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Über den Lungenkrebs bei Asbestose.

Von

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Als einzige haben bisher Nordmann und Sorge den Versuch unternommen, tierexperimentell an weißen Mäusen die Zusammenhangsfrage zwischen Asbeststaubinhalation und Lungenkrebs zu bearbeiten. Sie setzten 150 Mäuse zu ihren Versuchen an und bestäubten sie entsprechend der durchschnittlichen Lebens- und Arbeitsdauer des Menschen zwischen 1½ und 3 Monaten. Über die Hälfte der Tiere starb vorher. Keines überlebte die Inhalation länger als 9 Monate. 20% der überlebenden Tiere wiesen ein verhornendes multizentrisches Plattenepithelcarcinom und 42—57% epitheliale Neubildungen aller Stadien auf. Damit soll die ursächliche Bedeutung des Asbeststaubes für das primäre Lungencarcinom des Asbestarbeiters experimentell gestützt werden. Die Zahl der endgültig durch den Versuch gebrachten Tiere, aus denen die obigen Zahlen errechnet wurden, ist sehr klein. Nur 2 Tiere hatten Neubildungen, die als Krebs angesprochen wurden. Die Autoren wiesen selbst auf die Schwierigkeit der Abgrenzung von einfachen Metaplasien hin. Es muß einem erfahrenen Morphologen und Sachkenner überlassen bleiben zu entscheiden, wieweit die Schlüsse der Experimentatoren berechtigt sind und wieweit die erforderlichen Vorsichtsmaßregeln bezüglich Einheitlichkeit und Brauchbarkeit des Tiermaterials beobachtet wurden und wieweit in diesen Grenzen Spontantumoren in den Bereich der Erwägungen gezogen werden müssen. Nordmann und Sorge sind hierauf kurz eingegangen.

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

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

Tabelle 1.

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

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

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

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

Tabelle 2.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Zusammenfassung.

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

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[1] Die Originalarbeit lag dem Verfasser nicht vor.

Wir stellen also beträchtlich niedrigere als die Normwerte der Fe/B-Indexe fest, ja sogar die niedrigsten, bis jetzt aufgefundenen; und es scheint uns die Annahme nicht zu gewagt zu sein, daß, wenn der Befund teilweise auf die Eisenarmut des gesamten Organismus und deshalb auch des zirkulierenden Blutes zurückzuführen ist, andererseits auch auf die Neigung des Organismus, soviel wie möglich das Metall aufzusparen und es sofort für die Wiederherstellung des Farbstoffes, mit dem Endergebnis seiner raschen Entfernung aus dem Kreislauf, zu benutzen.

Wir haben versucht die Bedeutung und die Nutzbarkeit der Anwendung des Verhältnisses Fe/B bei der physiopathogenetischen Auswertung abnormer siderämischer Befunde und im allgemeinen des Verlaufes des Blutstoffwechsels mit praktischen Beispielen darzustellen. Im folgenden Diagramm wird das Verhalten des Verhältnisses Fe/B bei einigen Hämopathien dargestellt; unter den anämischen Formen ergeben sich durch ein höheres Verhältnis als die Norm charakterisiert im wesentlichen die aplastischen und hypoplastischen Anämien und in allgemeinen Krankheitszuständen, die durch funktionelle Trägheit der Erythropoiese charakterisiert sind.

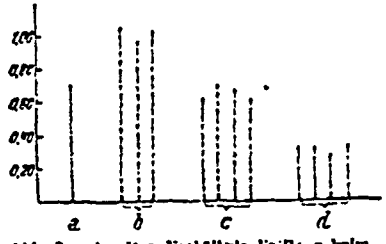

Abb. 2 a—d. Das Verhältnis Fe/B: a beim Normalen; b in 3 Fällen von aplastischer Myelose; c in 4 Fällen von ernstlicher Anämie (unbehandelt); d in 4 Fällen von „essentieller hypochromer Anämie".

Wir können zusammenfassen, daß, wie sich aus unserer Erfahrung ergibt — und die Eingriffsmöglichkeit umständlicher, die Aufspeicherungs- und Ausscheidungsvorgänge beeinflussender Faktoren ausgeschlossen — die Vergrößerung des Verhältnisses Fe/B in der Mehrheit der Fälle die Folge eines fehlenden oder ungenügenden Eisenverbrauches darstellt, und daß diese letzte Tatsache auf eine funktionelle Insuffizienz der hämopoietischen Gewebe hindeutet; während die Verminderung desselben Verhältnisses der Ausdruck eines sehr lebhaften Hämoglobinaufbaues und einer Neigung des Organismus zum „Sparen" des Eisens darstellen kann (diese zweite Möglichkeit ist bei Karenzzuständen des Metalls in Betracht zu ziehen, wie typisch bei „hypochromen essentiellen Anämien").

Literatur.

Für die Literatur siehe man nach: Oliva, G.: Il ricambio del ferro ed il comportamento della sideremia in condizioni normali e patologiche (im Druck).

(7)

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

Über den Lungenkrebs bei Asbestose.

Von

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(Eingegangen am 20. März 1943.)

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

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

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

die er wie folgt kurz abtut: „There has also been one case of squamous carcinoma of the pleura. There is no evidence at the moment that this was in any way related to the asbestosis".

1935 konnte Gloyne 2 weitere Beiträge zum Lungenkrebs bei Asbestose bringen. Dabei glaubte er, eine ätiologische Verknüpfung beider Krankheiten noch nicht behaupten zu können. Immerhin schienen ihm gewisse histologische Gesichtspunkte aber doch unbezweifelbar.

Die erste dieser beiden Beobachtungen betraf eine 35jährige Frau, die 8 Jahre Asbestspinnerin war und danach noch 9 Jahre ohne Staubexposition lebte. Sie starb — wie die Sektion zeigte — an einer mäßigen Asbestose, einem Gerinnsel im rechten Herzen, Milzinfarkt und einer meningealen Blutung. In der Basis des rechten Lungenoberlappens wurde eine klinisch nicht erkannte walnußgroße Geschwulst gefunden, die bis in die Spitze und verdickte Pleura hinaufreichte. Metastasen waren nicht vorhanden. *Das verhornende Plattenepithelcarcinom ging von einem kleinen Bronchus aus.*

Die zweite Beobachtung mit Sektion erstreckte sich gleichfalls auf eine Frau, die 71 Jahre alt wurde. Sie hatte 15 Jahre vor ihrem Tode je 1mal 6 und 13 Monate in der erfahrungsgemäß sehr staubreichen Mattratzen- und Aufbereitungsabteilung einer Asbestfabrik gearbeitet. Gloyne fand bei ihr anatomisch eine mittelschwere Asbestose mit zum Teil zerfallenem Tumor im rechten Lungenunterlappen, Ascites und Thrombose der linken Beinvene. Metastasen fehlten gleichfalls. Histologisch *handelte es sich auch um ein verhornendes Plattenepithelcarcinom.*

Der Krebs war in beiden Fällen nicht so ausgedehnt, daß er alleinige Todesursache zu sein schien. Das gleiche galt für die Asbestose.

In demselben Jahre (1935) kam aus USA. von Lynch und Smith eine Mitteilung über einen Lungenkrebs bei Asbestose, der eine ausführliche Krankengeschichte beigegeben war. Der dort beschriebene 57jährige Kranke, der 22 Jahre Baumwoll- und zuletzt bis zur Krankenhausaufnahme 21 Jahre Asbestweber gewesen war, hatte seit 5 Jahren über Kurzluftigkeit geklagt. Nachdem er 3 Jahre vor seinem Tode schon vorübergehend Schmerzen im Rücken und über den 3 letzten Rippen rechts gehabt hatte, erneuerten sich diese in den letzten Lebensmonaten. Er verfiel, hustete, wurde appetitlos, bekam Temperaturen, Blutauswurf sowie Belastungsdyspnoe. Der klinische Befund war für eine Asbestose charakteristisch. Rechts unten über der Lunge war das Atemgeräusch abgeschwächt. Die klinische Diagnose lautete auf Asbestose und chronisch indurierende Pneumonie mit Schwarte rechts unten. Pathologisch-anatomisch fand man neben der Asbestose mit rechtsseitiger Pleuritis und Bronchiektasen eine Zerfallshöhle im rechten Unterlappen, die makroskopisch für eine Tuberkulose gehalten wurde. Erst mikroskopisch stellte sich ein Plattenepithelkrebs heraus. Metastasen waren nicht vorhanden. Für eine Asbestose ungewöhnlich ist die Beschreibung von gleichzeitigen hyalinen Knötchen in der Lunge. Das Carcinom ging von einem Bronchus mit metaplastischem Epithel aus. Als Ursache dachten die Autoren an den chronischen Reiz auf die Bronchien. Sie sprachen bezüglich des Zusammenhanges zwischen Krebs und Asbestose von einer „possible relationship" und zogen Parallelen zu anderen Berufskrebsen der Lunge.

1936 berichteten Eglseer und Geiger (USA.) über eine weitere derartige Beobachtung, die sie — Gloynes Hinweis von 1933 ausgenommen — für die erste dieser Art überhaupt hielten. Der 41jährige Mann war 18 Jahre lang Asbestweber gewesen. Nach 9jähriger Arbeit bekleit er im Anschluß an eine Lungenentzündung Husten und Atemnot. 8 Monate vor der kurzen Krankenhausbehandlung bekam er heftige anfallsweise Rückenschmerzen. Er war abgemagert, wegen der Schmerzen schwer beweglich, hatte Husten, Cyanose und Atemnot sowie blutig-eitrigen Auswurf. Neben der Asbestose wurde links unten in der Lunge röntgenologisch ein Herd gefunden, der wie eine Atelektase oder ein pneumonischer

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

Gloyne konnte 1936 zu seinen 3 Beobachtungen eine weitere hinzufügen. Er fand ein entdifferenziertes Carcinom des linken Unterlappens bei einer Asbestose, dessen Träger 69 Jahre alt war und 21 Jahre im Asbestberuf gearbeitet hatte.

1938 machte Sparks ohne nähere Einzelheiten die Mitteilung, daß Gloyne bei seinen Sektionen 6 Fälle von Lungenkrebs bei Asbestose angetroffen habe. Hander erfuhr brieflich von Gloyne, daß sich diese 6 Krebse auf 60 Autopsien bezögen.

Nordmann erweiterte im gleichen Jahr unsere Kenntnisse um 2 neue Krebsfälle bei Asbestose, die er kurz hintereinander in Hannover sezieren konnte. Die erste Patientin war 35 Jahre alt. Sie hatte von ihrem 17.—26. Lebensjahr, genau 7 Jahre, in der Krempelei, Spinnerei und Weberei einer Asbestfabrik gearbeitet. 4—5 Jahre vor dem Tode bekam sie Husten und Atemnot. $^3/_4$ Jahr vor dem Tode trat sie unter dem Verdacht einer Tuberkulose in ärztliche Behandlung. Hornig stellte die Wahrscheinlichkeitsdiagnose auf Krebs im linken Unterlappen bei ausgeprägter Asbestose, weil klinisch die Zeichen einer Atelektase bestanden und tomographisch der Hauptbronchus verlegt war. Anatomisch handelte es sich um ein verhornendes Plattenepithelcarcinom mit walnußgroßer Zerfallshöhle, die Anschluß an den Unterlappenbronchus hatte, Pleuraverschwielung und Metastasen in Leber und Nieren.

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

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

1939 machte Wedler auf eine weitere Beobachtung in Deutschland aufmerksam, die von Bohne stammte, aber nicht mitgeteilt worden war. Der 58jährige Mann hatte von 1926—1935 10 Jahre zum Teil als Meister in einer Asbestfabrik gearbeitet. Wenige Jahre nach der Staubexposition bekam er schon Beschwerden von seiten der Atmungsorgane. 1928 war er 2 Monate verschickt. Später machte er öfter Heilstättenkuren, ohne daß Tuberkelbacillen bei ihm gefunden wurden. Wegen

zunehmender Verschlechterung seines Zustandes gab er ½ Jahr vor seinem Tode die Arbeit auf. Im Krankenhaus bot er Zeichen der allgemeinen Abmagerung, Cyanose und eines beginnenden unten über den Lungen wahrnehmbaren Katarrhs. Im Auswurf zahlreiche Asbestkörperchen, aber keine Tuberkelbacillen. Blutsenkung stark beschleunigt (57/93). Links über der 9. Rippe fand sich in der vorderen Axillarlinie eine mit der Haut verwachsene kastaniengroße Geschwulst, die entfernt wurde und sich als Krebsmetastase herausstellte. Röntgenologisch bestanden die Zeichen einer Asbestose sowie eine Zeichnungsvermehrung in den rechten Obergeschossen. Offenbar wurde nach den mir vorliegenden Unterlagen die Diagnose auf einen Lungenkrebs intra vitam nicht gestellt. Der Kranke starb bald nach der Excision der Metastase an Herzschwäche. Der Sektionsbefund wurde folgendermaßen beschrieben: „Die Lungen waren fest mit der Brustwand verwachsen. Das Herz war nicht vergrößert, die Muskulatur von braunroter Farbe und etwas schlaffer Konsistenz. Die linke Lunge war blut- und saftreich, der Unterlappen von derber Konsistenz und schiefriger Farbe. Die rechte Lunge fiel beim Herausnehmen im Bereich des Mittellappens ein. Sein Gewebe sah gelblich und völlig zerfallen aus und zeigte ausgedehnte Höhlen- und Knotenbildung. Der Oberlappen war blut- und saftreich, von fester Konsistenz und luftleer. Der Unterlappen war von schiefriger, graurötlicher Farbe und fester Konsistenz. Auch er erwies sich als luftleer. Die mikroskopische Untersuchung der Lungen ergab im rechten Mittellappen typisches Krebsgewebe, während im Unterlappen alle für Asbestose charakteristischen Veränderungen vorhanden waren. Vor allem fanden sich in allen Schnitten Asbestkörperchen."

Nach Bander (1939) sollen 9 Autoren in den Jahren 1935—1938 insgesamt 14 Krebsfälle bei Asbestose gesehen haben. Es geht aus dieser Mitteilung nichts Näheres hervor, so daß nach allen bisherigen Unterlagen, wie sie oben angeführt wurden, diese Angaben nicht in vollem Umfang bestätigt werden können.

