than in the general population. The last broad-based survey of Gloyne showed that in the autoptic material from his cases of pneumoconioses, the group with asbestosis had almost the lowest incidence of tuberculosis.

e) Pulmonary carcinoma in asbestosis. Pulmonary carcinoma in asbestosis is of practical and theoretical importance.

The carcinoma of the asbestos lung, observed in the past by Gloyne (1933, 1935), Lynch and Smith (1935) and by Egbert and Geiger (1936), has been recognized as an occupational cancer by all authors except Cureton, ever since Nordmann convincingly explained the relationship on the basis of four cases from the literature and two observations of his own. The number of cases has greatly increased during the past ten years. According

to Wedler (1943), 6 cases (=2 %) of the 29 of asbestosis that were autopsied and published in Germany, showed a pulmonary carcinoma, as did 14 cases (=16%) of the 92 cases of asbestosis that were reported in the whole literature. Wedler included in his figure two cases of pleural endothelioma, arguing that the pleura was involved in the transformation process. In 1947, Boemke studied a collective of almost the same size and found 17 cases and in 1953, he added two more cases to his one of 1947. Also to be mentioned are the cases of Weiss (one pleural endothelioma), Welz, and Werber. In 1950, Merewether reviewed 235 cases of autoptically confirmed asbestosis and determined that 13.2% of these had pulmonary carcinomas. Gloyne contributed 121 cases where 14.1% suffered from a carcinoma. Isselbacher, et al. determined a rate of carcinoma of 13.8% in a group of 603 cases of asbestosis (1953). In groups of living asbestos workers, a cumulation of lung cancers was also determined (Doll 1955).

In recent years, Bohlig and Jacob (1955, 1958) have raised objections to these statistics. By relating the figures for pulmonary carcinomas from autoptic statistics to the group of living asbestos workers, they arrived at the conclusion that lung cancer is no more frequent in asbestos workers than in the general male population. This is a surprising finding since Bohlig and Jacob consider the causal relationship between pulmonary asbestosis and bronchial carcinoma as a proven fact. In the very recent past, Böhme has in this archive cast doubt on the general validity of the results of Bohlig and Jacob. He not only used recent figures from the literature, but also studies of his own. In 92 asbestos patients from a certain asbestos plant, who had been continuously

examined, six had developed pulmonary carcinomas in 1959. In 125 cases of asbestosis registered by an occupational association, Böhme found 15 cases of lung cancer (=12%), 14 of whom have since died. Regarding the total number of deaths (n = 31), lung cancer with fatal outcome stands at 45%. Of the 20 cases which had been studied pathologico-anatomically, 11 had lung cancer. These figures demonstrate the dependence of statistical results on the selection of the reference system. In the material of Bohlig and Jacob, 34 patients have died since 1958, 11 of whom were autopsied. Among these, five asbestos carcinomas were found.

We object in principle to the assumption that autoptic material and the living population are comparable collectives. The sources of error inherent in such a situation become evident when one considers the question of the incidence of occupational cancers with a short life and a long latency period. Böhme has indicated this with respect to the asbestos carcinoma. A prerequisite for a comparison is that the groups are distinguished by only one characteristic. Pathologico-anatomical collectives must also meet this requirement as much as possible.

In this light, our collection of cases acquires particular interest. At 11 of 36 cases (=30.7%), the percentage of carcinomas of the lung and the pleura in our asbestosis group is higher than was expected in the light of the data in the literature. But a comparison to other statistics appears problematical, because the selection of the groups might be based on different principles as has already been said. But, if we use our general autoptic material from the years 1948 - 1958 (Nassehi) for the comparison and deduct all cases where death occurred before the age of

30 years and all cases of asbestosis, we retian 13,307 autopsied cases with 1,018 (=7.8%) pulmonary carcinomas (including pleural endotheliomas).

Since 10 of our 36 cases of asbestosis did not belong to the same autoptic material, it appears that sources of error of selection might interfere with equating our whole collection of cases with the group of the above 13,307 cases. In the remaining 26 cases, only 6 cases of asbestosis were clinically known and 4 were suspected. In 3 cases, the asbestosis was the cause of death. There is no argument against considering this autoptic group of 26 cases as being representative of the general asbestosis group as the simultaneously examined, general autoptic collective, with regard to the general population of the area that supplied all of these cases.

Among the 26 cases were 9 of lung cancer, i.e., 34.6%. This percentage can likewise not as yet be simply compared to that in the general autoptic material, since the ratio between men and women in the asbestos group was 1:1.9, while it is only 1:0.7 in the general autoptic material. If we examine the rate of lung cancer separately for the sexes, the men in the general autoptic material had 11.6% and those in the asbestos collective, 44.4% of lung carcinomas. For the women apply, correspondingly, rates were 2.1% and 29.4%. Table 9 gives a survey of these conditions. Regardless of which relationship is selected, it illustrates the increased incidence of cancer in the asbestosis group. This was especially evident for the female sex, an observation that was conceded by Jacob and Bohlig.

The large number of pleural endotheliomas that exceeded all expectations, confirms the assumption of Wedler. We also consider our cases as asbestosis carcinomas. Although we leave open the question as to the soil

TABLE 9. Comparison of the rate of incidence of pulmonary carcinoma in the autoptic material from asbestosis cases and in the general autoptic material of the Pathological Institute of the St. Georg Hospital, Hamburg.

	General autoptic material (cases from the 31st yr. of life on, minus the cases of asbestos), 1948-1958		Asbestosis cases in the general autoptic material 1948-1958		All asbestosis cases observed since 1939 at the Path. Inst. of St. Georg	
All cases	13307	100.0%	26	100.0%	36	100.0%
pulmonary carcinoma	1018	7,7%	9	34,6%	11	30,6%
pleural endotheliomas	102	0.77%	4	15,4%	4	11.1%
All cases in men	7817	100,0%	9	100.0%	13	100,0%
lung cancer	903	11.6%	4	44.4%	6	46,2%
All cases in women	5490	100,0%	17	100,0%	23	100,0%
lung cancer	115	2.1%	5	29,4%	5	21,7%

from which the pleural endothelioma came, it still appears sufficient to us for a justification of the occupational relationship that the above is a malignant tumor of the lung surface. It is this area that constitutes a site of predilection for the pulmonary reaction, as is indicated by the tendency toward a subpleural densification and the frequency of pleural callosities or indurations in uncomplicated cases of asbestosis.

Among the carcinomas listed in Table 9, six were located in the lower lobes, four were pleural endotheliomas, and one an upper carcinoma (case 26), which because of its location and its close relationship to a tuberculous scar, might also be interpreted as a scar carcinoma.

The increased danger of cancer in asbestosis is manifested not only by the rate of incidence, but also--in accordance with the concepts of

Schinz --by the shift of the ages at which the patients died toward the younger ages. In our material, the average age was 51.6 years and, thus, corresponded well to the age of 52 years reported by Wedler. Compared to this, Schenck determined an average age of 59 years for the patients who died of lung carcinoma and were autopsied at St. Georg . If one compares the data of Nassehi on the age distribution for lung carcinoma in the autoptic material at St. Georg during the past 50 years (1668 cases) to our figures by using summation curves, the proportions are the same (Figure 11).

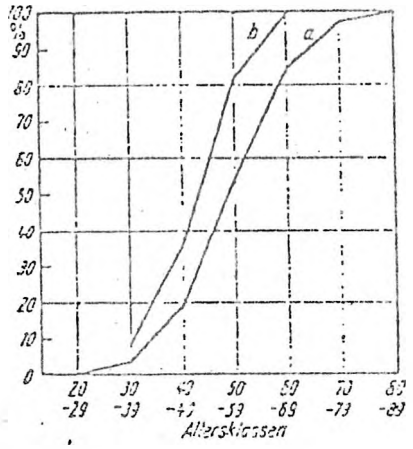


FIGURE 11. Age distribution for lung cancer in 1,668 cases of the general autoptic material of the Path. Inst. of St. Georg Hospital (using the data of Nassehi) and in 11 cases from autopsied patients who had asbestosis.
a) general autoptic material, and
b) asbestosis autoptic material.

But, the hazard cannot be evaluated by using the duration of the exposure, as can be seen from Table 10. There is a certain constancy—in agreement with previously published cases--regarding the period from the beginning of the exposure until death. We would like to call this period the latency period. Our own case, No. 16, is surpassed by one of Owen, where the exposure time was one year and the latency period was 20 years.

It also appears that the cancer hazard does not increase with the degree of severity of the asbestosis, as shown in Table 4, which is a

TABLE 10. Comparison of exposure time and latency period in six cases of asbestos carcinoma.

Case No.	years		
	Age	Exposure time	Latency period
9	53	24	24
10	47	15	26
13	39	11	24
16	45	2-1/2	23
23	41	10	24
30	54	9	18

surprising observation. When he studied the files of the occupational association, Böhme also arrived at the conclusion that the autopsied cases had apparently not suffered clearly from more severe asbestosis, a result that contrasted with the observations made in our own six cases. We shall return to this problem later with consideration of the histogenesis.

The male sex appears to be more endangered than the female one. Of the 13 men in our collection, 6 = 46.2% had a lung carcinoma, while of the 23 women, 5 = 21.7% were in the same position. Gloyne also found that a greater hazard exists for men: while in 19.6% of the male patients, a lung cancer was determined, this was the case in only 9.7% of the women. Wedler had already pointed to this sex distribution. The otherwise already sexual disposition in the case of lung cancer is here clearly demonstrated by the asbestos carcinoma. Of special interest in this connection is that the pleural endothelioma occurred only in female patients. Here also, a sexual predisposition is evident. For comparison, a look at the lung carcinomas that were autopsied from July 1, 1957 to December 31, 1958 at the St. Georg Hospital: of 133 carcinomas in men, 15 (=11.3%) were pleural endotheliomas; of 29 carcinomas in women, 11 were of this type (=38%).

The thought suggests itself that the asbestos carcinoma can in principle not be distinguished from carcinomas of unknown etiology appearing in the same location. This is supported by the fact that our material did by no means consist only of squamous cell carcinomas, as has been practically postulated in the past. Besides large-celled and pavement epithelial forms, there were also transitional types toward small-celled structures or clearly microcellular bronchial carcinomas. Transitions toward large cells or pavement epithelial cells were also observed in small-celled bronchial carcinomas of unknown etiology. Still, the forms that do not consist of small cells did predominate in our material. Another criterion of asbestos carcinoma, the multicentric development, is difficult to evaluate by macroscopic examination. The histologically varied pictures could mean just this, with a certain degree of probability in case 9. The site in the lower lobe of the carcinoma that has been emphasized in the literature, was clearly preferred in our material. It was striking, as has already been said, that pleural endotheliomas were so frequent. In two of four cases, it was limited to the lower lobes.

If we look at the group as a whole, the special position that has been assigned morphologically to the asbestos carcinoma is, after all, supported. But, if we examine only the individual case, then this special position would be justified only by the fact that we believe we know the etiology through statistical experience. If, according to K. H. Bauer, occupational cancers of the various organs cannot be distinguished from "spontaneous" cancers of the same organs, an opinion upheld by Hueck in connection with the Schneeberg lung cancer, the

asbestos carcinoma must gain our very special interest from the viewpoint of general pathology. If we succeed in defining the importance of the exogenous factor, our understanding of the conditions that attend upon the development of pulmonary carcinoma should improve.

f) Other carcinomas in asbestosis. The discussion of the relationship between asbestosis and pulmonary carcinoma should not exclude the fact that among the cases without lung cancer, there were 11 cases of other carcinomas. The high percentage of asbestosis carcinomas in our material, thus, did not come about at the expense of other malignant tumors with a different genesis. Found were: 4 stomach carcinomas, 3 peritoneal carcinomas, one esophageal carcinoma, one of the pancreas, one of the bladder, and one of the sigmoid colon. If we again use the general autoptic material for comparison, as we have done for the lung carcinomas, the data listed in Table 11 emerge. The rate of extrapulmonary carcinomas is, thus, relatively markedly raised despite the incidence of pulmonary carcinomas, a situation to which the stomach carcinoma contributed.