1941 folgte ein ausführlicher klinischer und pathologisch-anatomischer Bericht von Wedler und Linzbach über eine weitere einschlägige Krankengeschichte, die den ganzen Verlauf des Leidens brachte. Der 60jährige Mann hatte von 1921 bis 1939, im ganzen 18 Jahre, in einer Asbestfabrik gearbeitet. Er war nur die 3 ersten Jahre einer starken Staubeinwirkung (Vorbereitung) ausgesetzt. Die ersten Beschwerden traten bald nach Arbeitsaufnahme ein. 1938 bot er bereits das Bild einer unkomplizierten schweren Asbestose, die sich schleichend entwickelt hatte. Im Laufe des letzten Lebensjahres stellte sich über dem rechten Zwerchfell im rechten Lungenunterlappen eine zunehmende Verschattung mit den klinischen Zeichen einer Atelektase und späteren Zerfalls sowie starken neuralgiformen Schmerzen in dem zugehörigen Intercostalnervenbereich ein. Der Auswurf wurde blutig. Alle Anzeichen sprachen für einen Krebs, der schon klinisch diagnostiziert wurde. Bei der Sektion bestätigte sich die Diagnose eines zerfallenen verhornenden Plattenepithelcarcinoms, das vom rechten Unterlappenbronchus ausging. Metastasen waren nicht vorhanden.

In Deutschland liegen inzwischen noch 2 weitere Beobachtungen vor, die bisher nicht in das Schrifttum eingegangen sind.

Der erste Fall wurde von Teutschlaender gesehen, der darüber bereits 2mal kurz mündlich berichtete. Einer persönlichen schriftlichen Mitteilung entnehme ich dazu folgendes: 1938 sezierte Teutschlaender eine 40jährige Frau, die mit langen Unterbrechungen 19 Jahre in einer Asbestfabrik tätig war. Die klinische Diagnose lautete bei ihr: „Lungentumor rechts? Cirrhotischer Lungenprozeß rechts? Vikariierendes Emphysem links. Ascites. Hochgradige Kachexie." Bei der Sektion fand sich keine Tuberkulose, dagegen aber eine sehr ausgedehnte Asbestose mit massenhaften Asbestkörperchen und ein rechtsseitiges Pleurablastom, das sich histologisch als „peritheliocelläres Mesothelioma" herausstellte.

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

Die zweite Beobachtung stammt von Alwens. Die Sektion nahm Fischer-Wasels vor. Ich kam als Gutachter mit dem Fall in Berührung. Der 60jährige Mann (13. 8. 81 bis 19. 9. 41) hatte bis ½ Jahr vor dem Tode 42 Jahre in einer Asbestkautschukabteilung gearbeitet. Er erkrankte im Januar 1941 unter zunehmender Atemnot und Gewichtsabnahme mit den Zeichen eines linkseitigen Pleuraergusses. Absolute Dämpfung, aufgehobenes Atemgeräusch und Rechtsverdrängung des Herzens. Der Auswurf enthielt reichlich Asbestkörperchen. In dem mehrfach durch Punktion abgelassenen, gallertigen, rötlichen Erguß wurden reichlich Tumorzellen gefunden. Über der rechten Lunge unten waren vereinzelt feinblasige Rasselgeräusche zu hören. Die Blutsenkung stieg schnell an. Im Auswurf keine Tuberkelbacillen. Röntgenologisch wurde eine Asbestose mittleren Grades festgestellt und im rechten Hilus evtl. der Primärtumor vermutet. Die Sektion deckte eine leichte Asbestose mit einem diffusen primären schleimbildenden Drüsenzellcarcinom der linken Pleura von größtenteils adenomatösem Charakter und Metastasen an der Bauchseite der linken Zwerchfellkuppe, der Serosa des kleinen Beckens und der Brustmuskulatur links auf. Das Sektionsprotokoll der Brustkauorgane sei im einzelnen angeführt, da bisher darüber nicht berichtet wurde.

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

von zarter Wand. Geschwulstgewebe ist nirgends nachweisbar. Hilusdrüsen. knoten sind beiderseits von schwarzer Farbe und weicher Konsistenz. — Das Herz ist kaum so groß wie die Leichenfaust. Herzbeutelblätter glatt und spiegelnd. Subepikardiales Fettgewebe ist mäßig reichlich vorhanden. Der linke Ventrikel ist klein, der rechte etwas erweitert. Wand des linken 5 mm, des rechten 2—3 mm dick. Sämtliche Herzklappen zart und schlußfähig. Kranzarterien mittelweit und von zarter Wand. Das Myokard ist auf allen Schnitten gleichmäßig braunrot. Aorta in ganzer Ausdehnung zart und elastisch.

Mikroskopischer Befund.

Rechte Lunge. Die Lungenstruktur zeigt stellenweise geringe emphysematöse Veränderungen. Verschiedentlich findet man im peribronchialen Gewebe knötchenförmige Ablagerungen eines feinkörnigen schwarzen Pigmentes. In diesem Bereich zeigt das peribronchiale Gewebe eine deutliche hyaline Umwandlung und Fibrose. Neben den Ablagerungen des anthrakotischen Pigmentes sieht man aber auch teilweise frische, teilweise auch im Abbau begriffene typische Asbestosiskörper. Diese liegen in größeren Mengen stets mit dem Anthrakospigment zusammen. Man findet sie aber auch unabhängig von diesen in Lungenalveolen und im interstitiellen Gewebe für sich allein liegend. Reichlich Ablagerungen von Kohlestaub und Asbestkörperchen sieht man auch unter der Pleura. Die großen Bronchien enthalten teilweise Schleim und abgestoßenes Epithel. Die Bronchialen sind vielfach erweitert. Überall aber sind sie mit einschichtigem Flimmerepithel ausgekleidet. Epithelmetaplasien lassen sich nirgends nachweisen. Das Lungengewebe unmittelbar unter der Pleura zeigt einen leichten Kollaps der Alveolen. Das Alveolarepithel zeigt hier vielfach drüsigen, aber nirgends atypischen Charakter. Im übrigen nirgends pneumonische Veränderungen im Lungengewebe.

Linke Lunge. Am Gewebe der linken Lunge findet sich der Befund der Kollapsinduration mit desquamativem Alveolarkatarrh und Fibrose des Interstitiums. Im peribronchialen Gewebe genau wie rechts finden sich reichlich Anthrakoseablagerungen mit einer Hyalinose des umgebenden Gewebes. Reichlicher als rechts findet man in dieser Lunge typische Asbestosiskörperchen, und zwar solche in Anf- und Abbau. Erheblich seltener als diesen begegnet man freien Asbestnadeln. Die Gelhülle dieser Körperchen gibt in typischer Weise eine positive Eisenreaktion. In der linken Lunge findet man weiter umfangreiche Blutungen und von Blutungen durchsetzte Gewebsnekrosen. Diese sind meist alle jüngeren Datums, da Demarkationserscheinungen vollständig fehlen. Die Asbestosiskörperchen sind in diesen nekrotischen Partien überall erhalten und treten durch die Nekrosen des übrigen Gewebes sehr scharf hervor. Auch in dieser Lunge finden sich am Bronchialapparat die gleichen Veränderungen wie rechts. Epithelmetaplasien werden auch in dieser Lunge vermißt.

Diagnose. Zahlreiche Asbestosiskörperchen in beiden Lungen mit geringer umschriebener Fibrose (geringe Lungenasbestose). Kompressionsatelektase und Kollapsinduration der linken Lunge. Blutungen, Nekrosen und geringe Bronchopneumonie in der linken Lunge.

Pleuratumor links. Der Tumor wechselt in seiner Struktur. An einigen Stellen findet man solide Zapfen und Stränge umgeben von Zügen eines myxomatösen zartfibrillären Bindegewebes. Fast alle Geschwulstzellen besitzen große Schleimvakuolen; man sieht massenhaft Siegelringformen. Vereinzelt findet man Zellen mit geplatzten Vakuolen, wo der Schleim in das umliegende Bindegewebe ausgetreten ist. — An anderen Stellen bietet der Tumor das Bild dicht nebeneinanderliegender Hohlräume, die von einem glatten einschichtigen Epithel ausgekleidet sind. Auch diese Epithelzellen enthalten vielfach Schleim und lösen sich in Siegelringform aus dem Epithelverband ab, wobei sie in das Lumen der Hohlräume

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

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

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

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

Als einzige haben bisher Nordmann und Sorge den Versuch unternommen, tierexperimentell an weißen Mäusen die Zusammenhangsfrage zwischen Asbeststaubinhalation und Lungenkrebs zu bearbeiten. Sie setzten 160 Mäuse zu ihren Versuchen an und bestäubten sie entsprechend der durchschnittlichen Lebens- und Arbeitsdauer des Menschen zwischen 1½ und 3 Monaten. Über die Hälfte der Tiere starb vorher. Keines überlebte die Inhalation länger als 9 Monate. 20% der überlebenden Tiere wiesen ein verhornendes multizentrisches Plattenepithelcarcinom und 42—67% epitheliale Neubildungen aller Stadien auf. Damit soll die ursächliche Bedeutung des Asbeststaubes für das primäre Lungencarcinom des Asbestarbeiters experimentell gestützt werden. Die Zahl der endgültig durch den Versuch gebrachten Tiere, aus denen die obigen Zahlen errechnet wurden, ist sehr klein. Nur 2 Tiere hatten Neubildungen, die als Krebs angesprochen wurden. Die Autoren wiesen selbst auf die Schwierigkeit der Abgrenzung von einfachen Metaplasien hin. Es muß einem erfahrenen Morphologen und Sachkenner Überlassen bleiben zu entscheiden, wieweit die Schlüsse der Experimentatoren berechtigt sind und wieweit die erforderlichen Vorsichtsmaßregeln bezüglich Einheitlichkeit und Brauchbarkeit des Tiermaterials beobachtet wurden und wieweit in diesen Grenzen Spontantumoren in den Bereich der Erwägungen gezogen werden müssen. Nordmann und Sorge sind hierauf kurz eingegangen.

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

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

beeinträchtigen wird, da gewöhnlich für die Krebsentstehung eine lange Staubexposition und evtl. ein längeres staubfreies Intervall vorgelegen haben muß. Die wenigsten Arbeiter bleiben heute so lange in den gefährdeten Betrieben. Auch wirkt die Staubbekämpfung wünschenswerterweise dem Staubschaden an der Lunge entgegen. Immerhin haben wir heute bei den schweren Asbestosen meist noch Arbeiter vor uns, die ihren Staubschaden aus früherer Zeit mit sich tragen, wo die Arbeitsbedingungen wesentlich ungünstiger lagen.

Als zweiter Gesichtspunkt, der für die Zusammenhangsfrage zwischen Krebs und Asbestose wichtig ist, wäre zu erörtern, welche besonderen Verhältnisse beim Staubschaden und den Befunden am Orte der Krankheit angetroffen werden, die den Krebs verständlich machen und von anderen Lungenkrebsen unterscheiden.

Als Schlußstein des Beweises müßten experimentelle Erfahrungen belegen, daß die Krebserzeugung auch am Tier gelingt.

Wenden wir uns zunächst dem statistischen Weg zu. Hier können wir als wirklich zuverlässig nur die Sektionen mit genauer anatomischer Untersuchung der Lungen verwerten, weil bei den rein klinischen Diagnosen gewisse Irrtumsmöglichkeiten gegeben sind. Außerdem stehen rein klinische Arbeiten zu dieser Frage nicht zur Verfügung.

In Deutschland sind bisher 30 Asbestarbeiter seziert worden. Die angeschlossene Tabelle 1 gibt die Fälle nach Alter, Geschlecht, Arbeitszeit, Stadium der Asbestose und Todesursache — soweit sie außerhalb der Asbestose oder der durch sie bedingten Herzschwäche oder agonaler Pneumonie lag — wieder. Die ersten 18 Todesfälle sind bereits veröffentlicht worden. Die anderen 12 habe ich gesammelt. Das unter Nr. 29 mitgeteilte junge Mädchen kann hier vernachlässigt werden, da sie nur eine kurze Staubexposition hatte und anatomisch noch keine Asbestose bot. Von den verbleibenden 29 Sezierten hatten 4 einen Bronchialkrebs und 2 weitere ein malignes Pleuragewächs. Es errechnet sich hieraus eine Prozentzahl von rund 20% für maligne Geschwülste der Lunge bei sezierten Asbestosen in Deutschland. Andere maligne Neubildungen des Körpers wurden insgesamt nur 3mal gefunden, und zwar je eine des Magens, der Speiseröhre und der Prostata. Wenn auch der Lungenkrebs statistisch in den 3 letzten Jahrzehnten beträchtlich zugenommen hat, so steht er an großen Sektionsstatistiken doch immer noch hinter den Krebsen des Verdauungskanals deutlich zurück. Er nimmt an Häufigkeit in der Krebsstatistik der Organkrebse je nach den verschiedenen Autoren sonst den 4.—2. Platz ein. Bei der Asbestose liegt der Lungenkrebs in Deutschland weit im Vordergrund, wie die obigen Zahlen lehren. Auch ist das Durchschnittssterbealter der Lungengewächsträger erheblich niedriger als das der Träger anderer Carcinome (rund 51 Jahre zu 60 Jahre). Die

Tabelle 1.

a	b	c	d	e	f	g
Lfd. Nr.	Alter, Geschlecht	Staubarbeit Jahre	Freies Intervall Jahre	Stadium der Asbestose	Todesursache	Publiziert durch
1	33 J., ♀	?	?	III		Fahr 1914
2	47 J., ♂	26		III		Buresch/Loeweheke 1931
3	60 J., ♂	21		III		Beintker/di Biasi 1931/37
4	? ♂	29		III		Beintker/Path. Inst. Münster 1931
5	35 J., ♂	20		III		Stroebe/Beger 1933
6	31 J., ♀	8		II—III		Bohne 1936
7	64 J., ♀	11		III		Saupe/Letterer 1938
8	41 J., ♀	18		III		Saupe/Banlocki 1938
9	38 J., ♀	13		III		Wedler/Walkhoff 1939
10	45 J., ♂	16		III		Wedler 1939
11	63 J., ♂	12	0	III		Wedler/Koch 1939
12	59 J., ♀	10		III		Wedler 1939
13	61 J., ♂	10		II	Magen-Ca.	Wedler/Walkhoff 1939
14	35 J., ♀	7	9	II	Bronchial-Ca.	Nordmann 1938
15	56 J., ♂	7	12	III	Bronchial-Ca.	Nordmann 1938
16	38 J., ♀	12	7	III	Lungenabsceß, Empyem	Nordmann 1938
17	68 J., ♂	10	2	III	Bronchial-Ca.	Bohne/Wedler 1939
18	60 J., ♂	18	1	III	Bronchial-Ca.	Wedler/Linzbach 1940
19	70 J., ♂	16	1	III	Oesoph.-Ca.	di Biasi u. a.
20	60 J., ♂	42	?	I—II	Pleura-Ca.	Alwens/Fischer-Wasels
21	38 J., ♀	4	1	III		Bohne
22	54 J., ♂	27		III		Koopmann
23	59 J., ♀	4	0	III		Bohne
24	52 J., ♂	3,25	2	III		Holm u. a.
25	60 J., ♂	22	2	III	Prostata-Ca.	
26	42 J., ♀	0	10	I	Lungenabsceß, Amyloidose	Wedler/Poczka
27	60 J., ♀	12	2	III	Nierenins uff.	Wedler u. a.
28	36 J., ♂	5,5	0	II	Lungentbk.	Wedler u. a.
29	18 J., ♀	1,75		0	Lungentbk.	di Biasi u. a.
30	40 J., ♀	10	?	~III	Pleuragewächs	Teutschlaender

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

fällt das relativ niedrige Sterbealter von 36 bzw. 40 Jahren auf. Alle Krebsträger hatten eine ausgeprägte bis schwere Asbestose. Nur der Mann mit dem Pleuracarcinom (Nr. 20) wies eine mäßige Asbestose bei allerdings sehr langer, aber wohl nur geringer Staubexposition auf. Nordmann hat schon darauf aufmerksam gemacht, daß in allen Fällen eine längere Staubarbeit im Spiele ist. Das trifft nach obiger Tabelle für alle Krebsträger ohne Ausnahme zu. Die Expositionszeit liegt 2mal bei 7, 2mal bei 10 und je 1mal bei 18 bzw. 42 Jahren. Das staubfreie Intervall vor der greifbaren Erkrankung an Krebs, während dem das Asbeststaubdepot in der Lunge weiter wirken kann, war verschieden lang ($^1/_2$—12 Jahre). Imal war es nicht genau bekannt (Nr. 30 der Tabelle).

Diese Zahlen zeigen eindeutig, daß der Lungenkrebs die häufigste Komplikation bei der Asbestose ist, wenn man von agonalen Pneumonien und Herzschwäche absieht. Selbst die Tuberkulose, deren Häufigkeit ja sonst die des Krebses weit übertrifft, steht hier hinter dem Lungenkrebs ganz wesentlich zurück. Damit ist ein entscheidender Beweis für den engeren Zusammenhang von Asbestose und Lungenkrebs erbracht. Es ist erstaunlich, daß die heutigen Prozentzahlen aus dem größeren Ausgangsmaterial genau mit den von Nordmann früher angeführten Zahlen aus einem kleineren Beobachtungsgut übereinstimmen.

Im Ausland liegen die diesbezüglichen Verhältnisse bis heute wie folgt:

Die größten Erfahrungen besitzen in dieser Frage die Engländer. Es besteht nach dem englischen Schrifttum, das zu unübersichtlich ist, weil die Einzelfälle zum Teil mehrfach veröffentlicht wurden, ohne daß man sie noch trennen kann, leider nicht die Möglichkeit, die Einzelbeobachtungen genau wie oben aufzuführen. Man muß sich bis auf weiteres mit den Zahlen von Gloyne begnügen, der auf 60 Sektionen von Asbestosen (nach Bander) 6 Lungenkrebsfälle (wahrscheinlich einschließlich eines Pleuragewächses) gesehen hat. Es ergibt sich hiernach eine Lungenkrebshäufigkeit von 12% bei Asbestose.

Ganz ähnliche Zahlen liegen aus USA. vor. Ich habe dort aus der Literatur bis 1939 13 Sektionsfälle gesammelt. Die Zahl ist möglicherweise nicht ganz vollständig, da mir einige Arbeiten nicht zugänglich waren. Unter diesen sezierten Asbestosen traf ich auf 2 Bronchialkrebse, die oben angeführt wurden. Das entspräche einem Hundertsatz von rund 15%. Ein anderer Organkrebs wurde dort nicht aufgeführt. Relativ häufig ist über die Pneumonie als Todesursache (4mal) berichtet worden.

Aus Frankreich liegen eigenartigerweise zu unserem Thema überhaupt keine eigenen zweckdienlichen Angaben vor.

Ebensowenig wurde in anderen Ländern dazu etwas veröffentlicht.

In Italien, wo man die Asbestose sehr gut kennt, ist bisher kein Lungenkrebsfall gesehen worden (Viglani u. a.).

In der Weltliteratur übersehen wir also bisher 14 maligne Lungen-Lippenfellgewächse epithelialer Herkunft, die auf 92 Sektionen entfallen. Das sind rund 10% Krebsfälle bei sezierten Asbestosen.

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

Tabelle 2.

Lfd. Nr.	Alter, Geschlecht	Staub exp. Jahre	Freies Intervall Jahre	Stadium der Asbestose	Art des Gewächses	Lokalisation	Metastasen	Autor
1	35 J., ♀	8	0	I—II	verhorntes Plattenepithel-Ca.	rechter Oberlappen	keine	Gloyne
2	71 J., ♀	1,5	15	II	verhorntes Plattenepithel-Ca.	rechter Unterlappen	keine	Gloyne
3	67 J., ♂	21		III	Plattenepithel-Ca.	rechter Unterlappen	keine	Lynch und Smith
4	41 J., ♂	18		III	solides Ca.	linker Unterlappen	ausgedehnte Metastasierung	Egbert und Geiger
5	36 J., ♀	7	9	II	verhorntes Plattenepithel-Ca.	linker Unterlappen	Leber, Niere	Nordmann
6	66 J., ♂	7	12	II	verhorntes Plattenepithel-Ca.	linker Unterlappen	ausgedehnte Metastasierung	Nordmann, Kleiner Krebs, auch im rechten Unterlappen
7	58 J., ♂	10	2	III	?	rechter Mittellappen	ja	Bohne/Wedler
8	60 J., ♂	18		III	verhorntes Plattenepithel-Ca.	rechter Unterlappen	keine	Wedler, Linzbach
9	40 J., ♀	10	?	III	pseudoalveoläres Mesotheliom	rechte Pleura	Peritoneum	Teutschländer
10	60 J., ♂	42	$^1/_2$	I—II	adenomatöses Pleura-Ca.	linke Pleura	ausgedehnte Metastasierung	Alwens-Fischer-Wasels
11	59 J., ♂	21	?		entdifferenziertes Ca.	linker Unterlappen	?	Gloyne

Die Verteilung nach dem Geschlecht macht auf 7 Männer 4 Frauen aus.

Das Alter liegt zwischen 35—71 Jahren.

4 stehen davon allein in dem relativ jugendlichen Alter von 35 bis 41 Jahren.

Immer ist die Zeit vom Arbeitsbeginn bis zur Krebsentwicklung verhältnismäßig lang (zwischen 12—42 Jahren). Bei kurzer Staubexpositionszeit schiebt sich gewöhnlich ein längeres staubfreies Intervall ein, was zu beweisen scheint, daß die Staubeinwirkung — wenn überhaupt — erst sehr allmählich zu einer Krebsentwicklung führt.

Die Mehrzahl der befallenen Kranken hatte eine schwere Asbestose, ohne daß sie in dieser Form allerdings obligat sein müßte.

9mal lagen Lungen- und 2mal Pleuragewächse vor. Die Lungenkrebse scheinen alle — soweit das nachträglich noch sicher zu entscheiden ist — vom Bronchialepithel ausgegangen zu sein. Eine für einen Alveolarkrebs typische Beobachtung findet sich nicht darunter.

Dem histologischen Charakter nach überwiegen die verhornenden Plattenepithelkrebse. Von 8 histologisch näher bezeichneten Lungenkrebsen waren 5 verhornende Plattenepithelkrebse; ein weiterer Plattenepithelkrebs war nicht verhornt. Ein anderer Krebs gehörte der Gruppe der undifferenzierten Gewächse an und das letzte wuchs acinös.

Die 3 Pleuragewächse wurden als „pseudoalveoläres Mesotheliom", als adenomatöses Pleuracarcinom" und als „squamous carcinoma" beschrieben.

4 der Lungengewächse im engeren Sinne hatten keine Metastasen gesetzt.

Die Lokalisation der primären Lungenkrebse fällt allein 7mal auf die Unterlappen, wo die Asbestose immer am stärksten entwickelt ist. 4mal sitzt das Gewächs im linken, 3mal im rechten Unterlappen. Demgegenüber sind der rechte Mittel- und Oberlappen nur je 1mal mit einer Geschwulst vertreten.

Diese örtliche Übereinstimmung der Geschwulstlokalisation mit den stärksten asbestotischen Gewebsveränderungen in den Untergeschossen der Lunge ist auffällig.

Die zahlenmäßige Häufung des Lungenkrebses bei sezierten Asbestosebefallenen ist der erste einleuchtende Beweis für eine nähere ursächliche Verknüpfung dieser beiden Krankheiten. Der Prozentsatz von 16% Lungen- und Pleurakrebsen liegt weit über der sonst statistisch zu erwartenden Häufigkeit bei anderen Sektionen. Wenn die Lungenkrebshäufigkeit auch in den letzten Jahrzehnten sicher erheblich zugenommen hat, so macht sie nach großen Statistiken bei Sektionen im Durchschnitt doch nicht mehr als 2—3% aus. Wenn für die Asbestose die absoluten Zahlen — wie wir zeigen konnten — auch noch recht klein

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

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

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

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

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

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

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

Beobachtungen, die zum Teil vom Verf. selbst gemacht werden konnten, lehren uns, daß gera[illegible] bei der Asbestose der Staubschaden sich oft erst in diesem Intervall einstellt und zu einer zunehmenden Fibrose führt. Unter allen Lungenkrebsfällen bei Asbestose findet sich nicht ein einziger, bei dem nicht diese lange Einwirkungszeit des Asbeststaubes gegeben wäre. Hierin besteht eine sehr gute Übereinstimmung mit den Erfahrungen bei anderen Berufskrebsen.

Die sonstigen histologischen Befunde in der Asbestlunge ermöglichen uns ein weiteres Verständnis für die obigen Zusammenhänge. Man trifft in den Asbeststaublungen an den kleineren Bronchien meist ausgedehnte Epithelmetaplasien, die als präcanceröse Stadien angesprochen werden können. Höchstwahrscheinlich gehen aus ihnen im wesentlichen die carcinomatösen Neubildungen hervor. Nordmann hat in einem Falle sogar die Beobachtung gemacht, daß bei einem großen Carcinom des linken Unterlappens auf der anderen Seite ein eben beginnender kleiner Krebs vorkam, der nicht als Metastase, sondern als ein aus dem metaplastischen Bronchialepithel autochthon entstandener Krebs angesprochen werden mußte. Er hält deswegen die multiloculäre Krebsentstehung bei der Asbestose für besonders bezeichnend. Hier finden wir Parallelen zu dem Schneeberger Lungenkrebs.

Es hat den Anschein, als ob neben diesen Metaplasien auch die sonstigen histologischen Veränderungen in der Lunge bei der Krebsentstehung mitsprechen. Ihnen allen ist in erster Linie die stark gesteigerte Wachstumstendenz der Gewebe eigen. Hier sind zu nennen die reichlichen Epitheldesquamationen mit Formveränderungen der Deckzellen, die Bildung von zahlreichen Makrophagen und Fremdkörperriesenzellen sowie die Bindegewebswucherung. Dabei werden, worauf Linzbach Bezug nahm, die einzelnen Gewebe aus ihren normalen Beziehungen gelöst, ohne daß indes der Gewebsschaden so erheblich ist, daß Zelluntergang eintritt. In dieser gesteigerten Wachstumstendenz und Störung der normalen gewebl[illegible]chen Beziehungen sind Hilfskräfte für die Krebsentstehung wohl mit großer Wahrscheinlichkeit zu suchen.

Auch für die Pleuragewächse gelten diese Gesichtspunkte. Das Lungenfell ist in die Umbauprozesse einbezogen. Man findet dort Epitheldesquamationen, Fibrinauflagerung, Bindegewebsentwicklung, Verschwielung und Einlagerung von Asbestkrystallen und Asbestkörperchen (Gloyne u. a.).

Alle diese aufgeführten Gesichtspunkte fügen sich den Einsichten, die aus den statistischen Zahlen erwachsen, gut ein und bilden stützende Argumente für den inneren Zusammenhang zwischen Asbestose und Lungenkrebs.

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

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

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

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

Frage kommen. Die Einwirkung des Asbeststaubes auf die Lunge vollzieht sich wahrscheinlich über chemische und mechanische Schäden. Die chemische Wirkung suchen wir in der Kieselsäure, die sich aus dem leichter angreifbaren Serpentinasbest herauslösen dürfte. Daß sie eine cancerogene Wirkung besitzt, ist nach den Erfahrungen der menschlichen Pathologie und reichlichen Tierexperimenten ganz unwahrscheinlich und praktisch ausreichend widerlegt. Daß allerdings in den durch sie gesetzten, für die Asbestose örtlich anders angeordneten und ausgeprägten Gewebsveränderungen andere Verhältnisse als bei der Silicose gegeben sind, muß im Auge behalten werden. Diese andersartige Anordnung und Form der Gewebsneubildung kann immerhin andere biologische Reaktionsweisen des Gewebes auslösen. Darüber hinaus wird man aber gerade die mechanischen Rückwirkungen der vielen spitzen Asbestnadeln und Körperchen, die wahrscheinlich besonders dem Hornblendenasbest mit seiner starren, schwerlöslichen Beschaffenheit eigen sind, beachten müssen. Ihnen kommt wohl sicher für die eigenartige Gewebsreaktion durch die ständige mechanische Irritierung eine große Bedeutung zu.

Schließlich sei noch daran erinnert, daß besonders an den Bronchien bei der schwereren Asbestose sich entzündliche Reaktionen, zum Teil mit Bronchiektasenbildungen, abspielen, die ihrerseits gelegentlich einer Krebsentstehung Vorschub leisten können.

In diesen allgemeinen und vor allem örtlichen Gegebenheiten werden wir für die Asbestose bei unseren heutigen Kenntnissen die Erklärung für die Krebsentstehung suchen müssen. Viele der Schäden kommen ihrer Definition nach nicht über den Begriff der chronischen Reizwirkung hinaus. 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.

Wenden wir uns nun noch der klinischen Diagnosestellung des Krebses in der Asbeststaublunge zu:

Grundsätzlich werden hier alle diagnostischen Erwägungen Anwendung und Gültigkeit finden müssen, deren wir uns auch sonst bei der Krebserkennung der Lunge und Pleura bedienen. Da sich der Krebs aber hier auf eine Grundkrankheit aufpfropft, werden wir mit bestimmten Eigentümlichkeiten des Krankheitsbildes rechnen und bestimmte Vorkenntnisse aus der Symptomatologie der Asbestose mitbringen müssen.