What is conspicuous is the number of peritoneal carcinomas. The tumor in these cases was especially strongly developed. The diaphragm was always extended and shot through with proliferations. In one case, the tumor had invaded the right lower lobe on a broad front. We should not dismiss this occurrence of peritoneal carcinomas as coincidental. The coincidence of two such rare findings suggests a causal relationship. We refer to the case of Leicher. Since it has been proven that a generalization of asbestos particles can occur via the circulation, the suspicion (voiced for the first time by Leicher) of an interrelationship

TABLE 11. Comparison of the frequency of extrapulmonary carcinomas in the general autoptic material and in the material of the asbestosis cases of the Path. Inst. of the St. Georg Hospital, Hamburg.

	General autoptic material (cases from 31st yr. of life on, minus the cases of asbestosis 1948-1958		Asbestosis cases in the general autoptic material 1948-1958		All asbestosis cases observed since 1939 at the Path. Inst. of St. Georg Hosp.	
All cases	13307	100,0%	26	100,0%	35	100,0%
All carcinomas except pulmonary carcinomas	3135	23,6%	11	42,3%	11	30,6%
Stomach carcinomas	807	6,1%	4	15,4%	4	11,1%
Peritoneal carcinomas	22	0,16%	3	11,5%	3	8,3%

receives further support. The question would have to be investigated, with more evidence, whether the rate of extrapulmonary cancers is raised in asbestosis. In view of the present findings, one should at any rate consider an increased responsiveness of the peritoneum to a carcinogenic stimulus. One may draw a parallel with the lungs.

In examining the case histories, we encountered some problems for which there do not seem to be any solutions as yet. They concern the discrepancy between the clinical and the morphological picture, the importance of the time factor, especially that of the so-called free interval, for the progress of the lung changes, and of the substrate of the individual disposition. The question of the development of asbestosis carcinoma, whether caused by direct or indirect carcinogenic stimulus, remains open for the time being. Such questions lead to the study of the histogenesis of asbestosis.

2. Histogenesis.

Our histological findings in the lungs have essentially confirmed the morphological characteristics of asbestosis which prompted Fahr and Feigl, for example, to speak of a chronic indurating pneumonia, while Löschcke used the term cirrhosis of the lungs. These are characteristics which have been described in the detailed studies of Ströbe and, especially, Di Biasi. Commenting on a case, Di Biasi wrote: "Judging by the experiences that have been gathered so far and which have again been confirmed by the present case, asbestosis of the lungs consists of interstitial, indurating changes, a diffuse fibrosis of the lungs which involves both lungs, starting at the top and increasing downward." This statement agrees with the radiological findings. But what precedes this radiologically discernible fibrosis? In view of the findings, the question must be investigated whether the development of the diffuse fibrosis is the pulmonary process, as Nordmann believed: "Thus one must assume a diffuse, chronic irritation that causes the diffuse proliferation of the lungs."

At the meeting of pathologists in Kiel in 1949, Nordmann explained that in asbestosis, all of the enormous expanse of the organ offers itself as a surface for the dust to settle, since the particle size of the asbestos needles prevents the dust's being dispersed by the lymph tract. In 1949, at the dust lung meeting in Münster, Siegmund made this distinction: "Where the dust is concentrated, a silicotic granuloma or a silicotic induration develops, but where, as in asbestosis or aluminosis, the inhaled dust particles are diffusely distributed throughout the lungs, diffuse scleroses are the consequence."

The German literature contains some statements that seem to contradict this opinion and raise the question of whether a diffuse fibrosis exists from the beginning in all cases, or whether, possibly, local reactions at specific points and of another type precede the diffuse one.

Nordmann has pointed out expressly that the asbestos lung is fibrous only in parts. In a brief histological description of a case of Wedler, he said that the asbestos particles are found in the bronchi, the alveolar ducts and also in the callous tissue, i.e., that they are not diffusely distributed. Behrens emphasized the finding of a peribronchial fibrosis.

Numerous experiences have been reported in the Anglo-American literature. Gloyne and Wood observed in 22 cases that the first histological changes occurred at the respiratory bronchioles and at the alveolar ducts, where mononuclear phagocytes and giant asbestos cells were found. This was followed by reticular fibrosis. Sparks (1938) described the same processes. In experiments with guinea pigs, rabbits, and rats, Gardener and Cummings (1931-1933) had seen that the process began primarily at the respiratory bronchiole. In the English literature, the respiratory bronchiolus is called the "crucial site" for asbestosis.

The attempt of a chronological analysis of our findings must start with the fact that the asbestos particles are the permanent form of the asbestos needles in the lungs and that they are not diffusely distributed, but deposited at preferred sites. These preferred sites are the alveoli of the respiratory bronchioles and the alveolar ducts. We can confirm the observations of the British authors. Physical, anatomical, and functional considerations explain that deposition and reaction take place primarily at these sites.

Physical reasons: The dust passes through a system of ducts that is long in relation to the lumen. Such systems are suitable traps for dust whose components are needle-shaped or fibrous. The same principle of dust removal is used by the asbestos-processing industry, where air is pumped from the work rooms through long felt hoses along whose walls the dust adheres.

The dedusting of the air in the bronchial space takes place along wall areas of different composition of different design. In the bronchi and in the bronchioles, which are equipped with a ciliated epithelium and mucous glands, the asbestos needles are gripped by the cilia of the mucous layer which then slowly migrates toward the trachea ("like a rolling carpet," Hayek). In none of my cases have I been able to determine asbestos particles and needles in the walls of these sections of the air passages. Conditions are totally different in succeeding sections, in the terminal bronchioles, respiratory bronchioles, and the alveolar ducts. Here, conditions for catching the asbestos needles are particularly favorable. Because of the widening of the lumina in the area of the respiratory bronchioles and alveolar ducts, direction and velocity of the airstream are changed. The increasing numbers of needles that are deposited come in direct contact with the epithelium, without a mucous layer and a coat of cilia. But, the distribution is not even; there are cumulations in the alveoli which interrupt the wall of the duct like niches. The negative pressure that develops there during inspiration deflects the airstream that has so far been straight, and turbulences form. The tendency of the needle-shaped particles to deviate in their flight from the longitudinal direction of the bronchioles, is decisively

promoted at this point. Thus, these alveoli become the depositories for the dust. The dust that has not been held by the alveoli of the respiratory bronchioles enters the initial portion of the alveolar ducts and remains there under the same circumstances. This explains that only a few, and only the shortest, asbestos needles can be found in the alveolar sacs.

Moreover, these dust deposits take place in a contractile system of tubes. We must anticipate spastic occlusions even in the initial stages of asbestosis. The frequent finding of hyperplastic smooth muscles, also mentioned by Di Biasi and others, permits us to conclude such processes. An expression of this functional disturbance of ventilation is the rather diffuse emphysema that is observed in mild cases, a fact that was also pointed out by Eickhoff and Baader, among others. The bronchial spasms presumably force the needles into the tissue.

The first functional disorders in the sense of spasms of the bronchioles can, thus, take place in the respiratory bronchioles and the alveolar ducts. The first morphic reaction occurs: fixation of the asbestos needles that are transformed into asbestos particles by giant cells, which wander into the lumen, and by a granulation tissue that leads to a gradual narrowing of the lumen in the sense of an obliterating bronchiolitis. The spear-like nature of the foreign bodies, the shrinking that takes place as a consequence of the fibrous conversion of the granulation tissue and the walls, and the respiratory movements of the adjoining, free alveolar parenchyma, permit the foreign bodies to enter into the

surrounding areas of primary contact. Peribronchiolar fibroses result and a shrinking process again develops. The masses of asbestos particles that lie in this fibrous connective tissue can then be found, after decades without exposure to dust, surrounded by giant foreign body cells in callosities. The consequence of endo- and peribronchial fibrosis is a rigid fixation of the adjoining parenchyma, first in the longitudinal direction of the bronchiolus, which leads to a progressive ventilation disorder. As a secondary change--because of the ventilation disorders, which initially show an emphysemal character, but then increasingly turn into a telectases--there develops a diffuse fibrosis with atelectatic induration and ending in an obliteration of the parenchyma.

The fate of the bronchi in this situation differs. Either they become obliterated because of a progressive obliterating bronchiolitis, or they become dilated, sometimes in connection with the development of small, circumscribed foci of a highly substantive emphysema so that large-chambered systems are formed. In some cases, these show considerable post-infectious, mesenchymal proliferations and processes of rearrangement. Epithelial regeneration takes place and presents all transitional forms from regular to metaplastic or atypical epithelium. In these sections, adenoma-like elements develop with all transitional forms toward carcinoma. But, undoubtedly, the small bronchiolar lumina, which have remained intact in various segments of obliterated bronchioles, may also provide the ground for a carcinoma.

The concept that a diffuse distribution of the dust requires a diffuse stimulus, which then leads to a diffuse fibrosis, must be abandoned. The

diffuse fibrosis develops secondarily, as we have seen, without direct contact with asbestos particles, following a circumscribed, peribronchial fibrosis which stands in a definite local relationship to the described intracanalicular cumulation of dust.

The objection could be raised with respect to the above that dust elements whose size is below the line of visibility, enter the lungs in masses, a phenomenon which Nordmann felt is highly probable. According to Sundius and Bygden, et al., however, the fiber must be of a certain length in order to be able to induce fibrosis. Vorwald, Durban and Pratt also arrived at this position, as did Behrens via animal experiments. The hypothesis of the effect of invisible dust particles can probably be neglected, in our opinion, because the development of the fibrosis can easily be read from visible findings, as is shown by an examination of the formal genesis.

If one examines the process as a whole, two phases can be distinguished, as was rightly emphasized by Eickhoff; the phase of the functional and morphic reaction at the bronchiolus and the subsequent phase of the diffuse fibrosis. The first, the bronchiolar phase, already results in the decisive ventilatory disorder. The parenchymatous phase in the form of the diffuse fibrosis is the second chronological phase. It is not the cause of the ventilatory disorder, but its result.

3. Conclusions from the histogenesis.

These histogenetic concepts can contribute to finding the answers to the questions that have arisen from our examination of the material. Thus, they can help explain some peculiarities inherent in the clinical picture and the course of asbestosis.

a) Referring to the histogenesis, we can understand the discrepancy that arises between the clinical picture and the radiological and anatomical picture of the disease. The functional and morphological changes at the bronchioles and the alveolar ducts do not appear at all in the radiological picture initially, and later they occur as barely recognizable signs. This happens at a time, as was also emphasized by Eickhoff, when the disorder of pulmonary ventilation has already begun to develop, which in turn leads to parenchymatous fibrosis. It is understandable that the morphological changes one awaits in such cases in order to support the diagnosis, already belong to a relatively late phase of the disease at the time they become radiologically visible. Whether the symptoms appear early depends on the intensity of the bronchiolar reaction. We cannot decide to what extent late symptoms must be attributed to the bronchiolar process or to its sequelae, the diffuse fibrosis.

b) In accordance with our histogenetic ideas, the time factor (and thus also the free interval) is of great importance for the final development of the pulmonary changes. The amount of dust that has been deposited and the time are important factors that determine the extent of the progress of the disease. Our findings indicate that the peribronchiolar induration under the effect of the presence of the asbestos particles does not cease even in the course of decades. This is indicated by fragments, pieces that have separated from the particles, transformations at the gel sheath and rearrangements of the particles in rosette-like structures, all of which are typical of old and advanced asbestoses. It would be difficult to hold that these deposits, which must be considered as

typical amphibole derivatives, are irrelevant to the progression of the disease. We agree entirely with Beger that the asbestos particles maintain the fibrotic development indirectly via the peribronchiolar fibrosis, without wishing to belittle the importance of the asbestos needles for the initial processes. The nature of the fibrogenous irritation at any rate requires a long period of time, and it is possible that besides the mechanical irritation (Sundius and Bygden), a chemical one is added (Beger, Knox, and Beattie).

c) The histogenetic concepts also permit a better understanding of the role of individual disposition, as it became evident to us in our material, for example, as different degrees of intensity of the symptoms.