Für die Vorgeschichte wird es zunächst wichtig sein, eine genaue Berufsanamnese aufzunehmen und die Erfahrung zu berücksichtigen, daß Lungenkrebse bei Asbestose sich erst nach jahrelanger Staubexposition einzustellen pflegen, wobei die Dauer der Gefährdung zum Teil durch ihre Intensität aufgewogen werden kann. Wir kennen bisher nur eine einzige Beobachtung, wo die Arbeitszeit im Staub nur 1½ Jahre betrug, sonst erstreckte sie sich auf 7 Jahre und mehr. Bei kurzer intensiver Bestäubung scheint dennoch zur Krebsentstehung immer ein längeres staubfreies Intervall hinzukommen zu müssen. Es gibt bisher keinen Krankheitsfall, bei dem der Zeitraum vom Beginn der Staubarbeit bis zum Nachweisbarwerden des Krebses weniger als 12 Jahre betragen hätte. Man wird weiter gewöhnlich erwarten dürfen, daß der Krebs nur bei ausgesprochenen, wenn auch nicht immer schwersten Formen der Asbestose auftritt. Die obigen Beispiele belegen dies.

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

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

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

ist mit diesem Krankheitszeichen nicht viel anzufangen. Das gleiche gilt für die Atemnot. Etwas wichtiger scheint mir die Beachtung des Auswurfes zu sein. Er ist bei der unkomplizierten Asbestose meist spärlich und zäh schleimig, bei gröberer Bronchitis und Bronchiektasen aber auch reichlicher und eitrig. Ihm ist nur äußerst selten Blut beigemengt. Häufigere auch spärliche Blutentleerungen bedürfen einer besonderen Erklärung. Ich selbst habe Blut im Auswurf in Gestalt des Himbeergeleesputums nur bei einem komplizierenden Lungentumor gesehen. Im Schrifttum sind nur einzelne spärliche Angaben dieser Art auch für die einfache Asbestose vorhanden. Tumorzellen im Auswurf dürften nur sehr selten sein. Hornig will in seinem Falle von Tumor bei Asbestose reichlich Epithelzellen im Sputum gesehen haben. Wenn Zerfall des Lungengewebes einsetzt, wird sich dies unschwer an der Änderung des Auswurfes erkennen lassen. Bei meiner Beobachtung war dies sehr eindrucksvoll. Der Kranke warf plötzlich große Mengen körnig geballter nekrotischer Massen aus. Vielleicht gelingt es dabei auch einmal das Symptom der „asbestosis bodies in clumps" der Engländer zu finden. Es handelt sich dabei um rosettenförmige Haufen von Asbestkörperchen, die immer dann im Auswurf auftreten können, wenn Lungengewebe zerfällt (Abceß, Tuberkulose, Tumor). Sie sind den elastischen Fasern im Auswurf diagnostisch gleichwertig. Über die Bedeutung der Atemnot wurde oben schon gesprochen. Sie wird erst bei größerer Ausdehnung des Tumors oder Bronchialverschluß usw. auf ihn allein zu beziehen sein. Dagegen scheint mir den Schmerzen in der Brust eine größere Bedeutung zuzukommen. Sie sind bei der Asbestose allein gewöhnlich unerheblich und unbestimmt. Bei unserem Tumorfall traten sie mit Fortschreiten der Geschwulst ganz in den Vordergrund; sie nahmen einen typischen neuralgiformen Charakter an. Im Schrifttum finden sich ähnliche Hinweise. Die Ursache hierfür ist wohl in einem Übergreifen des Gewächses auf die parietale Pleura und evtl. die Intercostalnerven — wenn nicht gar auf Metastasen — zurückzuführen.

Diese Hinweise auf die allgemeinen und örtlichen Beschwerden, die größtenteils die Vorgeschichte an die Hand gibt, mögen genügen.

Für den sonstigen objektiven Befund mag folgendes bemerkt werden: Die Asbestose befällt die Lunge beiderseits. Streng einseitige Prozesse, um die es sich beim Tumor meist handelt, kommen nicht vor. Gewöhnlich herrscht auch eine weitgehende Symmetrie der Veränderungen vor. Man muß aber wissen, daß die rechte Lungenseite von der Fibrose auch normalerweise stärker betroffen sein kann. Über den Obergeschossen der Lunge finden wir nie gröbere Dämpfungen. Das Atemgeräusch ist hier meist rauh, nur selten abgeschwächt. Die abhängigen Lungenpartien bieten meist eine mäßige bis mittelstarke Schallabschwächung, die, wenn auch nicht ganz symmetrisch, so doch fast immer doppelseitig

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

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

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

verhält es sich mit der Bronchoskopie. Über diagnostische Lungenpunktionen bestehen keine Erfahrungen außer einigen Versuchen, bei denen Asbestkörperchen im Lungensaft gefunden wurden. Bei primären Pleuratumoren oder Metastasen vermag der Tumorzellnachweis im Punktat die Situation schlagartig zu erhellen. Dies war der Fall bei Alwens Beobachtung.

Metastasen werden die Diagnose immer schnell stellen lassen.

Daß länger bestehende Tumoren Fieber bedingen können, ist für die Diagnose unwesentlich, da Infekte die gleiche Folgen haben können.

Zum Blutbild und zur Senkungsbeschleunigung der roten Blutkörperchen sei bemerkt, daß Anämien nicht zur Asbestose gehören; eher kommen schon einmal hohe Farbstoff- und Zellwerte als Kompensationserscheinung vor. Begleitende Infekte dürften Ausnahmen veranlassen können. Zunehmende Anämien sind unter Ausschluß anderer vielfältiger Ursachen tumorverdächtig. Vom *Differentialblutbild* ist ein diagnostischer Anhalt für Tumor nicht zu erwarten. Die Blutsenkung ist bei unkompliziertet Asbestose an sich nicht beschleunigt. Dennoch findet man sie bei Serienuntersuchungen an zahlreichen Asbestosekranken verhältnismäßig oft in bescheidenem Grade erhöht, wahrscheinlich weil Infekte im Bronchialbaum dabei häufiger vorhanden sind. Stärkere und zunehmende Senkungsbeschleunigung ist immer zu beachten und nach den üblichen klinischen Regeln zu verwerten.

Damit wären die klinisch wichtigsten Gesichtspunkte zur Erkennung eines Lungentumors bei Asbestose aufgeführt. Die richtige Deutung ist immer Sache einer gediegenen klinischen Allgemeinschau und kritischen Verarbeitung der Einzelzeichen. Wichtig ist es, in diesem Zusammenhang das Krankheitsbild der Asbestose im allgemeinen zu kennen und an die Komplikationsmöglichkeit mit Tumor zu denken, der beinahe so häufig wie die aktive Tuberkulose in der Asbestlunge vorzukommen scheint. Sind doch in Deutschland bisher nur 10 aktive Tuberkulosen bei Asbestose gegenüber 6 Tumoren bekannt geworden.

Wenn das Ereignis des Auftretens von Krebs in der Asbeststaublunge so häufig ist, wie oben gezeigt wurde, und wenn auch sonstige gute Gründe für einen engeren ursächlichen Zusammenhang zwischen beiden Erkrankungen sprechen, so wird man, wenn auch die tierexperimentellen Unterlagen noch ausgeschaltet werden müssen, doch schon heute daran denken müssen, den gesetzlichen Versicherungsschutz auf diese Komplikation auszudehnen. In den wenigen bisher vorgekommenen Entschädigungsverfahren haben die Berufsgenossenschaften auf Grund einheitlicher Stellungnahme der befragten Gutachter den Zusammenhang anerkannt. In den von mir durchgesehenen diesbezüglichen Akten hat in Deutschland kein Gutachter einen ablehnenden Standpunkt eingenommen.

Zusammenfassung.

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

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[1] Die Originalarbeit lag dem Verfasser nicht vor.

Translation #

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LUNG CANCER IN ASSOCIATION WITH ASBESTOSIS

In the last 12-15 years, extensive experience with asbestosis has been presented in the German and foreign literatures so that we have now acquired far-reaching knowledge about the risk for asbestos workers and the picture of clinical illness of their job-related disease, as well as its course. Still a number of questions remain unanswered relative to its pathogenesis, which should be further explained from a standpoint of animal-experimental and chemical-physical studies. On the other hand, our knowledge of their complications and associated diseases rest on narrower and less certain foundations.

In recent times, an extensive contribution to the pattern of lung tuberculosis in this koniosis was made by the author. Informative and important, alike, is the question concerning the relation with lung cancer, which has received a large amount of attention in the last years due to the frequency with which it was found in association with asbestosis. Interest in this is not limited only to the sociological-medical and insurance-related field, but rather it extends further into the field of general medicine, because with this, a new example of an exogeneous cancer formation could be cited. The number of related observations so far is,to be sure, small, but so predominant in relation to the rarity of this disease, that a comprehensive representation seems permitted. It is also desirable because, so far, such a study from a clinical viewpoint is not yet available in literature.

First we would like to give a summary of the observations which have become known so far of lung cancer in association with asbestosis in world literature, we will add the new findings and illustrate the peculiarities of the picture of this disease as well as its clinical diagnosis.

We find the first mention of a cancerous tumor in an asbestos dust lung in 1933 by Gloyne, in a study concerning the pathological anatomy and histiology of asbestosis. He speaks there of asbestosis complications, which are connected with it originally (purulent bronchitis, bronchopenumonia, tuberculosis, emphysema, bronchiectasis) and of accompanying diseases, which, based on the status of the knowledge of the time, supposedly had nothing to do with the influence of the dust. Among the latter, he mentions an observation, which he quickly dismisses with the following: "There has also been one case of squamous carcinoma of the pleura. There is no evidence at the moment that this was in any way related to the asbestosis."

In 1935, Gloyne published two further contributions of lung cancer in association with asbestosis. He though he still could not prove an etiological link of the two diseases. Still, certain histiological criteria seemed to suggest this to him.

The first of these two observations concerned a 35 year old woman, who had been an asbestos spinner for eight years and then lived nine years more without any exposure to the dust. She died -- as the dissection indicated -- of moderate asbestosis, a clot in the right part of the heart, spleen infarct, and meningeal bleeding. At the base of the right upper lung lobe, a clinically unrecognized walnut-sized tumor was discovered, which reached into the top and thickened pleura. Metastases were not present. The callous squamous epithelium carcinoma originated from a small bronchus.

The second observation with dissection also involved a woman who lived to 71 years. Fifteen years before her death, she had worked one each for six months and then for 13 months in the matress and preparation department of an asbestos factory which was known to be very heavy in dust. Anatomically, Goyne found asbestosis of medium extent with a partly decayed tumor in the right lower lobe of the lung, ascites and thrombosis in the left leg vein. Again, metastases were not present. Histiologically, it was a callous squamous epithelium carcinoma.

In both cases, the cancer was not spread widely enough to appear as the only cause of death. The same was ture for the asbestosis.

In the same year, (1935), a report came from the U.S.A. by Lynch and Smith concerning lung cancer in association with asbestosis; it was accompanied by a detailed disease history. The 57-year-old patient described here, who had been a cotton worker for 22 years and then for 21 years (till he was admitted into the hospital) an asbestos worker, complained for years about short breath. The years before his death, he suffered temporary pains in the back and above the last three right side ribs; these pains flared up again in the last months of his life. He deteriorated, coughed, lost his appetite, developed fever, and experienced blood sputum, as well as stress dyspnea. The clinical findings were characteristic of asbestosis. Low on the right above the lung, the breathing noise had weakened. The clinical diagnosis was asbestosis with chronic pneumonia with callous slab low to the right.

Pathologically-anatomically, along with the asbestosis with pleuritis and bronchiectasis on the right side of the right lower lobe, was found, which macroscopically was thought to be a tuberculosis, decay (?). Only the microscope showed a squamous epithelium cancer. There were no metastases present. The description of simultaneous hyaline nodules in the lung is unusual for an asbestosis, the carcinoma started from a bronchus with metaplastic epithelium. The authors attributed the cause to chronic irritation of the bronchi. In regard to a connection between cancer and asbestosis, they spoke of a "possible relationship" and drew comparisons with other occupational lung cancers.

In 1936, Egbert and Geiger (U.S.A) reported a further observation of this type, which they considered except for Gloyne's 1933 study — the absolute first of this type. The 41-year-old-man had been an asbestos weaver for 18 years. After nine years of work, he retained cough and shortness of breath after he had had pneumonia. Eight months before the short hospital treatment, he suffered severe intermittant attacks of back pain. He lost weight, had difficulty moving because of the pain, suffered from coughing spells, shortness of breath, cyanosis (?) bloody sputum and (?) metastases into the left hilus and aorta glands to the right adrenal gland, into the stomach muscles, the pelvis, the spine and the skull. Along with the asbestosis, a focus was found by x-ray on the left side of the lower lung, which looked like an atelectasis or a pneumonic process, which however, was recognized as a tumor because metastases were present in the pelvis and spine. In the dissection along with the asbestosis, a 5:4:5 cm ascinsoc cancer was determined in the left lung underlap, which had sporea.

Origin of the tumor was a side branch of the left lower bronchus lobe. An etiological connection between the two diseases seemed plausible to them: "That the irritating effect of the inhaled asbestos particles may in this case been a significant factor concerned in the development of the primary lung cancer seems sufficiently plausible to be worthy of consideration."

In 1936, Gloyne added another observation to his three. He found a differentiated carcinoma of the left lower lobe in association with asbestosis. The carrier was 59 years old and had worked with asbestos for 21 years.

In 1938, Sparks revealed, without any further details, that in his dissections, Gloyne encountered six cases of lung cancer in association with asbestosis. Baader learned by letter from Gloyne that these six cancers were referred from 50 autopsies.

In the same year, Nordmann expanded our knowledge by two new cases of cancer in association with asbestosis, which he dissected in Hannover within a short time from one another. The first patient was 35-years-old. Of the 17-26 year of employment, she had worked for exactly seven years in (?), spinning and weaving of an asbestos plant. Four to five years before her death, she contracted shortness of breath and cough. 3/4 year before her death, she came under doctor's care for a suspected tuberculosis. Horning made the probable diagnosis of cancer in the left lower lobe in association with asbestosis, because clinically, the signs were present of atelectasis and the main bronchus was displaced tomographically.

Anatomically, this was a callous squamous epithelium carcinoma with a walnut-size decay cancer, which was connected with the lower lobe bronchus, pleura callousity and metastases in the liver and kidneys.

The second observation concerned a 55-year-old man who between the ages of 36 to 43 had worked seven years in an asbestos plant. Thirteen months before his death he lost a lot of weight and had bloody sputum. In the beginning, tuberculosis was suspected. Above the lower left lung, suppression and weaker breathing were found. The x-ray showed a shadow on the left lower segment. The doctors handling the case diagnosed it as asbestosis in association with lung cancer. The dissection confirmed this. The cancer in the left lower lobe and connected with the main bronchus was decayed to the size of a walnut and had spread off into the pericardium, the left chamber septum, the diaphragm, the peritoneum of the left upper stomach, the retroperitone tissue behind the spleen, the lymph nodes located there, and the lower (?) and upper lumbar spine. Again, histiologically, it was a callous squamous epithelium carcinoma. In the right lung lower lobe, a beginning of bronchial carcinoma was found, as well.

Nordmann followed up these observations with an exhaustive evaluation of the arguments which seemed to prove to him the existence of an occupation-related cancer. He was the first to clearly speak of occupational cancer of asbestos workers.

In Germany, 1939, Wedler directed the attention to a further observation which originated from Bohne, but which had not been published.

A 58-year-old man worked for ten years, from 1925 to 1935, as foreman in an asbestos factory. A few years after the exposure to dust, he became afflicted with problems to the breathing organs. In 1928, he was sent to a sanatorium for two months. Later he often underwent sanatorium cures, without any tubercule.bacilli having been found in him. Due to the steady deterioration of his condition, he left his job 1/4 year before his death. In the hospital he showed signs of general weight loss, cyanosis, and especially noticeable catarrh. In the sputum, numerous asbestos particles, but no tubercule bacilli showed. Hypostasis highly accelerated (57/95). On the left lung, above the 9th rib, in the front auxiliary line a chestnut-sized tumor intergrown with the skin was found, It was removed and turned out to be a cancer metastases.

The x-rays revealed symptoms of an asbestosis as well as an increase in the pattern of the upper part on the right side. Obviously, the diagnosis of lung cancer was not established - according to the accessible reports - in vivo. The patient died soon after the removal of the metastis from heart failure. The dissection findings were described as follows: "The lungs were firmly intergrown with the chest wall. The heart was not enlarged, the muscles were of brownish color and somewhat faccid consistency. The left lung was rich in blood and fluid, the lower lobe was coarse consistency and slatey color. The right lung tore when in the process of being removed, in the area of the middle lobe. The tissue looked yellowish and totally decayed, and presented extensive formation of caverns and nodules. The upper lobe was full of blood and fluid, of firm

consistency. It also proved to be without air. The microscopic examination of the lungs showed a typical cancerous growth tissue in the right middle lobe, whereas the lower lobe showed all changes which are characteristic for asbestosis. Above all, the sections contained asbestos particles.

According to Baader (1939) six authors supposedly observed, in 1935 to 1938, 14 cases of cancer in association with asbestosis. This report does not disclose any details, so that according to all reports up to now, as they were given above, these statements cannot be confirmed to the full extent.

In 1941, a detailed clinical and pathological-anatomical report by Wedler and Linzbach followed about a further clear history of the disease, which contained the full course of the suffering. The 60-year-old man had worked from 1921 to 1939, all in all, 18 years, in an asbestos factory. Only for the first three years was he exposed to a high level of dust (preparation). The first symptoms occurred not long after he began the employment. In 1938, he already presented an image of an uncomplicated asbestosis of a high degree, which had developed insiduously. In the course of his last year of life, there was, above the right diaphragm and in the lower lobe of the right lung an increasing shadow with the clinical signs of an atelectasis and later decay as well as very strong neuralgiform pain in the surrounding areas of the intercostal nerves.

The sputum became bloody. All signs pointed to cancer, which was clinically diagnosed. The dissection confirmed the diagnosis of a decayed callous squamous epithelium carcinoma, which originated from the bronchus of the right lower lobe. There were no metastases.

In the meantime, there are two more observations in Germany which are not yet part of literature.

The first case was observed by Teutschlender, who reported about it twice orally. Pertaining to this, the following can be seen from a personal written communication: In 1938, Teutschlaender dissected a woman of 40 years, who had been employed with long interruptions for ten years in an asbestos plant. The clinical diagnosis for her was: "lung tumor on the right (?), cirrhotic lung process on the right (?) vicarying emphysema on the left, ascites, cachexia to a high degree." The dissection did not reveal any tuberculosis, but rather a very extensive asbestosis, with a large number of asbestos particles, and a pleural blastoma on the right side, which was determined by the histiological examination as a: "Pseudo alveolar mesothelium." The peritoneum contained a large number of metastases in association with ascites. The left pleural cavity contained a hematoma of 50 cms. Compensatory emphysema of the left lung. The cachectic woman died of circulatory weakness due to the lung disease.

The second observation is by Alwens. The dissection was performed by Fischer-Wasels. I came in contact with the case in my role as a medical expert. The 60-year-old man (August 31, 81 till September 19, 41) had been employed up to half a year before his death for a total of 42 years in an asbestos caoutchouc department. He fell ill in January of 1941 with increasing shortness of breath and weight loss with the symptoms of pleural hematoma on the left side. Absolut- damping,

abnormal breathing noise, and displacement of the heart to the right. The sputum contained a great number of asbestos particles. The fluid that was tapped on several occasions contained a considerable amount of tumor cells and was reddish in color and gel-like in consistency. At times, small bubbly rattling noises could be hear above the right lung. The hapostasis rose fast. There were no tubercule bacilli in the sputum.

With the help of x-rays, an asbestosis of medium degree was diagnosed, and a tumor was suspected in the right hilus. The dissection revealed a slight asbestosis with a diffuse primary, mucus producing glandular cell carcinoma of the left pleura which was for the most part of adenomatose character, and it revealed metastases on the stomach side of the left diaphragm peak, the serosa of the small pelvis and the chest muscles on the left side. The dissection protocol of the chest organs shall be mentioned here in detail, since it has not been published so far.

Dissection of the chest:

Panniculus adiposus developed moderately. Thorax is moderately arched and elastic. The rib cartilege can be cut easily. The diaphragm is located on the right side at the level of the intercostal cavity, on the left side it is turned down and reaches far into the abdominal cavity. It lower pole here is lower than the pelvic comb. When applying the pneumo-thorax probe, almost 3000 cm of a yellowis-brown sticky fluid oozes out of the left pleural cavity. All of the mediastinum has been displaced to the right. The heart is suspended in drop-form in the mediastinum, its left edge is located in the middle line. The right lung is, except for a few strand-like growths, free in the pleural cavity. In the pleura costalis there are callous slabs the size of a palm, of white color, and coarse and sinewy with individual bulb-shaped, just as coarse with nodules. In the pleura of the right upper lobe, there is a large radiating scar. On the pleura of the right lung a moderately sticking, fine, grey and felty coating can be observed. The right lung itself is of appropriate size with medium air and fluid contents. The pleura and the cutting surface show moderately strong black netty patterning. Otherwise, the lung tissue is red in color. There are no diseased foci. The lower lobe branch of the right lung artery, there is on the intima, a brown-reddish blood clot. The lung arteries are empty. The left pleura is thickened slab-like over its full extent.

On the inner surface there are numerous, located closely to each other, up to walnut-size nodes, with a cauliflower type surface, which consists of gel-type tumor tissue which is white on the cutting surfaces. This exudes a sticky fluid when cut. Beside the tumor tissue there are several sinewy slabs as on the right side. At no place does the tumor tissue penetrate more deeply into the foundation, above all not into the lung tissue. Only in the area of the skin nodes mentioned in the beginning at the left side of the chest, there are tumor knots in the muscles between the ribs.

The left lung is highly atelectatic and adheres to the chest wall only in strand shaped growth. The lung tissue is of tough-coarse consistency, of greyish-red color, and shows on the surface and cuts a black, netty patterning, which is somewhat denser than the one on the right side. Nowhere can there be tumor tissue found. The lymph nodes of the hylus are on both sides of the black coloring and soft. The heart is barely as large as the first of the dead body. The sides of the pericardium are smooth and shiny. The fatty tissue beneath the pericardium is moderately sufficient. The left ventricle is small, the right one somewhat distended. The wall of the left one 5 mm, of the right on, 2-3 mm. Both cardiac valves are delicate and closable. The coronary arteries are of medium width and have a delicate wall. The myocardium is evenly brownish-red at all cutting surfaces. The aorta is all over delicate and elastic.

Microscopic Findings:

Right lung
The structure of the lung shows at places emphysematose changes. At several places there are in the peribronchial tissue nodular deposits, a finely grained black pigment. In this area, the per-bronchial tissue shows a clear hyaline change and fibrosis. Beside the deposits of the anthracotic pigment there are also fresh and also decaying asbestos corpuscles. These are always located in great quantities close to the anthracotic pigment. But they are also found independent from these in lung alveoli, and located by themselves, in interstitial tissue. There were also under the pleura, considerable deposits of coal dust and asbestos particles. The large bronchi contained in part mucus and discarded epithelium. The bronchioli were widened in many places. But all over they are lined with one-layered flickering epithelium. There are no epithelium metastases anywhere. The lung tissue just underneath the pleura shows a slight collapse of the alveoli. The alveolar epithelium here presents often glandular, but nowhere atypical characteristics. For the rest, there are no lung tissue pneumonic changes.

Left lung
The tissue of the left lung presents the finding of the collapse induration with desquamative alveolar catarrh and fibrosis of the interstitium. In the peribronchial tissue there is, just like on the right side, a considerable number of deposits of anthracosis with ophylanosis of the surrounding tissue. In this ling, there are more asbestosis corpuscles than on the right side, some fresh, some decaying. The free asbestos needles are to be found consider-ably less frequent than the asbestos corpuscles. The gel coating of these corpuscles gives, in a typical way, a positive reaction to iron. In the left lung there are many more hemorrhages and tissue necroses that are veined with hemorrhages. Most of these are of more recent origin, since there is no sign of demarcation.

In these necrotic segments the asbestosis corpuscles are preserved everywhere and they stand out considerably due to the necrosis in the rest of the tissue. In this lung, too, there are the changes in the bronchial structures as on the right. This lung also does not show any epithelial metaplasmas.

Diagnosis:
Numerous asbestosis corpuscles in both lungs with light, demarked fibrosis (slight lung asbestosis). Compression atelectasis and collapse induration of the left lung. Hemorrhages, necroses and slight bronchiopneumonia in the left lung.

Pleural tumor to the left. The tumor changes in its structure. In some places there are solid cones and strands surrounded by areas of myxomatous delicately-fibred connective tissue. Almost all tumor cells have large mucuous vacuoles; there are many ring shaped. In individual cases there are cells with burst vacuoles with the mucus having oozed out into the surrounding connective tissue. At different locations the tumor present the image caverns that are located close to each other and which are lined by a smooth one layered epithelium. These epithelium cells contain frequently mucus, and they separate from the epithelium group in ring-shape and enter the lumen of the cavities. In the interstitium there are also all over, loosely distributed mucuous tumor cells. Only in few places are there solid epithelium formations without the formation of mucus in the kind of the carcinoma solidum. The tumor is located all over the pleura parietalis and visceralis to the left and has, in some places grown into the subpleural layers of the lung tissue. There, they are mainly found in the septa and occasionally in the lymph vessels.

Diagnosis:
Primary, mucus-forming glandular cell carcinoma of the pleura, mostly of adenomatous character.

In question are the glassy knots of the stomach side of the left diaphragm peak and of the serosa of the small pelvis (?) , under the miscroscope, to be metastases of the same structure as the primary tumor.

This concludes that all cases observed so far and published in the world literature where pulmonary or pleural cancer occurred in association with asbestosis.

Up to now, Nordmann and Sorge were the only ones to attempt a solution to the question of a link between the inhalation of asbestos and pulmonary cancer with the help of animal experiments with white mice. They used 150 mice for their experiments, and they exposed them to dust from 1½ to 3 months, corresponding to the average life and employment span of humans. More than half of the animals died before the end of the experiment. None of them survived the inhalation more than 9 months. 20% of the surviving animals showed a callous, multiple squamous epithelium carcinoma; 42% to 57% showed epithelial new formations of all stages.

This is to confirm the causal meaning of the asbestos dust for the primary pulmonary carcinoma in the asbestos worker with the help of the animal experiments. The number of the animals that finally made it through the test, and from which the numbers above were calculated, is very small. Only two of the animals had growths, that were determined to be cancers. The authors themselves pointed out the difficulty of demarcation of simple metaplasias. An experienced morphologist and expert will utlimately have to determine whether the conclusions of the experimentors are justified, and in how far the necessary care had been taken regarding the unity and usability of the animal material and how far, within these limits, spontaneous tumors have to be included in the deliberations. Nordmann and Sorge discussed this briefly.

It is striking that so far, the animal-experiments with asbestos dust, that were admittedly conducted under different angles - did not show comparable observations. Dissections of animals (dogs, rats) that lived in asbestos plants, did not reveal such observations either. If there is to be a statement about an occupational cancer in a certain group of employees, first there will have to be the statistic proof that the cancer in question with increased frequency as compared to other groups of employees or populations. It will be difficult to fulfill the demand for the comparative numbers as matching in ages. The statistic method has also a further obvious difficulty for the asbestosis. It is a very rare disease in itself and there will always be small absolute numbers involved. One single, coincidental observation could bring about a large shift in percentages. Furthermore, one would have to consider with Nordmann that, especially in the last years, the turnover of workers in the asbestos plants will affect the results in a negative way, since usually the development of cancer is preceded by a long lasting exposure to dust, and possibly, a dust-free interval. Only few of the employees remain in the shops long enough that present a risk. Also, the attempt at cleaning up the dust contributes in a desirable way to the reduction of dust damage to the lungs. We have workers that are still carrying the dust damage from past times when the working conditions were far more unfavorable.

The second point that should be discussed for the question of the link between cancer and asbestosis, is which special conditions are found at the dust damage and the findings of the location of the disease which would render the cancer understandable and which would distinguish it from other forms of lung cancers.

The final step of the proof would have to be experimental observations which would prove that cancer can also be induced in animals.

Let us first discuss the statistical method. Here, we can use as dependable only the dissections with precise anatomic examination of the lungs, because the purely clinical diagnoses always leave certain room for error. Furthermore, there are no purely clinical studies concerning this question.