If the pulmonary parenchyma were from the beginning affected by the dust over its whole expanse, we would have to settle for those long-discussed factors enumerated in the recent past by Wedler, to which the decisive influence of individual disposition has been attributed. These are the manner of breathing and the removal of the dust by the respective nature and reactions of the upper respiratory paths. The validity of these ideas has already been doubted, for silicosis by Gessler and for asbestosis by Baader, who examined several hundred asbestos workers. Wedler likewise was not satisfied with them.

If the dust is deposited primarily in the bronchioles and if the first functional and morphic reactions take place in this area, we are inclined to view them as the basis for the individual disposition. It appears logical to assume that the reasons for an individual disposition

must lie especially in the intensity of the motor reaction of the respiratory bronchiolus. The shortness of breath, after all, developed in our cases after six years at the earliest (case 9) so that the first morphic reactions had presumably already taken place. But they are certainly coupled with a bronchiolar spasm of individual intensity, which determines the clinical picture. This spasm, in turn, may again be an important prerequisite for the transmural expansion of the morphic reaction in the bronchiolar wall.

d) The study of the formal genesis of asbestosis also provides us with some ideas relating to the question of the role of asbestosis in the development of a carcinoma.

It seemed justified that carcinogenic properties were attributed to the asbestos particles after it had become evident that carcinomas were frequently associated with asbestosis. The problem was to find out whether the cause was irritation from some foreign body or the effect of a chemical noxa that had dissolved (Baader). Among the most important chemical noxae, Hueper counted the anthracenes, the aromatic amines, tar, arsenic, etc., and asbestos (1950). That this effect could not be bound to free silicic acid was demonstrated, however, by the experiences gathered in connection with silicosis (. . . illegible, Baader, Merewether, Vorwald and Karr, Leicher, Ehrhardt, . . . [illegible], Mittmann).

Likewise, carcinogenic activities of such metals as magnesium, aluminum, and titanium have not become known, as was determined by Nordmann and . . . [illegible] . . According to Frank, et al., chrysotile asbestos contains as an impurity chrome and nickel. That such admixtures are not of great importance as carcinogens may perhaps be

concluded from the fact that in the countries where these asbestos types are obtained, asbestos carcinomas are not particularly frequent. The question cannot be answered whether chrysotiles with these impurities played any role at all in the histories of our cases. However, such a possibility has so far not been sufficiently considered.

It is best to base our considerations of the causal genesis on the concept that the carcinogenesis is the result of an interplay of different complementary factors of various degrees of importance, which all come together and produce the result--conditionally--roughly in the sense of a syncarcinogenesis (K. H. Bauer).

From this viewpoint, iron must be mentioned. The iron that is determined in the Prussion blue reaction is by itself probably meaningless regarding the development of pulmonary cancer as is revealed by the brown induration in the lungs. But in a table listing carcinogenic noxae, K. H. Bauer has also listed iron. From the literature, we know of the two cases of Dreyfuss (1936). The patients were siblings who both developed pulmonary carcinomas at the ages of 36 and 44 years. This cancer was related to the inhalation of iron oxide in the youth of the patients (clockmaking as a cottage industry). The only three cases of pulmonary carcinoma among a very large group of radiologically confirmed pneumoconioses (without asbestosis), came from an iron mine (Vorwald and Karr 1938). Otherwise, however, there have been no reports to my knowledge of lung cancer in workers employed in mining iron. In 1940, Campbell was able to induce cancer in animal experiments by iron oxide inhalation. These observations might mean that a combination of various effects of foreign bodies, where the effect of iron is not yet

known to us, might create suitable conditions for carcinogens, as has been discussed in connection with a case of pulmonary carcinoma caused by a splinter of a bullet that remained in the organism (König). The documentation that indicates carcinogenic importance of these two conditions are undoubtedly too sparse to justify any binding conclusions as to a carcinogenic activity of asbestos particles.

A review shows that the hypothesis of a chemical induction of cancer by asbestos cannot be sufficiently supported, a fact that has again been confirmed in the recent past by Behrens (1956). Linzbach felt that the cause for the development of an asbestosis carcinoma lies in the disorder of tissue relationships. Our findings have made it clear that epithelial proliferations of a regenerative nature can provide the matrix for the carcinoma on the basis of rearrangement processes at bronchiectases and constricted and dilated alveolar ducts. Sections of the respiratory tract seem to have been involved, whose epithelium has not had any contact with asbestos dust. The formation of an asbestos carcinoma can thus be explained by Virchow's irritation theory or by the regeneration theory of Fischer-Wasel. The chronic state of irritation has already been considered by Lynch and Smith as the cause of the asbestos carcinoma. Isselbacher, et al. have also held that chronic mechanical irritation is the essential carcinogenic factor. The objection that under such circumstances, tuberculosis or silicosis would have to lead to cancer more often, was refuted by Nordmann, who pointed to the fundamental difference of the morphological conditions in asbestosis on the one hand and the above-described pulmonary changes on the other. We must realize that to the diffuse process of asbestosis that spreads over the whole lungs

belong innumerable such regenerative foci. This makes it understandable that the probability that at any one of these sites a sudden change takes place that results in an autonomous proliferation of a malignant character is much greater than in lungs where the basis for such a development can lie only in one corresponding focus.

Thus, we approach concepts that apply to the genesis of pulmonary carcinoma as such. The importance of a chronic irritation for the development of a pulmonary carcinoma, according to Berkhan, can be recognized by the greater incidence of carcinoma in the right lung. He assumed that as a consequence of the straight course of the right main bronchus, the right lung inhales more dust than the left. W. Fischer attributed the differences in the incidence of carcinoma to the different volumes of the right and the left lung and, thus, introduced yet another aspect. The probability of the development of a cancer grows with the increase of a substrate. These general considerations are important for our observation that there is no relationship between the degree of severity of the asbestosis and pulmonary carcinoma. We must count on a quantitative factor, which is constituted by the extent of the process. We must assume that the chronic state of irritation at the respiratory bronchiole, distributed ubiquitously over the lungs, is sufficient for the growth of a carcinoma. But we must not settle for this exogenous factor. "That we are thus still far from a full understanding of the more complex relationships is a fact that this problem in asbestosis shares with that of carcinogenesis as such" (Wedler). That asbestos is only one factor was also emphasized by Hueper in 1957.

Further impulses that still elude our awareness must be assumed. "There are more endogenous and exogenous factors than one can dream of" (W. Fischer). The type of the inhaled asbestos, individual habits, general circumstances of life dictated by geography are, as far as can be judged, just as important participating factors as dispositional individual ones, which need the outside stimulus in the sense of a proliferative stimulus of sufficient duration, intensity, and, perhaps, type, in order to lead to cancer. At the 28th meeting of pathologists, Fischer-Wasel said, "Only if the typical special general disposition, the general readiness for cancer, is added, can a regenerative proliferation form the beginnings of a tumor, a malignant tumor." We refer in this context to the noteworthy sexual distribution of the asbestos carcinoma in our material, which corresponds to the general sexual disposition toward pulmonary carcinoma.

4. Conclusions resulting for the evaluating physician.

The findings presented above and their interpretation seem to bring us closer to the answers to some questions, particularly clinical ones and those that concern the genesis of the asbestosis carcinoma. Thus they may also acquire some importance for occupational medicine, individual prophylaxis and medical opinions.

The discrepancy between the clinical picture in its subjectivity, and the radiological (clinico-morphological) finding, creates a difficult situation for the physician who must give an opinion.

Any expert opinion will always seek an objective foundation for the classification of the severity of a disease, and will strive to express its judgments in a standardized manner in order to be generally understandable to the extent that the measure of help needed by the patient--

be it prophylactic, therapeutic or social in nature--can be determined. I refer to the classifications of Kruger, Rostoski and Saupe, Lanza and Buresch. Any critique of such an endeavor leads one to the recognition that a determination of degree cannot do justice to the clinical and radiological and pathologico-anatomical facts (Winkler).

In his last communication on pneumoconioses, Gloyne wrote that all attempts at classifying pulmonary changes have failed. They had to fail as long as one tried to correlate the severity of the clinical picture with the radiological one. Therefore, for example, it is not permissible to grant workmen's compensation only at the time when "the connective tissue transformation, the fibrosis of extensive parts of the pulmonary tissue with a cessation of their function for respiration and circulation" have been proven (Boemke). The preceding, long-lasting clinical disorders can then conceivably be neglected as warning signals and early indicators of asbestosis. In 1959, at the dust lung meeting at Münster, Jotten stated: "The functional examination is today, in contrast to the past, considered to be much more decisive than the radiological picture, which should be evaluated only as a criterion." The 5th regulation on occupational diseases of February 26, 1952, has largely taken this new concept into account.

Since the morphological examination of comprehensive autoptic material that contained pulmonary changes of all phases has shown that the pulmonary process is initiated by the functional and morphic reactions at the respiratory bronchiole and also that the fate of the further course is already decided in this bronchiolar phase, we wish to raise the question

alarming symptoms. This development can be ascertained at a time when there is not yet a sufficient radiological indication.

In conclusion, I wish to refer to the findings of carcinoma. The greater danger of carcinoma that threatens the asbestos lung in the central European area can, in our opinion, be considered to be largely factual. The retreat to a "in dubio pro aegroto" (Oettel) does not seem necessary if one uses comparable samples from the central European region as a foundation of judgment. Pleural endothelium can also be included among asbestos lung cancers.

A case from the literature (Leicher), a cumulation of cases in our material and the proof that a hematogenous generalization of asbestos particles is possible, raise the question of whether the peritoneal carcinoma in asbestosis is to be recognized as a complication of asbestosis and, thus, as an indemnifiable occupational disease.

SUMMARY

1. This is a report on 36 cases of asbestosis which were examined at the Pathological Institute of the General Hospital St. Georg in Hamburg. Data on asbestosis as a disease of civilization, on asbestos, its processing, on the dust and the intrapulmonary asbestos particles, as they are needed for a general understanding, precede the report.

2. Tables list the histories and most important clinical and autoptic findings. The macroscopic and microscopic findings of the lungs and the regional lymph nodes are described. A brief report follows on the findings which indicate a hematogenous distribution of the asbestos particles.

3. The autoptic material, stemming from 13 male and 23 female patients, includes all morphological degrees of severity of asbestosis.

In 7 cases, the asbestosis was presumably the main disorder; in another 11, a carcinoma was found, 4 of which were pleural endotheliomas. In 18 cases, the chief disorders were other conditions. In a number of cases, the asbestosis was recognized only at autopsy.

4. The opinion held in Germany, that the diffuse effect of dust on the respiratory parenchyma in its totality leads directly to a diffuse fibrosis, cannot be confirmed. Rather, most of the dust is deposited in the respiratory bronchiole, as has long been described by British authors. The functional and morphic reactions at the bronchiole introduce the first phase, which we would like to call the bronchiolar one. It leads to peribronchiolar fibrosis. The rigid fixation of the elastic parenchyma begins the second, parenchymatous phase, which finally leads to diffuse fibrosis. Besides an obliterating bronchiolitis, bronchiolectasis also develop. Under the conditions of post-infectious states of irritation and functional losses, considerable processes of epithelial regeneration get under way and these are the prerequisites for the development of a pulmonary carcinoma.

5. The knowledge of the histogenesis moves us close to answers concerning some problems of asbestosis.

a) The discrepancy between the severe clinical picture and the more or less negative radiological picture can be explained through the peculiarity of the bronchiolar phase. The functional disorders in this phase may be considerable, while there still need not be any radiological symptoms. Unelucidated remains the discrepancy that can exist in the parenchymatous phase between a sparse symptomatology and a more or less marked morphological finding.

b) The degree of severity of pulmonary changes depends not only on the exposure time and the (mostly unknown) dust concentration at the work place, but also on the time. The histological findings make it probable that the disease progresses gradually even during the course of the free interval.

c) A substrate of individual disposition can be seen in the respiratory bronchiole. The intensity, differing from one case to the next in the functional and morphic reactions that influence each other, determines the clinical picture and the time frame of the progression and, thus, it also affects the degree of severity of the lung changes.

6. The opinion voiced during recent years that pulmonary carcinoma is no more frequent in asbestos workers than in the general population, is contradicted. Of 13 men in our sample, 6 (= 46.2%) and of 23 women, 5 (= 21.7%) showed a pulmonary carcinoma (or a pleural endothelioma). If we consider, in the interest of a statistically acceptable comparison, only the cases seen at the St. Georg Hospital among the autoptic material between 1948 and 1958, the higher expectation of cancer compared to the general autoptic material during this period becomes quite clear: in the men at the rate of 44.4% (compared to 11.6% in the general autoptic material), in the women at 29.4% (compared to 2.1% in the general autoptic material). Among the 11 lung carcinomas were 4 pleural endotheliomas. The average age at the time of death and the duration of the latency periods agreed with the data in the literature. There was no relationship in our material between pulmonary cancer and the degree of severity of the pulmonary changes. This appears understandable if one considers the histogenesis.

7. The percentage of extra-pulmonary carcinoma was likewise raised. Stomach carcinoma occurred at the rate of 11.1% (or 15.4%, related to the asbestosis autoptic material from 1948 to 1958), compared to 6.1%. The suspicion, voiced by Leicher, of a relationship between peritoneal carcinoma and asbestosis was supported by our findings, since three peritoneal carcinomas were found in our material, i.e., 8.3% (or 11.5%, related to the autoptic material with asbestosis from 1948 to 1958), compared to 0.16% in the general autoptic material.

8. The conclusions to be drawn from our results for the authors of medical expert opinions are discussed.

In view of the difficulty of reconciling the clinical and radiological pictures, it is proposed that a distinction be made between asbestosis and asbestos lung.

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Über die Asbestose*

Von

J. König, Hamburg

Mit 11 Textabbildungen

(Eingegangen am 22. April 1960)

Einleitung

1951 konnte König auf der Tagung der nordwestdeutschen Pathologen an Hand von 16 Fällen des Pathologischen Institutes St. Georg, Hamburg, über die *Histogenese der Asbestose* und des Asbestose-Carcinoms in der Lunge berichten. Die Untersuchungen waren dadurch gefördert, daß die beobachteten Fälle überwiegend nicht mit einer Asbestose als Hauptleiden zur Sektion gekommen waren. In einem großen Teil der Fälle wurde die Asbestose erst bei der pathologisch-anatomischen Untersuchung aufgedeckt. Dieses so geartete Material ist inzwischen auf 36 Fälle angewachsen. Es bietet einige der klinisch erörterten Probleme in der Sicht des Pathologen. Sie können auf Grund der vertieften Kenntnisse der Histogenese einer Lösung nähergebracht werden. Deshalb glauben wir uns zu einer Veröffentlichung verpflichtet.

Die Asbestose als Zivilisationskrankheit

Angesichts der Seltenheit der Asbestose erscheint es zweckmäßig, zur Einführung kurze Angaben über ihre Bedeutung als Zivilisationskrankheit, über ihre Entstehungsbedingungen und über den Asbest vorauszuschicken.

Wann die Asbestose zuerst aufgetreten ist, wissen wir nicht. — Als feuerfestes, verspinnbares Material bereits im Altertum verwendet und beschrieben (Cooke 1924, ausführliche Darstellung bei Frank, 1952), wurde Asbest doch erst seit der Mitte des vorigen Jahrhunderts im Sinne der modernen Industrie verarbeitet. Die wichtigsten Produkte sind It-Platten, Asbestpappen, Asbestzementplatten und -röhren, Bremsbänder und -beläge, Dichtungen, Packungen, Filter und Dichtungsmaterial bei Säuren. Die moderne Technik ist ohne den Asbest nicht denkbar.

Die Asbestose wurde zuerst in England beobachtet (Montague Murray 1900), dann in Kanada (1912, Wedler) und in Deutschland (Fahr und Feigl 1914). Das eigentliche Schrifttum der Asbestose begann in *England* 1924 (Cooke). 1927 erschienen zahlreiche englische und südafrikanische Arbeiten; 1930 wurde in England die Asbestose als Berufskrankheit anerkannt. 1951 gab Gloyne einen

* Herrn Prof. Heine in Dankbarkeit und Verehrung zum 35. Geburtstag.

Tabelle 2. *Übersicht über die Fälle mit bekannter beruflicher Vorgeschichte*

Lfd. Nr.	S Nr.	Alter	Geschlecht	Expositionszeit		Freies Intervall in Jahren	1. Symptome		Klinische Diagnose	Röntgenbefund
				Datum	Dauer in Jahren		Datum	Jahre vor dem Tod		
3	1016/39	63	♀	1916—1933	17	6	invalidisiert wegen Asthma 1933	6	Verdacht 1939	negativ
4	1999/39	41	♀	1918—1930	12	9	Bronchitis 1930	9	1933	vermutlich positiv
6	G 2053/41	59	♂	?	15	?	?	—	ja	positiv
9	491/48	53	♂	1924—1948	24	0	1930	18	70% Invalidität 1938	vermutlich 1938
10	835/48	47	♂	1922—1937	15	11	1935	13	30% Erwerbsminderung („Silikose“) 1937	positiv
11	993/48	49	♀	1927—1933	6	15	vor 1947	?	1947	positiv 1948
12	436/50	75	♂	?	30	?	?	—	nein	positiv, aber keine Diagnose
13	823/50	39	♀	1926—1937	11	13	1935: Asthma im Anschluß an Erkältung	15	bis 1949: nein, 1950: Verdacht	1949: negativ, 1950: Verdacht
14	227/51	61	♀	1907—1912 1927—1930	5 3 } 8	15 21	1938: Bronchitis (Asbestkörperchen im Auswurf)	13	sicher seit 1938	?
15	276/51	55	♀	1925—1930	5	21	1950	1—2	nein	positiv, aber keine Diagnose
16	567/51	45	♀	1928—1931	$2^1/_2$	20	1950	1	nein, obwohl berufliche Anamnese bekannt	vermutlich negativ
17	630/51	44	♀	1928—1935, etwa 1941—1949	7 8 } 15	2	?	—	Verdacht wegen beruflicher Anamnese	vermutlich negativ
20	851/52	60	♀	1910—1917	7	35	1951	1	nein	?
22	923/52	59	♀	1946—1952(?)	6	0	vermutlich keine	—	nein	—
23	198/53	41	♂	1929—1939	10	14	Lungenfürsorge wegen Tbc ab 1939	14	nein	vermutlich negativ
24	967/54	45	♂	1928—1936	8	18	keine	—	nein	nein
29	1318/55	55	♂	1937—1955	18	0	1952	2—3	30% Erwerbsminderung 1955	1944, 1951, 1953: negativ, 1955: positiv
30	1428/55	54	♂	1937—1946	9	9	1952	2—3	1955 Verdacht wegen beruflicher Vorgeschichte	negativ
31	1493/56	72	♀	?	25	?	1956	10 Wochen	Verdacht, Einweisung wegen „Staublunge“	1956: Verdacht
34	393/57	47	♀	1928—1932, 1947	4 1 } 5	15 9	1950	7	1950	vermutlich positiv

Tabelle 3. *Übersicht über die Fälle mit unvollständiger Vorgeschichte*

Lfd. Nr.	S Nr.	Alter	Geschlecht	1. Symptome Datum	Jahre vor dem Tode	Klinische Diagnose	Röntgenbefund
1	G 209/39	46	♀	1935: „Lungenleiden"	4	14 Tage vor dem Tode	positiv
2	G 2110/39	55	♀	?	—	?	?
5	2076/39	52	♀	keine	—	wahrscheinlich nein	—
7	G 1665/48	48	♀	?	—	ja	—
8	109/48	67	♂	1928(?): trockene Pleuritis	20(?)	nein	Asbestose negativ
18	15/52	46	♀	1928: Kur, 1940: Pleuritis	24 12	nein nein	seit 1928 „Verschwartung"
19	248/52	62	♂	keine	—	nein	nein
21	852/52	79	♀	vermutlich keine	—	nein	—
25	1051/54	60	♂	Asthma, Datum?	?	nein	vermutlich negativ
26	1122/54	56	♀	keine	—	nein	negativ
27	558/55	52	♀	?	—	nein	?
28	879/55	63	♀	1955	10 Wochen	nein	—
32	15/57	61	♀	nein	—	nein	negativ
33	296/57	57	♀	nein	—	nein	negativ
35	1063/57	65	♂	?	—	nein	negativ
36	1089/57	77	♂	1953: „Emphysembronchitis" angeblich schon einmal vor 46 Jahren	4 (46?)	nein	positiv aber keine Diagnose

erkennen, daß die Asbestkörperchen die Alveolen vollkommen ausstopfen. Sie liegen wirr durcheinander, meist ziemlich dicht. Zwischen sie sind Makrophagen und Riesenzellen eingedrungen, oder es liegt ein Granulationsgewebe vor, das in feinster Aufsplitterung das Häufchen durchdringt und ein zartes Gitterfasernetz bildet (Abb. 4). Die Asbestkörperchen sind gelegentlich — besonders in den Schwielen — radiär geordnet, derart, daß das knopfförmig verdickte Ende peripher liegt (Abb. 5). Die Alveolarwand kann trotz nicht unbeträchtlicher

Tabelle 4. *Übersicht über die wichtigsten Sektionsbefunde*
Grad der Asbestose: 1 = gering, 2 = mittelschwer, 3 = schwer (Näheres s. Text); Grad der Anthrakose: — = in der Sektionsdiagnose nicht erwähnt; mäßig = alle Fälle, die in der Diagnose nicht ausdrücklich als schwer, stark usw. hervorgehoben sind.

Lfd. Nr.	Hauptleiden Todesursache	Asbestose-Grad	Lungencarcinom	Lungentuberkulose	Anthrakose-Grad
1	Einsendungsgut (vermutlich Asbestose)	vermutlich 3	—	—	?
2	Einsendungsgut (vermutlich Asbestose)	vermutlich 3	—	—	?
3	Tuberkulose, Rechtsinsuffizienz	2	—	Starke Verschwielung der Oberlappen, des Mittellappens und der apikalen Abschnitte der Unterlappen. Frischere Verkäsungen im re. Unterlappen, Pleuritis re.	—
4	Asbestose, Rechtsinsuffizienz	3	—	—	—
5	Sepsis	1	—	—	—
6	Lungencarcinom (Einsendungsgut)	2—3	li. Unterlappen	—	?
7	Einsendungsgut (vermutlich Asbestose)	2—3	—	—	?
8	Tuberkulose, Lungenembolie	2	—	Indurierende Tuberkulose im re. Oberlappen mit einzelnen exsudativen Herden. Empyem 1000 cm³, Kaverne und chronische Pneumonie im re. Unterlappen	—
9	Lungencarcinom	3	li. Unterlappen mit diffuser Infiltration, knotige Metastasen im re. Unterlappen	—	mäßig
10	Lungencarcinom	3	re. Unterlappen, Einbruch in das Mediastinum	—	stark
11	Magencarcinom	3	—	—	stark
12	Hydronephrotische Schrumpfniere, Urämie	2—3	—	Schiefrige Induration des re. Oberlappens	—

Tabelle 4 (Fortsetzung)

Lfd. Nr.	Hauptleiden Todesursache	Asbestose-Grad	Lungencarcinom	Lungentuberkulose	Anthrakose-Grad
13	Pleura-endotheliom	3	über dem re. Unterlappen, ausgedehnte Ausbreitung auch im re. Unterlappen	—	stark
14	Asbestose	2	—	—	mäßig
15	Glomerulonephritis, Urämie	3	—	—	mäßig
16	Pleura-endotheliom	2	über der li. Lunge, ausgedehnte Einbrüche subpleural und im Hilus	—	—
17	Peritoneal-carcinom	2—3	—	—	mäßig
18	Peritoneal-carcinom	2—3	—	—	stark
19	Harnblasencarcinom, Urämie	1	—	—	mäßig
20	Magencarcinom, Herzinfarkt	1	—	Karnifizierende und vernarbende Spitzentuberkulose beider Oberlappen mit Kreideherden	mäßig
21	Kardiacarcinom	1	—	—	stark
22	Oesophagus-carcinom	1	—	Kreideherd im re. Oberlappen	mäßig
23	Lungencarcinom	1	re. Unterlappen	Chronisch-cirrhotische Spitzentuberkulose bds. mit kleinsten Kavernen	stark
24	Lungenembolie nach Harnröhrenverletzung	3	—	Schiefrige Spitzennarben bds	stark
25	Asthma bronchiale, Rechtsinsuffizienz	1	—	Spitzennarben in beiden Oberlappen	—
26	Lungencarcinom	1	li. Oberlappen innerhalb einer tuberkulösen Verschwielung	Schwielige Spitzentuberkulose mit frischen Verkäsungen	mäßig
27	Pleura-endotheliom	vermutlich 1	über der re. Lunge	—	mäßig