So far in Germany, there have been 30 dissections of asbestos workers. The following chart 1, lists the cases according to age, sex, time span of employment, stage of the asbestosis and cause of death - as long as they lay outside the asbestosi or heart insufficiency or fatal pneumonia that were caused by the asbestosis. The first 18 fatal cases have already been published. The other 12 were collected by me. The young girl that is listed under no. 29 can be neglected in our context since she had only a short exposure to dust, and anatomically did not yet show an asbestosis. Of the remaining 29 dissected patients, four had bronchial cancer, two more had a pleural malignant growth. From this, a percentage figure of around 20% was established for malignant tumors of the lungs for dissected asbestosis in Germany. Other malignant new growths of the body were found only three times: one of stomach, one of the esophagus, and one of the porstate. Even if pulmonary cancer has increased considerably in the statistics of the last three decades, it is still, in the large dissection statistics clearly behind the cancers of the digestive tract. With its frequency in the cancer statistics of the carcinoma of the organs, lung cancer occupies 4-2 rank, depending on different authors. As the numbers above show, lung cancer is by far the most important in association with asbestosis in Germany. The average age of death is considerably lower for the carriers of lung tumors than for the carriers of other carcinoma (approximately 51 to 66 years). But for now, the small numbers do not yet allow for special conclusions to be drawn from this. In the distribution according to sex we have four men and two women with pulmonary growths. For the distribution of sex for lung cancer, usually there are numbers of 3/4 to 1. Of course, the quota of the asbestos workers with lung cancer is also dependent on the number of the women and men working in the plants. In Germany, there are far more women. For the two men mentioned above, the relatively low age of death is striking; 35 and 40 respectively. All cancer carriers had a clear to bad asbestosis. Only the man with the pleural carcinoma (no. 20) had a moderate asbestosis with a very long, but only light exposure to dust. Nordmann already pointed out that in all cases a long time of employment in the is involved. This is true, without exception, according to the chart above, for all cancer carriers. The time span of exposure is twice 7, twice 10, and once each 18 and 42 years respectively. The dustfree interval, before the diagnosis of cancer could be made and during which the deposit of asbestos dust in the lung can be effective, varied in length (½ to 12 years). In one case we do not have precise information. (no. 30 of the chart).

These numbers clearly show that lung cancer is the most frequent complication with asbestosis, if heart insufficiencies and fatal pneumonias are disregarded. Even tuberculosis, which usually surpasses cancer in frequency, in this case clearly falls behind lung cancer. This provides an important proof for the close link behind lung cancer. It is striking that the percentage of today, gained from the more extensive material, coincides exactly with the numbers that Nordmann had gained earlier from a much smaller amount of observation material.

Abroad, the conditions pertaining to this, are up to now, as follows: In this area, the British have most experience. But according to the English literature, which is diverse, because some of the individual cases have been published several times, unfortunately it is not possible to list the individual cases as we did above. Till further developments take place, the numbers provided by Gloyne have to suffice. He observed six cases of lung cancer (one probably a pleural tumor) in 50 dissections. This shows a frequency of lung cancer in association with asbestosis at 12%. The numbers from the US.are very similar. I have found in the literature up to 1939, 13 cases of dissection. This number is probably not quite complete, since some studies were not accessible to me. Among these dissected asbestoses I found two bronchial cancers, which were listed above. This would correspond to a percentage of approximately 15%. There was not any mention of a different organ cancers. Relatively frequent (four times) is the pneumonia as given cause of death. Strangely enough, there is no report pertaining to this matter from France.

And just as little was published about this problem in other countries. In Italy, where asbestosis is a very well known disease, no case of pulmonary cancer has been observed (Vigliani and others).

Therefore, in the world literature, we see so far 14 malignant pulmonary-pleural tumors of epithelial origin, which came from 92 sections. This means approximately 16% cases of cancers in dissected asbestosis.

Of these 14, only eleven have so far been described in detail so that statistical results could be gained from them, (cf. chart 2). The distribution according to sex shows seven men and four women. The ages are between 35-71 years. Four are in the relatively young age group of 35 to 41.

In all cases the time between the beginning of the employment to the occurrence of the cancer is relatively long (between 12 and 42 years). If the exposure to the dust was short, usually a longer dust-free interval will follow, which seems to prove that the effect of the dust will if at all, lead only gradually to an occurrence of cancer.

The majority of the affected patients had a bad asbestosis without it having to be obligatory in this form.

In nine cases there were lung tumors, in two cases pleural tumors. All of the lung tumors, as far as this can be determined, seemed to originate from the bronchial epithelium. There is no observations among them that would be typical for an alveolar cancer.

According to histological character the callous squamous epithelium cancers were in the majority. Among the eight histologically closer defined lung cancers five were callous squamous epithelium cancers. One further cancer of the squamous epithelium was not callous. One further cancer belonged to the group of non-differentiated growths and the last one was acinous.

The three pleural growths were described as "pseudo-alveolar mesothelium", as "adenomatous pleural carcinoma" and as "squamous carcinoma."

Four of the lung tumors in the limited sense had not spread into metastases. The localization of the primary lung cancers is seven times alone in the lower lobes, where, at all times the asbestosis is developed most of all. Four times the tumor is located in the left , three times in the right lower lobes. Compared to this, the right side middle and upper lobes are represented only once each with a tumor.

The matching localization of the tumors with the strongest changes in the tissue as triggered by the asbestosis in the lower parts of the lung is striking.

The numerological frequency of lung cancer in dissected asbestosis patients is the first convincing proof for a close causal link of these two diseases.

Sixteen percent of pulmonary and pleural cancers surpasses, by far, the otherwise statistically expected frequency of other dissections. Even if the frequency of the occurrence of lung cancer has risen considerably in the last decades, it still does not show up in the over all statistics of dissections more than 2%-6% on the average.

And even if for asbestosis the absolute numbers - as we have shown- are still relatively small, they still are convincing through the fact that they were established with even frequency at totally different places (Germany, England, U.S.A.).

To these numerological conditions further positive points can be added from the above deductions, which were already presented by Nordmann, in small numbers.

First, we shall present the age of the cancer carriers. Four of the men were still young, 35-41 years. Even if lung cancer does occur in adolescents, its greatest frequency is not before the ages of 50-60. Six patients from our study belonged to this age group. The distribution according to sex shifted here towards women, contrary to the number ratios which are usually valid. There are four women among 11 cases. The large statistics list, otherwise a distribution ratio for the distribution according to sex as 3-4 to 1 between men and women. Still, one has to remember that in Germany and England, in contrast to the U.S., women surpass men as employees in asbestos plants.

Especially striking seems to be the frequent coincidence of the location of the tumor with the location of the worst changes of the asbestosis in the lower segments of the lung, as we reported above.

Further, the histological character of the lung tumors is striking. Where numbers are concerned, mostly the callous, squamous epithelium carcinoma is of importance. Among eight bronchial cancers that were described in detail, six alone were such. The number ratio which is common in lung cancers among the individual growth forms is totally changed and shifted in favor of the squamous epithelium carcinoma. If the histological distinction is made into the three groups of undifferentiated cells, squamous and cylinder epithelium cancers, the first group contains by far the cases according to the larger statistics with approximately 2/3 of all cases. Since the squamous epithelial cancers have the least inclination to form metastases, it may be understandable why the observations of four of the cases did not show any metastases. The histological character of the lung cancers speaks for its independent position among the lung cancers.

The cancer was always observed after a relatively long effect of the dust. It may be that the time of employment in the asbestosis dust was very long or that, at a short time of work there with a considerable exposure there was a longer interval, in which the dust damage could be further effective. A series of clear observations, which were made in part by the author himself, show us that the dust damage in asbestosis will often only occur after this interval, and will lead to an increasing fibrosis. Among all the cases of lung cancer in association with asbestosis there is not a single one that would not show this long span of the effect of the asbestos dust. This is in agreement with observations of other occupational cancers.

The other histological findings of the asbestos lung give us a further understanding of the links discussed above. There are, in the asbestos dust lungs, at the small bronchi mostly extensive epithelial metaplasias, which can be viewed as pre-cancerous stages. Most likely they are generally the origin of the carcinomatous new formations. Nordmann has even made the observation, in one case, that at a large carcinoma of the left lower lobe there was on the other side a small, just beginning cancer, that could not be a metastasis, but a bronchial cancer originated epithelium in an authochthonous fashion. Therefore, he believes the origin of the cancer in association with asbestosis in several places to be especially characteristic. Here, we find parallels to the Schneeberg lung cancer.

It seems that beside these metaplasias, the other histological changes in the lung also play a role in the development of cancer. The most characteristic one is the highly increased tendency of the tissue to grow. Here are the numerous epithelium despamations with changes in shape of the covering cells, the formation of numerous macrophagi and foreign body giant cells as well as wild growth in the connective tissues. As Linzbach pointed out, this triggers the individual tissues' removal from their normal relationship, without however, the damage to the tissue being bad enough to cause death of the cells. In this heightened growth tendency and the interruption of the normal inter-relations of the tissues, in all probability the triggering forces of the occurrence of cancer have to be seen.

These points hold also true for the pleural growths. The pleura is included in these processes of restructuring. Epithelial desquamations, deposits of fibrin, growth of connective tissue are to be found there, the same as callousities and deposits of asbestos crystals and asbestos particles (Gloyne and others).

These points fit well into the results that come from the statistic numbers, and they form confirming arguments for the inner link between asbestosis and lung cancer.

Besides the increased rate of cancer carriers with asbestosis there has to be, to be further convincing, the possibility to reproduce these conditions in animal experiments. This point can not yet be seen as fulfilled for the asbestosis. But this is not the consequence of negative results in experiments, but rather in the fact that this question has not been tackled yet in a larger scope. Nordmann and Sorge conducted the first experiments with a result that seemed striking in its agreement. We discussed this earlier. But, to be careful, one will have to wait for further confirmations and acceptance of these complicated conditions by other experts.

In any case, all facts gained so far speak with high probability for the fact that Nordmann's theory about the occupational cancer of the asbestos workers is justified. The other authors, too, like Gloyne, Lynch, and Smith, Egbert and Geiger and Linzbach show the tendency to suspect closer causal links. No side has so far tried to disprove this assumption. If we now ask ourselves the question of where to look for the carcinogenic effect of the asbestos dust, we have to separate general and local effective factors. It is assumed everywhere that the development of a cancer is based on a general disposition for cancer. But it is hard to say of which it consists. It is known from the generally human and the experimental pathology that the disposition for cancer is dependent on genetic factors. This is expressed in the fact that under equal conditions for the experiment and roughly even exposure to carcinogenic damage for people, the

quota of cancer carriers is always only a part of the ones at risk. The observation material that is accessible to us for asbestosis did not allow an analysis of cancer occurrence in the family in a satisfactory manner.

We do not know how far and in what way the asbestos dust damage creates such a general disposition for cancer. The assumption remains a hypothesis. It does not seem to be the case that this general disposition has such a strong effect that it would also trigger the occurrence of cancer in other organs. The given numbers do not speak for that at all. It always seems to be of greatest importance how the surrounding area is affected. We have discussed above in detail their morphological expression in the changed tissue reactions of the lung. As their cause, primarily chemical and mechanical factors have to be considered. Since asbestos is chemically simply defined, the conditions here are tolerably clear. It can probably be stated right in the beginning that substances from the group of the familiar carcinogenic agents are not in question. The affect of the asbestos dust on the lung takes place probably through chemical and mechanical damage. For the chemical damage we look to the silicic acid, which proably dissolves from the more easily affected serpentine asbestos. It is hight unlikely and practically unproven that it has a carcinogenic effect, as was shown from observations of human pathology and animal experiments. But it must be kept in mind that the conditions are different for silicosis and that the tissue changes are at different locations and of different character for the asbestosis. This different arrangement and type of new tissue formation could indeed trigger different bilogical reactions of the tissue. Beyond that, one will have to give special attention to the effect of the many pointed asbestos needles and particles, which are probably especially characteristic to the hornblende asbestos with its rigid, hard to dissolve quality. They have great importance for the continuous mechanical irritation which trigger the reaction of the tissue.

Finally, it should be recalled, that in bad cases of asbestosis inflammatory reactions take place at the bronchi in part with formation of bronchiectasis, which in turn, could favor the development of cancer.

In general, and above all, local conditions, we will probably have to look at the present status of our knowledge for the explanation of the occurrence of cancer in association with asbestosis. A great deal of the damage does not exceed in its definition as the term of chronic irritation. The problems of the association with asbestosis and the origin of cancer have in common that we are still far away from a full understanding of the finer inter-relations.

Let us now discuss the clinical diagnosis of cancer in the asbestos dust lung:

In general, all diagnostic deliberations will have to be applied and are valid, which we also use in general cases of pulmonary or pleural cancer determination. But since the cancer here builds on a foundation disease, we will have to expect certain characteristics of the way the disease presents itself, and we will have to be in possession of certain knowledge from the symptology of the asbestosis. For the history if will first of all be important to take down a complete occupational anamnesis, and to keep in mind that lung exposure to the dist,with the duration of the risk sometimes being compensated for by the intensity. So far, we are only familiar with a single observation for which the employment in the asbestos dust lasted only 1½ years, in all the other cases it was seven year or longer. If the exposure to the dust is short but intense, there seems to be a longer, dust-free interval necessary for the occurrence of cancer. So far, we do not have case of the disease, for which the time period from the beginning of the work in the dust to the diagnosis of the cancer would have been less than 12 years. One should expect in general that the cancer would occur only in association with clear, if not always worst, cases of asbestosis. The examples above show this.

The first symptoms of a developing lung cancer, which in themselves don't have anything characteristic or pathognomonic, will not be as striking as they would be in a person who was previously healthy, since shortness of breath, coughing, sputum and a certain discomfort in the chest area are complaints that are very familiar to the asbestosis patient. Even a certain deterioration of the general strength, which does not even have to go hand in hand with a lung cancer in the beginning, weight loss, loss of appetite are often symptoms in cases of bad asbestosis. And acute deterioration in the general condition, including the local lung pain, are often an expression of secondary infections which are difficult to overcome. But overall, one would have to observe the rule for the previous history of asbestosis, that the process of the disease is a deterioration which is very gradual, drawn out over years and even decades. If this development shows sudden instances of obvious local and general deterioration, then the thought of a development of cancer will have to appear. Responsible for this condition are, beside the cancer, unspecific infections with bronchitis, penumonia or abscesses. The complicating tuberculosis is, according to our observations, of minor importance, but it is much too often diagnosed. Of course, it will always be within the realm of the possible. So far, there has been no information regarding an association with lung lues or fungal disease.

Among the general symptoms, fast weight loss is important, but does not prove it. The same is true, as has been said, of the loss of appetite, bad coloring of the face and perspiration at night. If these symptoms are based alone on the increasing asbestosis, they are usually accompanied by an increased shortness of breath, cyanosis, possibly drummer's fingers and other local complaints of the lung, but one has to keep in mind that a lung tumor can also trigger the increase in such complaints. Overall, the situation will not be clarified from the previous history alone.

It is not very different where the local complaints are concerned. Since asbestosis mostly causes bad irritation cough, this symptom cannot be used for determination. The same is true for the shortness of breath. Of somewhat greater importance seems to be the observing of the sputum. In a case of uncomplicated asbestosis it is of small quantity, sticky and mucuous, in case of bronchitis and bronchiectases it can be more copious and purulent. Only in rare occasions does it contain blood. Frequent even if sparse bloody sputum requries an explanation. I myself have seen sputum in the form of raspberry sputum only in the case of a complicated lung tumor. The literature has only few mentions of this kind for the simple asbestosis. Tumor cells in the sputum are probably rare. Hornig claims to have seen a large number of epithelium cells in the sputum of his case of a tumor in association with asbestosis. When the decay of the lung tissue begins, this will be easily detected from the change in the sputum. This was very impressive in my observation. The patient suddenly delivered great quantities of granular necrotic substances. Maybe we will be successful at some point to find the symptom of the British "asbestosis bodies in clumps." These are rosette-shaped piles of asbestos particles, which can only be found in the sputum, if there is decaying lung tissue (abscess, tuberculosis, tumor). Diagnostically speaking, they are the same as the elastic fibers in the sputum. The importance of the shortness of breath was discussed above. Only when the tumor reaches a larger extent or if there is a bronchial blockage will it have to be related to it only. On the other hand, I find pains in the chest to be a more significant sign. In the case of asbestosis they are usually insignificant and undefined. In our tumor case they became more and more prevalent with the growth of the tumor; they assumed a typical neuralgiform character. There are similar hints in the literature. The cause is probably to be seen in the spreading of the tumor to the pleura parietalis and possibly the intercostal nerves.

These hints for the general and local complaints, which are in most cases suggested by the previous history, may be sufficient.

The following shall be remarked for the rest of the objective finding: asbestosis attacks the lung on both sides. There are no strictly one-sided process, which is typically the case for tumors. Usually, there is also a symmetry regarding the changes. One has to know, though, that the right side of the lung can be attacked more strongly by the fibrosis in normal cases also. We never find dampings above the upper segments of the lungs. In most cases, the breathing noise is rough, only rarely weakened. The dependent lung segments offer mostly a moderate to medium damping of the noise, which, even if it is not quite symmetrical, is almost always on both sides. Only coarse callouses or specific or unspecific complications can be responsible for exceptions. The breathing noise is usually weaker in the lower part than above. Only in rare cases is it reversed. Foreign noises are more prevalent in the lower part than above; differences in the side do not mean much. If there are clear signs of an atelectasis on one side, there is high suspicion concerning a tumor. But it is a matter of course that this symptom does not have to obligatory be a lung tumor.

Hematoma, especially of hemorrhaging nature, are practically non-existant in the common asbestosis. Signs of melting can be a sign for either a tumor, an ascess and tuberculosis. Bronchiectasia in the form of a cylindrical widening of the windpipe are not rare in cases of bad asbestosis. They will, on occasion, create difficulties in the definition of against caverns in the clinical examination.

There will always have to be an explanation given for strong asymmetries of the rib cage, displacement of the pleura in the middle area and of the diaphragm.

The x-ray method will always be the most important method for examining and determing a tumor. There it has to be kept in mind that the bad asbestosis not always, as could be believed in the literature, leads only to delicate, symmetrical densing of the lung tissue. Beside certain asymmetries there are also flat cloudy blotches of circumscribed type in the lower segments,especially in the middle. But the dense shadows are not as compact and like a tumor, but more of stripe patterning and not clearly defined. Hard or tomographic exposures will show the bronchia system as open, possibly even enlarged. So far there have been no reports about bronchus stenosis in association with asbestosis. Compact, one-sided, defined shadows in the lung, possibly with a bronchial blockage, are practically proof for a tumor. In this area belongs shifting of the mediastinum, either continuously or changing with breathing, as well as paralysis of the diaphragm, the recurrent or in processes of the upper lobes also often a Horner's symptom complex. Defined densities of the upper segments are never characteristic of asbestosis. Here, the conditions are much clearer and simpler than they are for silicosis. Rough formations of shadows occur in asbestosis mainly through unspecific inflammation. Thuberculosis is by far less frequent than has been suspected. Its first occurrence in the lower segments is rare for asbestosis. For completeness sake, it may be mentioned here that the tomo and bronchiography may be of value for the recognition of a tumor of the lung within the framework of general customary diagnostic evaluation, with the usual rules of evaluation applicable.

The bronchioscopy is of similar value. There are no observations about the diagnostic value of lung tappings except for a few experiments, when asbestos particles were found in the lung fluid. In the case of a primary pleural tumor or metastases the proof of tumor cells in the tapping fluid can explain the situation very suddenly. This was the case in Alwen's case.

Metastases will always allow fro their diagnosis to be established very fast. Since infections can have the same consequence it is irrelevant for the diagnosis that long-lasting tumors can cause fever. Concerning the blood situation and the increase in the hyposatasis of the red corpuscles it should be noted that anemia is not a sign of asbestosis, it would be more likely to find high pigment and cell values as compensatory symptoms. Accompanying infections may be able to cause the exceptions. Increasing anemias are, when other multiple causes have been ruled out, suspicious of tumors. No diagnostic hint for a tumor is given with the differential blood analysis. The hypostasis is not accelerated for uncomplicated asbestosis. It is, however, found to be slightly increased for a great number of asbestos workers as is

established in routine examinations, probably because infections in the bronchial trunk are more frequent. Stronger and increasing acceleration of the hypostasis must always be checked, and they have to be evaluated according to the customary clinical rules.

This concludes the most important clinical points for the recognition of a lung tumor in association with asbestosis. The correct interpretation is always dependent on a careful clinical general examination and the critical understanding of the individual signs. It is important in this context to be familiar with the image of the disease of asbestosis and to keep the possiblity of a complicating tumor in mind, which seems to be as frequent in the asbestos lung as tuberculosis. In Germany, so far, there were only reports of about 10 active tuberculosis in association with asbestosis as compared to six tumors.

If then the occurrence of the development of cancer in the asbestos dust lung is as frequent as was shown above, and if still other good reasons speak for a close causal link between the two diseases - even if the results from the animal experiments cannot be included - there should be, even today, some thought given to include this complication in the insurance coverage. In the few cases that have come up so far in compensatory procedures, the insurance associations have accepted the link due to the agreement in all statements of the experts that were questioned. In the files pertaining to this subject matter and which I examined there was no expert in Germany that would have denied the request.

SUMMARY

The report is about the only so far known cases of malignant lung and pleural growths in the world literature. The reasons which suggest a causal link between both diseases, are given. The clinical picture of the lung tumor is discussed and the inclusion of this complication into the insurance coverage is believed to be appropriate.

Chart 1

a	b	c	d	e	f	g
nr.	age sex	years of exposure to dust	dustfree interval in yrs	stage of asbestosis	cause of death	published by
13					stomach ca	
14					bronchial ca	
15					bronchial ca	
16					lung abscess empyema	
17					bronchial ca	
18					bronchial ca	
19					esophagus ca	
20					pleural ca	
25					prostate ca	
26					lung abscess amyloidosis	
27					kidney failure	
28					lung tuberculosis	
29					lung tuberculosis	
30					pleural tumor	

Chart 2

nr.	age sex	dust exp. yrs	dustfree interval	stage of asbestosis	type of tumor	localization	metastases	author
1					callous squamous epithelium ca	upper right lobe	none	
2					callous squamous epithelium ca	right lower lobe	none	
3					squamous epithelium ca	right lowe lobe	none	
4					acinous tumor	left lower lobe	wide spreading	
5					callous squamous epithelium ca	left lower lobe	liver kidney	
6					callous squamous epithelium ca	left lower lobe	wide spreading	
7					?	right middle lobe	yes	
8					callous squamous epithelium ca	right lower lobe	none	
9					pseudo-alveolar mesothelium	right pleura	peritoneum	
10					adenomatous pleural ca	left pleura	wide spreading	
11					non-differenciated ca	left lower lobe	?	

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See also 44-1

Wedler, H.W.

Lung cancer in asbestosis patients

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GERMANY

LUNG CANCER IN ASBESTOSIS PATIENTS

[Article by Dr. H. W. Wedler; German; Dtsch. Arch. Klin. Med. 191, 1943, pp. 189-209]

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In the last 12-15 years, such extensive experience in the field of asbestosis has been reported by both German and foreign literature that we are now quite familiar with the dangers to which asbestos workers are subjected, and the clinical picture as well as the development of this occupational disease. Nevertheless, there are still many unanswered pathogenesis-related questions which will eventually be answered through animal experimentation and chemical-physical processing. However, our knowledge of accompanying diseases and complications is based on a much narrower and uncertain basis. At this time, the editor could publish an extensive report on the behavior of lung tuberculosis patients suffering from this type of pneumoconiosis. One question which is as important as it is conclusive is that concerning the correlation to lung cancer, whose incidence in asbestosis patients has been repeatedly observed over the last few years. The interest that this creates is not limited to the fields of social medicine and legal insurance regulations, but extends far into the field of general medicine, since this would produce a new example of the exogenetic appearance of cancer. The number of such observations reported in itself is very small, but is nevertheless so significant in relation to the rare occurrence of this disease that we feel it warrants the publication of a detailed report. This is also justified by the fact that, as yet, from a clinical side, no such work has ever been published.

We shall first mention observations previously published in worldwide literature concerning lung cancer in asbestosis patients, and conclude with the latest experience in that field, as well as the characteristics of the respective clinical image and its diagnosis.

[illegible] of a carcinomatous tumor in the lungs of an asbestosis [illegible] made in 1933 by Gloyne, while working with the pathological anatomy and histology of asbestosis patients. He mentions complications in asbestosis patients which were thought to be related to the origin of the disease (purulent bronchitis, bronchopneumonia, tuberculosis, emphysema and bronchiectasis) and accompanying diseases which, based on the status of medical knowledge at that time, were thought to be correlated to the effects of the dust. Under the latter, he makes the following observation: "There has also been one case of squamous carcinoma of the pleura. There is no evidence at the moment that this was in any way related to the asbestosis".

In 1935, Gloyne was able to provide two additional reports on lung cancer detected in asbestosis patients. At that time, he still was not able to make a definite statement as to the possible etiological correlation of both diseases. Nevertheless, certain histological aspects did appear to indicate this.

The first of these two observations concerned a 35-year-old female who had worked for a period of 8 years as an asbestos spinner, and had then lived 9 years for 9 years without any exposure to the dust. She died, as shown by the autopsy, of moderate asbestosis with a coagulum in the right section of the heart, spleen infarct and a meningeal hemorrhage. On the basis of the right lung upper lobe, a clinically non-identifiable tumor was found, which was approximately the size of a walnut and which extended into the tip of the enlarged pleura. There were no metastases to be observed. The cornified pavement epithelium carcinoma originated from a small bronchus.

The second observation and autopsy also concerned a female who was just turning 71 years of age. Fifteen years prior to her death, she had once worked for a period of 6 months, and another time for a period of 13 months, in a hazardous dusty mattress and processing department of an asbestos plant. In this patient, Gloyne found a moderate case of asbestosis, with a partly-collapsing tumor in the right lung upper lobe, ascites and thrombosis of the left leg vein. Here too there were no metastases to be observed. Histologically, this was also a cornified carcinoma of the pavement epithelium.

In both cases, the cancer did not appear to be spread to the extent that it could promote death by itself. The same applied to asbestosis.

In the same year (1935), a report was issued by Lynch and Smith of the United States concerning lung cancer in asbestosis patients, in which a detailed history of the disease was given. The 57-year-old patient whose case is described had worked for 22 years in a cotton weaving plant, and for 21 years in an asbestos plant, until his hospitalization; he had been complaining of shortness of breath for about 5 years. Three years prior to his death, he started having occasional pains in the back and over the three last ribs on the right, and again complained of shortness of breath in the last few months of his life. He became weak, coughed, lost his appetite, his temperature rose, he had blood in his sputum and suffered

[illegible] The clinical findings were characteristic of asbestosis. Underneath to the right above the lungs, the respiratory sounds were weakened. The clinical diagnosis was asbestosis and chronic indurative pneumonia, with rind (skin) to the bottom right. In addition to asbestosis with right lateral pleuritis and bronchiectasis, a decomposed cavity was found in the right lower lobe through pathological-anatomical examination, which was macroscopically taken as tuberculosis. Only through the microscopic examination was it possible to detect cancer of the pavement of the epithelium. There were no metastases to be observed. It is unusual to speak of simultaneous hyaline nodes in the lungs of asbestosis patients. The carcinoma originated from a bronchus with a metaplastic epithelium. The authors felt that this had been caused by chronic irritation of the bronchii. They spoke of the correlation between cancer and asbestosis as a "possible relationship" and tried to find parallels to other occupational diseases of the lungs.

In 1936, Eghert and Geiger (USA) reported on an additional observation which they felt was the first one of this type (with the exception of Gloyne's 1933 report). The 41-year-old male had worked for 18 years as an asbestos weaver. After 9 years in this job, he had a case of pneumonia, followed by coughing and shortness of breath. Eight months prior to a short treatment in the hospital, he began to have occasional back pains. He was emaciated and had trouble moving because of the pain; he coughed, had cyanosis and shortness of breath, as well as bloody and purulent expectoration. In addition to asbestosis, x-rays showed a cluster in the left bottom part of the lung, which had the appearance of an atelectasis or a pneumonic process, but which was recognized as a tumor, due to the fact that metastases were present in the pelvis and in the spinal column. In addition to asbestosis, autopsy revealed a 5:5:4 cm acinose cancer in the left lower lobe of the lung, which had caused the appearance of metastases in the lungs, in the left lateral hilus and aortic glands, in the right suprarenal gland, in the abdominal musculature, the pelvis, the spinal column and the skull. The origin of the tumor was formed by a large secondary branch of the left bronchial lower lobe. He felt that there was very likely an etiological correlation between the two diseases: "That the irritating effects of the inhaled asbestos particles may in this case have been a significant factor concerned in the development of the primary lung cancer seems sufficiently plausible to be worthy of consideration."

In 1936, Gloyne was able to add an additional observation to his three initial ones. He found a non-differentiated carcinoma of the left lower lobe in a 59-year-old male suffering from asbestosis, who had worked for 21 years in the asbestos industry.

In 1938, Sparks, without specific data, stated that in his autopsies, Gloyne had encountered 6 cases of lung cancer in patients suffering from asbestosis. Baader learned from Gloyne himself that these 6 cases of cancer were based on 50 autopsies.