Tabelle 4 (Fortsetzung)

Lfd. Nr.	Hauptleiden Todesursache	Asbestose-Grad	Lungencarcinom	Lungentuberkulose	Anthrakose-Grad
28	Peritonealcarcinom, Tuberkulose, Herzinfarkt	wohl 3	—	Chron-kavernöse Tuberkulose beider Lungen, karnifizierende Pneumonie im li. Oberlappen, frische Streuung	—
29	Pankreascarcinom	2—3	—	—	stark
30	Lungencarcinom	2	li. Unterlappen	—	stark
31	Asbestose	3	—	Alte indurierende Tuberkulose mit frischer Aussaat	mäßig
32	Pleura-endotheliom	2	bds., besonders re. Unterlappen	—	stark
33	Carcinom des Colon sigmoid.	2	—	—	mäßig
34	Dermoid des li. Ovars, Magencarcinom	3	—	—	mäßig
35	Lungencarcinom	1	li. Unterlappen, Ausbreitung in Pleuraschwarten bds.	Schiefiger Spitzenherd re.	stark
36	Asbestose	3	—	—	stark

Ansammlung noch ziemlich zart sein. Meist ist sie aber verdickt und kleinzellig infiltriert.

Bronchiolus und *Ductus alveolaris* sind oft nur andeutungsweise zu erkennen, wenn sich ein kleinzellig infiltriertes Granulationsgewebe in der Schleimhaut entwickelt hat und fibrös wird. Hierbei wird die Lichtung eingeengt und die vollgestopfte Alveole von der Lichtung abgeschnürt, so daß kompakte Häufchen von Asbestkörperchen völlig isoliert in schwielig umgewandelter Bronchiolenwand liegen können (Abb. 3). Die Lichtung, soweit sie in diesen Abschnitten noch vorhanden ist, ist von Schleimhaut entblößt und enthält einzelne Asbestkörperchen und reichlich desquamierte Makrophagen. Das Granulationsgewebe dringt in die zellerfüllte Lichtung vor. Es zeigen sich Bilder einer Bronchiolitis obliterans (Abb. 4). Sowohl in den Bronchiolen als auch besonders deutlich in den Ductus alveolares finden sich erhebliche Verdickungen der glatten Muskulatur (Abb. 1 und 2). Sie sind selbst im Schwielengewebe teilweise noch deutlich nachweisbar.

Durch den Anbau von fibrös-kollagenem, zur Hyalinisierung neigendem Material in den lockeren *peribronchiolären Bindegewebsschichten* ist

die Fälle 4, 10, 13 und 29 die Annahme, daß in den Fällen mit kürzerer Expositionszeit verhältnismäßig mehr Staub aufgenommen wurde. In den Fällen 11, 15, 24 müssen wir dagegen annehmen, daß die in der relativ kurzen Expositionszeit aufgenommene Staubmenge nicht ausreichend war, um in baldiger Folge Symptome zu verursachen. Sie beeinflußte aber einen progredienten Prozeß von schleichendem Charakter, der weit in das freie Intervall, d. h. in die Zeit vom Ende der Exposition bis zum Tode, reichte. Die Bedeutung der Zeit für die Entwicklung des Lungenprozesses wird an diesen Fällen besonders augenscheinlich.

Tabelle 7. *Vergleich von Expositionszeiten mit der Zeitdauer vom Beginn der Exposition bis zum Auftreten erster Symptome bei Fällen mit schwerer Asbestose*

Fall	Expositionszeit	1. Symptom Jahre nach Beginn der Exposition	Freies Intervall	Dauer der gesamten Anamnese
13	11	9	13	24
4	12	12	9	21
10	15	13	11	26
29	18	15	0	18
11	6	etwa 19	15	21
15	5	etwa 25	21	26
24	8	—	18	26

Die Unterschiede in der Reaktion des Einzelfalles, seien sie zeitlicher, seien sie quantitativer Natur, sind aber sicher nicht allein auf die Unterschiede der (nur zum Teil bekannten oder abschätzbaren) exogenen Faktoren zurückzuführen. Zu diesem Ergebnis kommen auch KNOX und BEATTIE. An der Mitwirkung einer *individuellen Disposition* kann nicht gezweifelt werden, wenn auch ihre Bedingungen noch ungeklärt sind (BAADER. WEDLER). Die anamnestischen Unterlagen reichen für die Abschätzung dieses Faktors nicht aus.

Eine eingehendere Betrachtung der Art und der Entwicklung des Lungenprozesses kann sich also letztlich nur auf das Lungenbild und seine zeitliche Ordnung stützen. d. h. auf das Studium der *Histogenese*.

d) Welche Lungenbefunde von allgemeiner Bedeutung sind in unseren Fällen mit der Asbestose zusätzlich kombiniert? Mischpneumokoniosen im engeren Sinne liegen in unserem Material nicht vor. Ein Fall nur weist histologisch kleine hyaline Schwielen, die Verdacht auf Silikose erwecken, auf. Die Verteilung der *Anthrakose* auf unsere Fälle gibt Tabelle 8 wieder. Danach zeigen die Männer häufiger eine schwere Anthrakose als die Frauen. Der Schweregrad der Asbestose geht dem der Anthrakose nicht parallel.

Tuberkulöse Veränderungen wurden in 12 Fällen gefunden. In 7 Fällen handelte es sich um ältere, weitgehend abgeheilte Prozesse, die mehr oder minder die apikalen Oberlappenabschnitte betrafen. In dieser Gruppe war der Anteil der Fälle mit leichter Asbestose unverhältnismäßig groß ($n = 5$). In weiteren 3 Fällen fanden wir eine frische Streuung, zweimal (Fall 8, 31) bei einer indurativen Tuberkulose der Oberlappen, einmal (Fall 28) bei einer doppelseitigen kavernösen Tuberkulose. In den restlichen 2 Fällen bestand eine frischere käsige Tuberkulose, im Fall 26 in beiden Lungen, im Fall 3, der eine starke Verschwielung beider Oberlappen zeigte, im rechten Unterlappen. In diesen 5 Fällen noch aktiver Tuberkulose zeigten zwei (Fall 8, 26) eine leichte, einer (Fall 3) eine mittelschwere, und zwei (Fall 28, 31) eine schwere Asbestose. In den Fällen 3, 8 und 28 war die Tuberkulose wahrscheinlich wesentlich an der Todesursache beteiligt. Das Sterbealter betrug 63, 63 und 67 Jahre. In den beiden übrigen Fällen war einmal die Asbestose (Fall 31), das andere Mal ein Narben(?)-Carcinom der Lunge (Fall 26) die Todesursache; das Sterbealter war 72 und 56 Jahre. Diese Zusammenstellung läßt unseres Erachtens keinen Schluß auf eine gegenseitige Abhängigkeit von Lungentuberkulose und Asbestose zu. Die Abhängigkeit von allgemeinen Zeitumständen wird einige Bedeutung haben. An Hand großer Statistiken konnte WEDLER nachweisen, daß die Lungentuberkulose bei Asbestarbeitern nicht häufiger ist als in der allgemeinen Bevölkerung. Die letzte große Übersicht von GLOYNE zeigt, daß im Sektionsgut seiner Pneumokoniosen die Asbestosegruppe fast die geringste Häufigkeit an Tuberkulose aufwies.

Tabelle 8. *Die Beziehung zwischen dem Schweregrad der Asbestose und der Anthrakose*

Geschlecht	Schweregrad der Asbestose	Schweregrad der Anthrakose: leichtmittel *n* Fälle	schwer *n* Fälle	nicht erwähnt *n* Fälle
♂	1	1	2	2
	2		1	
	2—3		1	1
	3	1	3	
♀	1	4	1	1
	2	2	2	1
	2—3	2	1	1
	3	3	2	3

e) Das Lungencarcinom bei Asbestose. Eine ganz besondere Bedeutung in praktischer und theoretischer Hinsicht hat das *Lungencarcinom bei Asbestose*.

Das Carcinom der Asbestlunge, schon früher von GLOYNE (1933, 1935), von LYNCH und SMITH (1935) und von EGBERT und GEIGER (1936) beobachtet, gilt, seit NORDMANN mit 4 Fällen der Weltliteratur und zwei eigenen Beobachtungen überzeugend den Zusammenhang mit der Lungenasbestose dargelegt hatte, unwidersprochen als Berufskrebs, wenn man von Einwänden CURETONS absieht. In den letzten 10 Jahren ist die Zahl der Fälle wesentlich vermehrt worden. Nach WEDLER (1943) zeigten von den 29 in Deutschland sezierten und bekannt gewordenen Fällen von Asbestose 6 (20%) und von 92 im Weltschrifttum mitgeteilten Fällen 14 Fälle (16%) ein Lungencarcinom. WEDLER rechnete zu seinen Fällen auch 2 Pleuraendotheliome mit der Begründung, die Pleura sei in den Umbauprozeß mit einbezogen. BOEMKE stellte 1947 bei einem fast gleich großen Kollektiv 17 Fälle fest und fügte 1953 seinem Fall von 1947 zwei weitere Fälle hinzu. Es müssen weiterhin die Fälle von WEISS (ein Pleuraendotheliom), WELZ und WERBER

erwähnt werden. Merewether übersah 1950 235 Fälle autoptisch gesicherter Asbestosen mit 13,2% Lungencarcinom, Gloyne 121 Fälle mit 14,1%. Isserbacher u. Mitarb. fanden bei 603 Fällen des Schrifttums eine Häufigkeit von 13,8% (1953). Auch in Gruppen von lebenden Asbestarbeitern konnte eine Häufung des Lungencarcinoms beobachtet werden (Doll 1955).

In den letzten Jahren sind von Bohlig und Jacob (1955, 1958) Bedenken gegen diese Statistiken erhoben worden. Indem sie die durch Sektionsstatistiken ermittelten Zahlen von Lungencarcinom auf das Kollektiv der lebenden Asbestarbeiter beziehen, kommen sie zu der Feststellung, daß der Lungenkrebs bei Asbestarbeitern nicht häufiger sei als in der allgemeinen männlichen Bevölkerung. Das ist überraschend, da Bohlig und Jacob ursächliche Zusammenhänge zwischen Lungenasbestose und Bronchialcarcinom als erwiesen ansehen. In jüngster Zeit hat Böhme in diesem Archiv die Allgemeingültigkeit der Ergebnisse von Bohlig und Jacob in Zweifel gezogen. Er stützt sich nicht nur auf neuere Zahlenunterlagen des Schrifttums sondern auch auf eigene Erhebungen. So entstanden bei 92 Asbestosekranken, die — aus einem bestimmten Asbestwerk stammend — laufend untersucht wurden, bis 1959 6 Lungencarcinome. Weiterhin fand Böhme in 125 berufsgenossenschaftlich erfaßten Fällen 15 Lungenkrebse (= 12%), von denen 14 gestorben sind. In bezug auf die Gesamtzahl der Verstorbenen ($n = 31$) ergibt sich für den Lungenkrebs mit tödlichem Ausgang eine Rate von 45%. Unter den 20 Fällen, die pathologisch-anatomisch bearbeitet waren, zeigten 11 einen Lungenkrebs. Diese Zahlen zeigen die Abhängigkeit statistischer Ergebnisse von der Auswahl des Bezugssystems. In dem Material von Bohlig und Jacob sind übrigens bis 1958 34 Fälle verstorben, von denen 11 seziert wurden; unter diesen wurden 5 Asbestosecarcinome festgestellt.

Wir haben grundsätzliche Bedenken, Sektionsgut und lebende Bevölkerung als vergleichbare Kollektive anzusehen. Die Fehlerquellen werden allein schon augenscheinlich, wenn es sich um die Frage der Häufigkeit von Berufskrebsen mit kurzer Lebensdauer und langer Latenzzeit handelt. Böhme hat das für das Asbestosecarcinom angedeutet. Die Voraussetzung eines Vergleichs ist, daß sich die Kollektive nur in einem Merkmal unterscheiden. Auch pathologisch-anatomische Kollektive müssen dieser Forderung möglichst nachkommen.

In dieser Hinsicht gewinnt unsere Fallsammlung besonderes Interesse. Mit 11 von 36 Fällen (= 30,7%) ist der Anteil des Lungen- und des Pleuracarcinoms an unserem Asbestosekollektiv größer als nach dem Schrifttum zu erwarten war. Ein Vergleich mit anderen Statistiken erscheint jedoch problematisch, weil die Auswahl der Kollektive unterschiedlich sein könnte, wie schon betont. Ziehen wir aber zum Vergleich unser allgemeines Sektionsgut von 1948—1958 heran (Nassehi),

so ergeben sich nach Abzug aller Fälle mit einem Lebensalter bis zu 30 Jahren und der Asbestosefälle 13307 Sektionen mit 1018 (= 7,8%) Lungencarcinomen (einschließlich der Pleuraendotheliome).

Da 10 von unseren 36 Asbestosefällen nicht dem gleichen Sektionsgut angehören, erscheint eine Gleichsetzung unserer gesamten Fallsammlung mit dem Kollektiv der 13307 Fälle durch die Fehlermöglichkeiten der Auswahl belastet. In den verbleibenden 26 Fällen waren nur 6 als Asbestose klinisch bekannt, in 4 Fällen bestand ein Verdacht. In 3 Fällen war die Asbestose Todesursache. Es spricht nichts dagegen, diesem Sektionskollektiv von 26 Fällen die gleiche Repräsentanz für das allgemeine Asbestosekollektiv zuzusprechen, wie dem gleichzeitig beobachteten allgemeinen Sektionskollektiv für das allgemeine Kollektiv der Bevölkerung des Einzugsgebietes.

Unter den 26 Fällen finden sich 9 Lungencarcinome, das sind 34,6%. Auch dieser Prozentsatz ist noch nicht ohne weiteres mit dem des allgemeinen Sektionskollektivs zu vergleichen, da das Verhältnis der Männer zu den Frauen im Asbestosekollektiv 1:1,9, im allgemeinen Sektionsgut aber nur 1:0,7 beträgt. Vergleichen wir die Häufigkeit des Lungencarcinoms für die Geschlechter getrennt, so finden sich bei

Tabelle 9. *Vergleich der Häufigkeit von Lungencarcinom im Sektionsgut der Asbestosefälle und im allgemeinen Sektionsgut des Pathol. Instituts des Krankenhauses St. Georg*

	Allgemeines Sektionsgut (Fälle vom 31. Lebensjahr an, minus Asbestosefälle) 1948—1958		Asbestosefälle des allgemeinen Sektionsgutes 1948—1958		Alle Asbestosefälle, die seit 1939 im Path. Institut von St. Georg beobachtet wurden	
Alle Fälle	13307	100,0%	26	100,0%	36	100,0%
Lungencarcinome .	1018	7,7%	9	34,6%	11	30,6%
davon Pleuraendotheliome	102	0.77%	4	15,4%	4	11,1%
Alle männlichen Fälle	7817	100,0%	9	100,0%	13	100,0%
Lungencarcinome .	903	11.6%	4	44,4%	6	46,2%
Alle weiblichen Fälle .	5490	100,0%	17	100,0%	23	100,0%
Lungencarcinome .	115	2,1%	5	29,4%	5	21,7%

den Männern des allgemeinen Sektionsgutes 11,6%, bei denen des Asbestosegutes 44,4% Lungencarcinome. Für die Frauen gelten entsprechend die Sätze 2,1% und 29,4%. Eine Übersicht über die Verhältnisse gibt Tabelle 9. Sie macht, welchen Bezug man auch wählt, die erhöhte Krebsbelastung des Asbestosekollektivs deutlich. Besonders deutlich erscheint das für das weibliche Geschlecht, eine Beobachtung, die auch Jacob und Bohlig einräumend hervorheben.

Die über jede Erwartung hinausgehende Häufung von Pleuraendotheliomen bestätigt die Annahme von Wedler. Wir betrachten

auch unsere Fälle als Asbestose-Carcinome. Wenngleich wir die Frage, welchem Mutterboden das Pleuraendotheliom entstammt, offen lassen, so erscheint uns für die theoretische Begründung der geweblichen Beziehung doch ausreichend, daß es sich um einen malignen Tumor d. Lungenoberfläche handelt; gerade dieser Bereich ist ein Prädilektionsort der Lungenreaktion, wie die Neigung zu subpleuraler Verdichtung u. die Häufigkeit von Pleuraverschwartungen in unkomplizierten Fälle von Asbestose zeigen.

Unter den in Tabelle 9 angeführten Lungencarcinomen findet sich neben den 6 Unterlappen-Carcinomen und den 4 Pleuraendotheliomen ein Oberlappen-Carcinom (Fall 26), das wegen seines Sitzes und seiner engen Beziehung zu einer tuberkulösen Narbe auch als Narbencarcinom gedeutet werden könnte.

Die größere Krebsgefährdung bei Asbestose kommt nicht nur in der Häufigkeit sondern auch — entsprechend den Vorstellungen von Schinz — in der Verschiebung des Sterbealters in Richtung der jüngeren Jahrgänge zum Ausdruck. Das Durchschnittsalter beträgt in unserem Material 51.6 Jahre und entspricht damit recht gut dem von Wedler angegebenen Alter von 52 Jahren. Demgegenüber fand Schenck für das Lungencarcinom im St. Georger Sektionsgut ein Durchschnittsalter von 59 Jahren. Vergleichen wir die Angaben von Nassehi über die Altersverteilung für das Lungencarcinom im St. Georger Sektionsmaterial der letzten 50 Jahre (1668 Fälle) mit unseren Zahlen an Hand von Summationskurven, so ergeben sich entsprechende Verhältnisse (Abb. 11).

Die Gefährdung läßt sich aber nicht aus der Dauer der Exposition ableiten, wie Tabelle 10 zeigt. Eine gewisse Konstanz liegt — in Übereinstimmung mit den bereits veröffentlichten Fällen — in dem Zeitraum vom Beginn der Exposition bis zum Tode. Wir möchten diesen Zeitraum als Latenzzeit bezeichnen. Unser eigener Fall 16 wird noch von dem Fall Owens übertroffen, bei dem die Expositionszeit 1 Jahr die Latenzzeit 20 Jahre dauerte.

Die Gefährdung scheint auch nicht mit dem Schweregrad der Asbestose zuzunehmen, wie Tabelle 4 zeigt, eine überraschende Feststellung. Auch Böhme kam auf Grund seines Studiums der berufsgenossenschaftlichen Akten zu dem Schluß, daß bei den sezierten Fällen ein deutliches Überwiegen der schweren Asbestosen anscheinend nicht beobachtet worden war, ein Ergebnis, das im Gegensatz zu den Beobachtungen der eigenen 6 Fälle stand. Wir werden auf dieses Problem noch einmal unter Berücksichtigung der Histogenese zurückkommen.

Das männliche Geschlecht ist offenbar mehr gefährdet als das weibliche. Von 13 Männern unserer Sammlung haben 6, d. h. 46,2% ein Lungencarcinom, während von den 23 Frauen 5, d. h. 21,7% betroffen

sind. Eine stärkere Krebsgefährdung des männlichen Geschlechts stellte ebenfalls Gloyne fest: während bei Männern in 19,6% der Fälle ein Lungencarcinom gefunden wurde, war dies bei Frauen nur in 9,7% der Fall. Schon Wedler weist auf diese Geschlechtsverteilung hin. Die auch sonst bekannte Geschlechtsdisposition für das Lungencarcinom tritt uns damit deutlich beim Asbestosecarcinom entgegen. Von besonderem Interesse ist in diesem Zusammenhang, daß das Pleuraendotheliom nur bei den weiblichen Fällen aufgetreten ist. Auch hier wird eine Geschlechtsdisposition deutlich. Betrachten wir zum Vergleich etwa die Lungencarcinome, die vom 1. Juli 1957 bis 31. Dezember 1958 in St. Georg seziert wurden: von 133 Carcinomen beim Mann

Tabelle 10. *Vergleich von Expositionszeit und Latenzzeit in 6 Fällen von Asbestose-Carcinom*

Fall Nr.	Jahre		
	Alter	Expositionszeit	Latenzzeit
9	53	24	24
10	47	15	26
13	39	11	24
16	45	$2^1/_2$	23
23	41	10	24
30	54	9	18

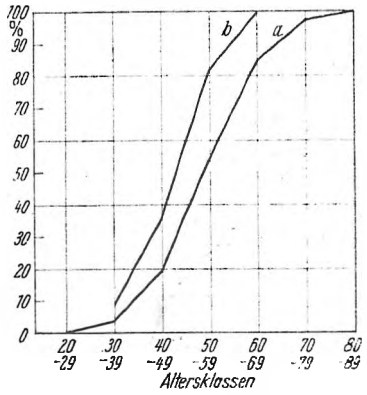

Abb. 11. Die Altersverteilung des Lungencarcinoms bei 1668 Fällen des allgemeinen Sektionsgutes des Path. Institutes St. Georg (unter Verwendung der Angaben von Nassehi) und bei 11 Fällen des Asbestose-Sektionsgutes. *a* Allgemeines Sektionsgut; *b* Asbestose-Sektionsgut

waren 15 (=11,3%) Pleuraendotheliome, von 29 Carcinomen bei der Frau 11 (=38%).

Es drängt sich die Vorstellung auf, daß das Asbestosecarcinom prinzipiell nicht von Carcinomen mit unbekannter Ätiologie in gleicher Lokalisation unterschieden werden kann. In diesem Sinne spricht, daß unser Material durchaus nicht nur Plattenepithelcarcinome zeigt, wie früher geradezu postuliert wurde. Es finden sich in einigen Fällen neben großzelligen und plattenepithelialen Wuchsformen auch Übergänge zu kleinzelligen Strukturen oder das ausgesprochene Bild des kleinzelligen Bronchialcarcinoms. Übergänge zu großzelligen oder plattenepithelialen Strukturen kann man auch in kleinzelligen Bronchialcarcinomen unbekannter Ätiologie beobachten. Immerhin stehen die nichtkleinzelligen Wuchsformen in unserem Material mehr im Vordergrund. Ein weiteres Kriterium des Asbestosecarcinoms, die multizentrische Entstehung, ist makroskopisch schwer zu beurteilen. Die

alveolären Parenchyms bewirken ein Übertreten der Fremdkörper in die Nachbarschaft ihres primären Kontaktes. Es entstehen *peribronchiolare Fibrosen* und wiederum Schrumpfungen. Die in diesem fibrösen Bindegewebe liegenden Asbestkörperhaufen können dann nach jahrzehntelangem, staubfreiem Intervall von Fremdkörperriesenzellen umschlossen innerhalb von Schwielen gefunden werden. Die Folge der endo- und peribronchiolären Fibrose ist eine *starre Fixierung* des benachbarten Parenchyms zunächst *in der Längsrichtung* des Bronchiolus, die zu einer fortschreitenden Belüftungsstörung führt. Als *sekundäre* Veränderung — infolge der Belüftungsstörungen, die anfänglich noch Emphysemcharakter zeigen, dann aber zunehmend in Dystelektase übergehen — entwickelt sich eine *diffuse Fibrose mit Kollapsinduration* und Ausgang in Verödung des Parenchyms.

Die Bronchiolen erleiden dabei ein verschiedenes Schicksal. Entweder veröden sie infolge einer fortschreitenden Bronchiolitis obliterans, oder sie erweitern sich, gelegentlich im Zusammenhang mit der Entwicklung kleiner umschriebener Herde eines hochgradigen substantiellen Emphysems, so daß großkammerige Systeme entstehen. Diese zeigen dann in manchen Fällen erhebliche post-infektiöse mesenchymale Proliferationen und *Umbau*vorgänge. Hierbei kommt es zu epithelialen Regenerationen, die alle Übergänge von regelrechtem zu metaplastischem oder atypischem Epithel aufweisen. In diesen Abschnitten entwickeln sich adenomartige Bilder mit allen Übergängen zum *Carcinom*. Zweifellos können aber auch die kleinen Bronchiolenlichtungen, die in einzelnen Abschnitten verödeter Bronchiolen erhalten geblieben sind, den Boden für ein Carcinom bereiten.

Die Vorstellung, eine diffuse Verteilung des Staubes setze einen diffusen Reiz, dieser führe dann zu einer diffusen Fibrose, müssen wir aufgeben. Die diffuse Fibrose entwickelt sich, wie wir sehen, *sekundär*, ohne selbst einen Kontakt mit Asbestkörperchen aufzuweisen, im Anschluß an eine umschriebene, peribronchioläre Fibrose, die in einer sicheren örtlichen Beziehung zu der geschilderten intracanaliculären Anhäufung des Staubes steht.

Gegen diese Überlegung könnte eingewendet werden, daß Staubelemente, deren Größe unter der Grenze der Sichtbarkeit liegt, in Mengen in die Lungen geraten, was Nordmann für sehr wahrscheinlich hält. Nach Sundius und Bygden u. a. muß aber die Faser eine bestimmte Länge haben, um eine Fibrose erzeugen zu können. Zu diesen Vorstellungen kamen auch Vorwald, Durban und Pratt sowie Behrens auf tierexperimentellem Wege. Die Hypothese der Wirkung unsichtbarer Staubteilchen kann unseres Erachtens wohl auch deshalb vernachlässigt werden, weil sich, wie eine Betrachtung der formalen Genese ergibt, die Entwicklung der diffusen Fibrose zwanglos aus den sichtbaren Befunden ablesen läßt.

Es sind, überblickt man den ganzen Prozeß, *zwei Phasen* zu unterscheiden, wie Eickhoff schon mit Recht hervorgehoben hat, die Phase

der funktionellen und morphischen Reaktion am Bronchiolus und die anschließende Phase der diffusen Fibrose. Die erste, die *bronchioläre Phase*, führt bereits zu der entscheidenden Belüftungsstörung; die *parenchymatöse Phase* in Form der diffusen Fibrose ist die zweite, zeitlich nachgeordnete Phase. Sie ist nicht Ursache der Belüftungsstörung sondern ihre Folge.

3. Folgerungen aus der Histogenese

Diese Vorstellungen von der Histogenese sind geeignet, zur Lösung der Fragen, die sich bei der Betrachtung unseres Materials ergaben, beizutragen und damit einige Eigentümlichkeiten, die am klinischen Bild und am Verlauf der Asbestose auffallen, verständlich zu machen.

a) Auf diesem Wege verstehen wir die *Diskrepanz* zwischen dem *klinischen* Befund und dem *röntgenologischen* und *anatomischen* Bild. Die funktionellen und morphologischen Veränderungen am Bronchiolus und am Alveolargang werden anfänglich keine und später relativ schwach erkennbare Zeichen im Röntgenbild geben können, wie auch Eickhoff betont, während sie schon jene Belüftungsstörung der Lunge einleiten, die ihrerseits zur Parenchymfibrose führt. Es ist verständlich, daß die morphologischen Veränderungen, auf die man in solchen Fällen zur Erhärtung der Diagnose wartet, schon einer verhältnismäßig späten Phase des Krankheitsverlaufes angehören müssen, um röntgenologisch sichtbar zu werden. Von der Intensität der bronchiolären Reaktion hängt es ab, ob ein Fall frühzeitig Symptome zeigt. Wir können nicht entscheiden, wieweit Spätsymptome dem bronchiolären Prozeß oder seinen Folgen, der diffusen Fibrose, zuzuschreiben sind.

b) Dem *Zeitfaktor* und damit auch dem *freien Intervall* kommt nach unseren histogenetischen Vorstellungen eine erhebliche Bedeutung für die endgültige Ausbildung der Lungenveränderungen zu. Die einmal abgelagerte Staubmenge und die Zeit sind wichtige Bedingungen für das Maß der Progredienz. Unsere Befunde sprechen dafür, daß die peribronchioläre Verschwielung unter dem Einfluß der Asbestkörperchen auch im Laufe von Jahrzehnten nicht zur Ruhe kommt. Dafür sprechen Brüche, Absprengungen von den Körperchen, Umformungen an der Gelhülle und Umgruppierungen der Körperchen zu Rosettenstrukturen, alles Befunde, die für alte und fortgeschrittene Asbestosen typisch sind. Es fällt schwer, diese Ablagerungen, die als typische Hornblendenderivate anzusehen sind, als belanglos für die Progredienz aufzufassen. Wir sind mit Beger völlig einig, daß die Asbestkörperchen die Fibrosebildung mittelbar über die peribronchioläre Fibrose unterhalten, ohne die Bedeutung der Asbestnadeln für die initialen Prozesse schmälern zu wollen. Die Natur des fibrogenen Reizes ist jedenfalls auf einen

entkräftet. Vergegenwärtigen wir uns, daß dem diffusen, über die ganze Lunge verbreiteten Prozeß der Asbestose unzählige solcher Regenerationsherde zugehören, dann wird ohne weiteres verständlich, daß die Wahrscheinlichkeit, daß an irgendeiner Stelle der Umschlag in eine autonome Wucherung malignen Charakters erfolgt, größer ist als in jenen Lungen, in denen der Boden zu einer solchen Entwicklung nur in einem entsprechenden Einzelherd zu suchen ist.

Wir nähern uns damit Vorstellungen, die für die Genese des Lungencarcinoms überhaupt gelten. Die Bedeutung eines chronischen Reizes für die Entstehung des Lungencarcinoms glaubt Berkhan in dem stärkeren Befall der rechten Lunge mit Carcinom erkennen zu können, wobei er annimmt, daß infolge des gradlinigen Verlaufes des rechten Hauptbronchus die rechte Lunge mehr Staub einatmet als die linke. Wenn W. Fischer die Unterschiede in der Häufigkeitsverteilung auf die Unterschiede des Volumens der rechten und linken Lunge zurückführt, so wird damit ein weiterer Gesichtspunkt berücksichtigt; es wächst die Wahrscheinlichkeit der Krebsentstehung mit der Zunahme des Mutterbodens. Diese allgemeinen Überlegungen sind für unsere Beobachtung, daß keine Beziehung zwischen Schweregrad der Asbestose und Lungencarcinom besteht, von Bedeutung. Wir müssen mit einem quantitativen Faktor rechnen, der in der Ausdehnung des Prozesses liegt. Wir müssen annehmen, daß der chronische Reizzustand am Bronchiolus respiratorius, ubiquitär in der Lunge verteilt, für die Carcinomentstehung ausreicht. Aber wir dürfen uns mit dem exogenen Faktor nicht begnügen. „Daß wir damit noch weit von einem vollen Verständnis der feineren Beziehungen entfernt sind, hat dieses Problem bei der Asbestose mit dem der Krebsentstehung überhaupt gemeinsam" (Wedler). Daß der Asbest nur *ein* Faktor ist, betonte 1957 auch Hueper. Es müssen weitere Impulse, die sich unserem Wissen noch entziehen, angenommen werden. „Es gibt mehr endogene und exogene Faktoren als sich träumen läßt" (W. Fischer). Die Art des inhalierten Asbestes, individuelle Lebensgewohnheiten, allgemeine geographisch bedingte Lebensumstände sind, soweit zu übersehen, von ebenso mitwirkender Bedeutung wie anlagebedingte individuelle Faktoren, Faktoren, die erst des äußeren Anstoßes im Sinne des Proliferationsreizes von genügender Dauer, Stärke und vielleicht bestimmter Art bedürfen, um zum Krebs zu führen. Schon Fischer-Wasels sagte auf der 28. Pathologen-Tagung: „Aber nur, wenn die typische besondere Allgemeindisposition, die allgemeine Krebsbereitschaft noch hinzukommt, bildet eine Regenerationswucherung eine Geschwulstkeimanlage, eine bösartige Geschwulst." In diesem Zusammenhang verweisen wir auf die bemerkenswerte Geschlechtsverteilung des Asbestose-Carcinoms in unserem

Material, die der allgemeinen Geschlechtsdisposition für das Lungencarcinom entspricht.

4. Schlußfolgerungen für die Begutachtung

Die vorgelegten Befunde und ihre Deutung scheinen geeignet, Fragen vor allem von klinischer Seite und jene, die die Genese des Asbestose-Carcinoms betreffen, einer Lösung näherzubringen. Sie gewinnen damit vielleicht auch eine gewisse Bedeutung für die Arbeitsmedizin, die individuelle Prophylaxe und die Begutachtung.

Die Diskrepanz zwischen dem klinischen Bild in seiner subjektiven Färbung und dem röntgenologischen (klinisch-morphologischen) Befund stellt den Begutachter vor eine schwierige Entscheidung.

Die Begutachtung wird immer nach objektiven Unterlagen einer Klassifizierung der Schwere einer Erkrankung suchen und bestrebt sein, ihre Urteile in genormter Ausdrucksweise zu formulieren, um soweit allgemein verständlich zu sein, daß das Maß der Hilfeleistung für den Betroffenen — sei es eine prophylaktische, eine therapeutische oder eine soziale — festgelegt werden kann. Es sei auf die Einteilungen von KRÜGER, ROSTOSKI und SAUPE, von LANZA und von BURESCH hingewiesen. Die Kritik an diesen Bemühungen führt immer wieder zu der Feststellung, daß eine Gradeinteilung den klinischen *und* röntgenologischen *und* pathologisch-anatomischen Gegebenheiten nicht gerecht werden kann (WINKLER).

GLOYNE schrieb in seiner letzten Mitteilung über die Pneumokoniosen, daß alle Klassifizierungen der Lungenveränderungen gescheitert sind. Sie müßten scheitern, solange man die Schwere des klinischen Bildes mit einem Röntgenbild zu identifizieren versuchte. Es ist daher z. B. nicht angängig, eine Rente immer erst dann zu gewähren, wenn die „bindegewebige Umwandlung, die Fibrose ausgedehnter Lungengewebsanteile mit Ausfall ihrer Funktion für Atmung und Kreislauf" nachgewiesen ist (BOEMKE). Die vorausgehenden, lang anhaltenden klinischen Störungen werden damit unter Umständen als Alarmzeichen und frühzeitige Indicatoren der Asbestose völlig vernachlässigt. 1949 stellte JÖTTEN auf der Staublungentagung in Münster fest: „Die funktionelle Untersuchung wird jetzt im Gegensatz zu früher wesentlich höher bewertet als das Röntgenbild, das nur als ein Kriterium bewertet werden soll." Die 5. Berufskrankheiten-Verordnung vom 26. Februar 1952 trug dieser neuen Auffassung schon weitgehend Rechnung.

Nachdem uns nun die morphologische Untersuchung eines größeren Sektionsmaterials, das — einheitlich gesichtet — Lungenveränderungen aller Phasen enthält, gezeigt hat, daß der Lungenprozeß durch die funktionellen und morphischen Reaktionen am Bronchiolus respiratorius eingeleitet wird, ferner daß sich in dieser bronchiolären Phase bereits das Schicksal des weiteren Verlaufes entscheidet, möchten wir die Frage aufwerfen, ob es gutachtlich richtig ist, erst dann von einer Asbestose zu sprechen, wenn im Röntgenbild die Veränderungen der Fibrose

sichtbar werden. Zweifellos wird die Antwort auf diese Frage von der Entwicklung der Röntgentechnik beeinflußt sein; so etwa von der Möglichkeit, durch Vergrößerungsaufnahmen Frühdiagnosen zu stellen (KRAUSLER und SEYSS). Aber damit wird die Diskrepanz zwischen dem morphologischen Befund und dem klinischen Bild nicht geringer. Das Ergebnis unserer Untersuchung liefert unseres Erachtens den Beweis, daß BURESCH recht hatte, als er bereits 1931 schrieb: „Diese Unterscheidung von Staublunge und Staubkrankheit erscheint als durchaus glücklich gewählt." Damit hat BURESCH zwei Begriffe unterschieden, die üblicherweise gemeinsam mit der Bezeichnung Asbestose benannt werden.

Eine Voraussetzung, die Schwierigkeiten der Beurteilung und der Begutachtung zu überwinden, sind klare Begriffe, die einem objektiven Denken zugänglich sind, die deutlich und nicht vertauschbar sind. Begriffe bedürfen eindeutiger Benennung. Zur Erreichung einer eindeutigen Nomenklatur auf dem Gebiet der Pneumokoniosen hat der englische Arbeitsmediziner MEREWETHER die Bildung internationaler Gremien gefordert.

Dem Vorschlage von BAADER, GORALEWSKI, HAGEN, HOLSTEIN und KOELSCH, das Organ und die schädigende Noxe in der Bezeichnung zu vereinen, folgend, möchte ich die durch Asbest morphologisch veränderte Lunge als Asbestlunge bezeichnen. Hiernach kann jemand an einer *Asbestose* leiden, ohne daß mit den Mitteln der klinischen Morphologie, wenn man von dem Nachweis der Körperchen im Sputum absieht, eine *Asbestlunge* nachgewiesen wird. Ebenso sollte man aber auch mit der Möglichkeit rechnen, daß sich eine mittel- oder sogar hochgradige Asbestlunge ohne alarmierende Symptome entwickeln kann; diese Entwicklung kann zu einem Zeitpunkt festgelegt werden, zu dem röntgenologisch noch kein ausreichender Anhalt gegeben ist.

Abschließend möchten wir auf unsere *Krebs*befunde hinweisen. Die höhere Krebsgefährdung der Asbestlunge im mitteleuropäischen Raum kann unseres Erachtens nach wie vor als weitgehend sichergestellt angesehen werden. Der Rückzug auf ein „in dubio pro aegroto" (OETTEL) scheint nicht erforderlich, wenn man vergleichbare Kollektive des mitteleuropäischen Raumes zur Grundlage der Urteilsbildung macht. Zum Krebs der Asbestlunge ist auch das Pleuraendotheliom zu zählen.

Ein Fall aus dem Schrifttum (LEICHER), eine Häufung von Fällen in unserem Material und der Nachweis, daß eine hämatogene Generalisation von Asbestkörperchen möglich ist, werfen die Frage auf, ob auch das *Peritoneal-Carcinom* bei Asbestose als Komplikation der Asbestose und damit als entschädigungspflichtige Berufskrankheit anzuerkennen ist.

Zusammenfassung

1. Es wird über 36 Fälle von Asbestose, die im Arbeitsbereich des Pathologischen Institutes des Allgemeinen Krankenhauses St. Georg in Hamburg untersucht wurden, berichtet. Einige zum allgemeinen Verständnis notwendige Angaben über die Asbestose als Zivilisationskrankheit, über den Asbest, seine Verarbeitung, über den Staub und die extrapulmonal gebildeten Asbestkörperchen werden vorangestellt.

2. Die Anamnese, die wichtigsten klinischen und Sektionsbefunde finden sich in Tabellen. Die makroskopischen und mikroskopischen Befunde der Lungen und der regionären Lymphknoten werden zusammengefaßt dargestellt. Es folgt ein kurzer Bericht über Befunde, die eine hämatogene Streuung der Asbestkörperchen erkennen lassen.

3. Das Sektionsgut, das von 13 männlichen und 23 weiblichen Fällen stammt, enthält alle morphologischen Schweregrade der Asbestose ziemlich gleichmäßig. In 7 Fällen ist die Asbestose vermutlich das Hauptleiden, in 11 weiteren Fällen besteht ein Lungencarcinom, davon in 4 Fällen ein Pleuraendotheliom. In 18 Fällen sind andere Befunde als Hauptleiden zu bezeichnen. In einer Reihe von Fällen wurde die Asbestose erst pathologisch-anatomisch erkannt.

Dieses Material schien geeignet, die Vorstellungen von der Histogenese zu überprüfen, auf dieser Grundlage einige klinische Probleme einer Klärung näherzubringen und erneut Stellung zu der in den letzten Jahren wieder aufgeworfenen Frage des Asbestose-Carcinoms zu nehmen.

4. Die in Deutschland vertretene Auffassung, eine diffuse Staubeinwirkung auf das atmende Parenchym in seiner Gesamtheit führe unmittelbar zur diffusen Fibrose, kann nicht bestätigt werden. Der Staub wird vielmehr überwiegend im Bronchiolus respiratorius abgefangen, wie es die englischen Autoren schon seit langem beschreiben. Die funktionellen und morphischen Reaktionen am Bronchiolus leiten die 1. Phase, die wir die bronchioläre nennen möchten, ein. Sie führt zur peribronchiolären Fibrose. Die starre Fixierung des elastischen Parenchyms am indurierten Bronchiolus leitet die 2., die parenchymatöse Phase ein, die schließlich zur diffusen Fibrose führt. Neben einer Bronchiolitis obliterans entwickeln sich auch Bronchiolektasen. Hier wie dort kommt es unter den Bedingungen postinfektiöser Reizzustände und funktioneller Ausschaltung zu erheblichen epithelialen Regenerationen. Sie sind die Voraussetzung für das Lungencarcinom.

5. Die Kenntnis der Histogenese bringt einige Fragen zur Asbestose einer Klärung näher.

a) Die Diskrepanz zwischen dem schweren klinischen Bild und dem mehr oder minder negativen Röntgenbild kann mit der Eigenart der bronchiolären Phase erklärt werden. In dieser Phase können die funktionellen Störungen erheblich sein, während röntgenologische Zeichen noch fehlen müssen. Unklar bleibt die Diskrepanz, die in der parenchymatösen Phase zwischen einer dürftigen Symptomatologie und einem mehr oder minder ausgeprägten morphologischen Befund bestehen kann.

b) Der Schweregrad der Lungenveränderung ist nicht nur abhängig von der Expositionszeit und der (meist nicht bekannten) Staubkonzentration am Arbeitsplatz sondern auch von der Zeit. Die histologischen Befunde machen die Annahme einer schleichenden Progredienz auch im Verlaufe des freien Intervalls wahrscheinlich.

c) Ein Substrat der individuellen Disposition kann im Bronchiolus respiratorius gesehen werden. Die von Fall zu Fall unterschiedliche Intensität der sich gegenseitig beeinflussenden funktionellen und morphologischen Reaktionen bestimmt das klinische Bild und das Zeitmaß der Progredienz und beeinflußt damit auch den Schweregrad der Lungenveränderung.

d) Wir lehnen — in Übereinstimmung mit dem Schrifttum — eine unmittelbare cancerogene Wirkung des Asbestes ab: die Ubiquität von Herden mit epithelialen Regenerationen erhöht allein schon die Wahrscheinlichkeit für die Entstehung eines Lungencarcinoms.

6. Der in den letzten Jahren geäußerten Ansicht, daß das Lungencarcinom beim Asbestarbeiter nicht häufiger als in der allgemeinen männlichen Bevölkerung sei, können wir nicht zustimmen. Von 13 Männern zeigen in unserer Sammlung 6 (= 46,2%), von 23 Frauen 5 (= 21,7%) ein Lungencarcinom (bzw. ein Pleuraendotheliom). Berücksichtigen wir, um einen statistisch einwandfreien Vergleich durchzuführen, nur die Fälle des St. Georger Sektionsgutes von 1948—1958, so ist die höhere Krebserwartung gegenüber dem allgemeinen Sektionsgut dieses Zeitabschnittes unverändert eindeutig: bei den Männern mit 44,4% (gegenüber 11,6% im allgemeinen Sektionsgut), bei den Frauen mit 29,4% (gegenüber 2,1% im allgemeinen Sektionsgut). Unter den 11 Lungencarcinomen finden sich 4 Pleuraendotheliome. Das durchschnittliche Sterbealter und die Dauer der Latenzzeit entsprechen den Angaben in der Literatur. In unserem Material besteht keine Beziehung zwischen Lungenkrebs und Schweregrad der Lungenveränderung. Unter Berücksichtigung der Histogenese erscheint das verständlich.

7. Der Anteil der extrapulmonalen Carcinome ist ebenfalls erhöht. Das Magencarcinom kommt mit 11,1% (oder 15,4%, bezogen auf das Asbestose-Sektionsgut von 1948—1958) gegen 6,1% gehäuft vor. Die schon von Leicher ausgesprochene Vermutung eines Zusammenhanges von Peritonealcarcinom und Asbestose erhält eine Stütze, da sich in unserem Material 3 Peritonealcarcinome finden, d. h. 8,3% (oder 11,5%, bezogen auf das Asbestose-Sektionsgut von 1948—1958) gegenüber 0,16% im allgemeinen Sektionsgut.

8. Schlußfolgerungen aus unseren Ergebnissen für die Begutachtung werden besprochen.

Wegen der Schwierigkeit, klinische und röntgenologische (anatomische) Bilder zur Deckung zu bringen, wird vorgeschlagen, in der Begutachtung begrifflich zwischen Asbestose und Asbestlunge zu unterscheiden.

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Archiv für Gewerbepathologie und Gewerbehygiene 18, 205—219 (1960)

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(Leit. Arzt: Prof. Dr. Nordmann)

Asbest-Zementstaub-Lunge

(Pneumokoniose bei Mischstaub oder gemischtem Staub?)

Von

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Mit 5 Textabbildungen

(Eingegangen am 14. Juni 1960)

Die Kombination von Asbest und Zement kommt bei der Herstellung von Platten, die zu Wänden und Dächern benutzt werden oder auch von Behältnissen und Isolierkörpern vor, die in der Elektroindustrie Verwendung finden. Bei der Bearbeitung von Asbest-Zement kann es stauben, wenn die gehärteten Platten zersägt werden.

Zementstaub gilt als ungefährlich, jedenfalls steht die Zahl der Menschen, die ausnahmsweise durch Zementstaub geschädigt werden, in keinem Verhältnis zu der Menge der in der Zementindustrie Beschäftigten.

Asbest bewirkt bekanntermaßen eine Asbeststaub-Lunge (Asbestosis), die erst nach vielen Jahren eine Beeinträchtigung der Atmungsorgane bewirkt und durch Kombination mit rezidivierenden Lungenentzündungen, Tuberkulose und Krebs das Leben gefährdet.

Die Kombination von Asbest und Zement als Ursache einer Staublunge mit autoptischer Bestätigung ist im bisherigen Schrifttum noch nicht beschrieben worden. Eine Erkrankung und gar ein Todesfall nach Exposition von Asbest-Zementstaub sind offenbar selten; angesichts der vermeintlichen Harmlosigkeit des Zementes wäre nur eine Asbestlunge zu erwarten gewesen.

Der von uns behandelte Fall hat noch eine dritte Staubart im Werkstoff: Talkum, allerdings in einem sehr geringfügigen Prozentsatz, der trotzdem nicht unbeachtet gelassen werden soll.

Bei unserer Beobachtung handelt es sich um den 68jährigen N., der sehr lange Zeit in einer kleinen Fabrik mit einem sehr kleinen Personenkreis gearbeitet hat, die aus eigener Anschauung zunächst beschrieben werden soll.

Die Arbeitsstätte

Der Fabrikationsbetrieb — ein kleiner Familienbetrieb im Hinterhof eines mehrstöckigen Wohnhauses — beschäftigt 6 Arbeiter und läuft in einem niedrigen Schuppen ab, der in 2 Räume geteilt ist, in denen die Maschinen stehen. Im ersten Raum wird ein erdfeuchtes Gemisch von Asbest und Zement angerührt und in einer Druckpresse