In the same year, Nordmann provided us with two new observations of cancer cases in asbestosis patients that he had previously and consecutively

[illegible] cases. The first was a 55-year-old female. Between her [illegible] year of life, she had worked for exactly 7 years in the [illegible] and weaving departments of an asbestos paint. Four [illegible] prior to her death, she began to cough and have shortness of breath. Two months before she died, she was treated for suspected tuberculosis. Boenig gave a probable diagnosis of cancer in the left lower lobe, due to extensive asbestosis, since there were clinical symptoms of atelectasis and the main bronchus was tomographically found to be displaced. Anatomically, this was a cornified carcinoma of the pavement epithelium, with a walnut-sized decomposed cavity, which also affected the lower lobe bronchus, with pleura callosities and metastases in the liver and kidneys.

The second observation concerned a 55-year-old male who, between his 36th and 43rd years of his life, had been involved the preparation processes of an asbestos plant, for a total of 7 years. Thirteen months prior to his death, there was sudden loss of weight accompanied by bloody expectoration. He was first suspected of suffering from tuberculosis. Above the left lung underneath, respiration was suppressed and weak. X-rays showed a shadow around the left lower field. His treating physician gave a diagnosis of asbestosis with lung cancer. This was confirmed by the autopsy. The cancer, which was in the left lower lobe, had also caused a walnut-sized decomposition of the main bronchus, and also affecting the pericardium, the left chamber wall, the diaphragm, the peritoneum of the left upper part of the abdomen, the retroperitoneal tissues behind the spleen, the lymph node and the lower breast and upper lumbar spinal column. Histologically, this was again a cornified carcinoma of the pavement epithelium. Bronchial carcinoma had also begun to appear in the right lung lower lobe.

In this observation, Nordmann included an evaluation of the various aspects which could possibly lead to occupational cancer. For the first time, there was a definite mention of occupational cancer in asbestos workers.

In 1939, Wedler reported on one additional observation made in Germany, which had originally been made by Bohne, but which had not been reported at that time. The 58-year-old male had, between 1925 and 1935, worked as a part-time craftsman in an asbestos plant. A few years following his exposure to the particles, he began to have respiratory troubles. In 1928, he was transferred for a period of two months. Later, he often underwent cures at cure centers, without tubercle bacillus ever being detected. Because of a worsening of his condition, he stopped working 3 months prior to his death. In the hospital, he showed symptoms of general emaciation, cyanosis, and a probable catarrh, particularly under the upper part of the lung. His sputum contained numerous asbestos particles, but no tubercle bacilli. His blood sedimentation rate sharply accelerated (57-95). To the left above the ninth rib, there was a tumor the size of a chestnut, which had grown together with the skin in the anterior axillary line, which was removed and found to be a carcinogenic metastasis. X-rays showed symptoms of asbestosis as well as multiple indications in the right upper field. Judging from the documents in my possession, there was no intra vitam

[illegible] The patient died of cardiac insufficiency [illegible] the metastasis. The autopsy findings were [illegible] as follows: "The lung had grown together with the chest wall. [illegible] was not enlarged, the musculature was brownish-red in color and [illegible] somewhat flaccid. The left lung was filled with blood and fluid, the lower lobe was firm and slate-gray colored. The right lung ruptured in the area of the middle lobe when removed. Its tissue was a reddish-yellow, and was decomposed and showed widespread formation of cavities and nodes. The upper lobe was filled with blood and fluid, its consistency was firm and air-free. The lower lobe was slate-gray and reddish-gray in color, and firm to the touch. It was also found to be air-free. The microscopic examination of the lungs showed typical cancerous tissue in the right middle lobe, and all the alterations which are characteristic in the case of asbestosis were present in the lower lobes. More particularly, there were asbestos particles in all the parts examined."

According to Baader (1939), six authors saw a total of 14 cases of asbestosis cancer between the years 1935 and 1938. However, this report did not include any details and, judging from the available documents which are listed above, this cannot be completely confirmed at this time.

In 1941, a detailed clinical and pathological-anatomical report was published by Wedler and Linzbach on an additional patient history which described the complete course of the disease. The 60-year-old male had, between 1921 and 1939, worked a total of 18 years in an asbestos plant. He was only exposed to the strong effects of the particles (preparation) for the first three years. His first problems were experienced shortly after his employment. In 1938, he already presented the picture of an uncomplicated and severe case of asbestosis, which had developed chronically. During the course of his last year of life, an increasing shadow developed over his diaphragm in the right lung lower lobe, with clinical symptoms of atelectasis and later decomposition, as well as severe neuralgic pains in the respective intercostal nerve area. Blood appeared in his sputum. All symptoms seemed to indicate cancer which had already been diagnosed clinically. The autopsy confirmed the diagnosis of a collapsed cornified carcinoma of the pavement epithelium, originating from the right lower lobe bronchus. There were no metastases to be found.

In the meantime, two additional observations have been reported in Germany, but no documentation is as yet available.

The first case was observed by Teutschlaender, who reported twice verbally on the subject. Following is a quotation from a personal communication on the subject: "In 1938, Teutschlaender performed an autopsy on a 40-year-old female, who had been employed in an asbestos plant for a period of 10 years with long interruptions. In her case, a clinical diagnosis was as followed: 'Lung tumor on the right? Lung process on the right? Secondary emphysema on the left, ascites, severe cachexia'. The autopsy revealed no tuberculosis, but rather a widespread asbestosis with massive accumulation of asbestos particles and a right-sided pleure blastoma which was histologically found to be pseudo-alveolar mesothelium. Tumors

[illegible] peritoneum with ascites. The left pleural cavity [illegible] discharge. There was compensatory emphysema in the [illegible] lung. The cachectic female died of cardiac insufficiency following [illegible] lung disease."

The second observation was made by Alwens. The autopsy was performed by Fischer-Wasels. As a consultant, I became involved with this case. The 60-year-old male (6/13/81 to 9/19/41) had been working in an asbestos rubber plant for 42 years, until 6 months prior to his death. He became ill in January of 1941 with increasing shortness of breath and loss of weight, with symptoms of left pleural secretion. The respiratory sounds were totally suppressed and sustained, and there was right cardiac repression. His sputum contained considerable amounts of asbestos particles. In the jelly-like red secretion, mostly obtained through puncture, numerous tumorous cells could be found. Above and under the right lung, individual fine bubble-like rattling sounds could be heard. The sedimentation rate quickly increased. There were no tubercle bacilli to be found in the sputum. Based on the x-rays, a moderate asbestosis was diagnosed, with the primary tumor thought to be in the right hilus. The autopsy revealed a mild case of asbestosis, with a diffuse primary mucus-forming glandular cell carcinoma in the left pleura of mostly adematous character, and metastases on the abdominal side of the left diaphragm cupola, the serosa and the small pelvis, and the left side of the chest musculature. The autopsy report on the thoracic organs is quoted here, since no report has yet been made on the subject.

Autopsy of the chest. Moderately developed panniculous adiposes. The thorax is moderately expanded and flexible. The rib cartilage can easily be cut. The diaphragm is on the right, at the level of the fifth intercostal space; on the left side it is folded under, and penetrates far into the abdominal cavity. Its bottom pole here is lower than the neck of the pelvis. In the pneumothoracic test, almost 3,000 ccm of yellowish-brown fibrous fluid is released by the left pleural cavity. The entire mediastinum is displaced to the right. The heart hangs in the shape of a drop in the mediastinum; its left edge lies along the median line. The right lung floats freely in the pleural cavity up to small string-type growths. In the pleura costalis, there are gray and white tendon-like scales about the size of the palm of the hand, with isolated tubular nodes which are also gray and white. In the pleura of the right lung upper lobe, there is a large radiating scar. On the pleura of the right lung, there is a fine moderately firm adhering gray felt-like layer. The right lung itself is normal in size and filled with a moderate amount of air and fluid. The pleura and the surface of the cut show moderately severe black mesh-type markings. Generally, the lung tissues are red in color. There are no clusters to be observed. In the lower lobe branching of the right pulmonary artery, a small brownish-red blood thrombus adheres to the intima. The pulmonary arteries are empty. The left pleura is entirely covered with rind-like skin. On the inner surface, there are massive, tightly-packed tuberosities reaching the size of a walnut, with a mulberry-type surface consisting of blister-like (white on the surface of the cut) tumorous tissues. When cut, the latter secretes a

In addition to tumorous tissue, we can also observe [illegible] patches. The tumorous tissue does not penetrate any [illegible] deeper than its base, particularly not the lung tissue. Only in the area of the cutaneous nodes on the left side of the chest, as mentioned in the introduction, can tumorous nodes be found in the intercostal musculature. The left lung is highly atelectatic, and only adheres to the chest wall through a series of growths. The lung tissue is tenacious and grayish-red in color, and shows a black mesh-type marking on the surface of the cut and on the surface itself, which is somewhat thicker than on the right side. No tumors were detected in the lung tissue. The trachea and bronchi of both lungs are normal in size, and the wall is tender. No tumorous tissue was observed here. The hilary lymph nodes are bilaterally black in color, and soft in consistency. The heart is barely the size of the dead patient's fist. The pericardium is smooth and shiny. There is some sub-epicardial fatty tissue. The left ventricle is small; the right one somewhat expanded. The wall of the left ventricle is 5 mm thick; that of the right ventricle 2-3 mm. The entire cardiac valve is soft and conclusive. The coronary artery is moderately enlarged, and its wall is soft. Cardiac musculature is of the same brownish-red in all cuts. The complete aorta is soft and flexible.

MICROSCOPIC FINDINGS

Right lung. The lung structure shows small isolated emphysemal changes. Occasional nodular deposits with a fine granular black pigmentation can be found in the peribronchial tissue. In this area, the peribronchial tissue shows a definite hyaline alteration and fibrosis. In addition to the anthracotic pigmentation deposits, typical asbestosis particles can be seen which are partly fresh and partly disintegrating. For the most part, these are parallel to the anthracotic pigmentation. However, independent from the latter, these can also be found by themselves in the pulmonary alveoli, as well as in the interstitial tissues. Massive accumulations of coal dust and asbestos particles can also be seen underneath the pleura. The large bronchi contain some amounts of mucus as well as epithelial discharge. The bronchioli are greatly expanded. However, they are covered with one layer of glittering epithelium. No epithelial metaplasia can be found. The lung tissue directly underneath the pleura shows a mild collapse of the alveoli. The alveolar epithelium shows a considerable glandular, but never non-typical, character. Generally, there are no pneumonic changes in the lung tissue.

Left lung. In the tissue of the left lung, we find a collapsed induration with desquamitous alveolar catarrh and fibrosis of the interstitium. In the peribronchial tissue, as on the right side, we find considerable anthracotic deposits with hyalinosis of the surrounding tissue. In this lung, we find a larger amount of typical asbestosis particles, both in the development stage and in the decomposition stage. Asbestos needles are considerably more rare. The jelly-like envelope of the particles gives a characteristically positive reaction to iron. In the left lung, moreover, we find several hemorrhaging areas, as well as areas of tissue necrosis saturated with the hemorrhaging blood. These mostly occurred recently, since there are absolutely no signs of demarcation. In these necrotic

[illegible] particles present, and penetrate sharply through [illegible] of the remaining tissue. In this lung, the same [illegible] as in the bronchial system are found as in the right lung. No epithelial [illegible] can be found in this lung either.

Diagnosis. Numerous asbestosis particles in both lungs with minimal fibrosis (mild pulmonary asbestosis). Compression atelectasis and collapsed induration of the left lung. Hemorrhage, necrosis and minimal bronchopneumonia in the left lung.

Pleural tumor on the left. The tumor grows in its own structure. In a few areas, there are firm cones and strings surrounded by the stromae of a myxomatous, slightly fibrillar, connective tissue. Almost all tumorous areas have large mucus vacuoles; several signet-ring shapes can be seen. Some cells with ruptured vacuoles can be seen where the mucus has penetrated to the surrounding tissue. In another area, the tumor has the appearance of a collection of tightly-packed hollow cavities, which are covered with a smooth, single-layer epithelium. These epithelial cells also contain large amounts of mucus, and are released from the epithelial accumulations in the form of signet-rings, and thus end up in the lumen of the hollow cavities. In the interstitium, however, loose, stringy mucus-forming tumorous cells can be found. Firm epithelial formations without mucus formation of a solid carconoma type can only be found in isolated areas. Tumors can be found all over the pleura parietalis and visceral pleura on the left, and, in some areas, there is minimal growth in the subpleural layers of the pulmonary tissue. Here they are particularly in the septum and some isolated ones can be found in the lymphatic tract.

Diagnosis: Primary mucus-forming glandular cell carcinoma of the pleura of mostly adenomatous character.

The glassy nodes in question on the abdominal side of the left diaphragm tip and on the serosa of the small pelvis are mocroscopically found to be metastases with a structure similar to that of the primary tumor.

This completes the observations found in world-wide literature on published cases of lung and pleural cancer in asbestosis patients.

Nordmann and Serge were the first to undertake a study of the correlation between asbestos particle inhalation and lung cancer through animal experiments on white mice. For these experiments, they used 150 mice, which they sprayed with amounts corresponding to the average amounts received by humans (taking into consideration average age and duration of employment) for a period of 1 1/2 and 3 months. More than half of the animals died prior to the experiment. None of the animals survived for longer than 9 months following inhalation. Twenty per cent of the remaining animals were found to have a cornified multi-centric carcinoma of the pavement epithelium, and 42-57% epithelial regeneration in all stages. Experimentally, this is in support of the importance of asbestos dust in promoting primary pulmonary carcinomas in asbestos workers. The number

[illegible] experiment, and to which the above-[illegible] is very small. Only 2 animals had new growth [illegible] to be cancerous. The authors themselves referred to the [illegible] in differentiating from simple metaplasia. We must leave it to [illegible] experienced morphologist and specialist to decide to what extent the conclusions of the experimenters are valid and to what extent the necessary measures with regard to uniformity and use of the animal material were observed, and, within these limits, which spontaneous tumors are to be classified under the type which is the subject of this work. Nordmann and Sorge gave a short report on this.

It is evident that no similar observations have ever been made before in animal experiments with asbestos dust; these experiments in fact concerned other aspects of the disease. Moreover, various dissections of animals (dogs, rats) living in asbestos plants also did not lead to these observations.

In discussing occupational cancer in a specific industry, it is first necessary to produce statistical data in support of the fact that there is a higher incidence of cancer in that industry than in other industrial or social groups, in which case comparative figures of age groups which are similar (as much as possible) are difficult to produce. Even in the case of asbestosis, the statistical method also presents one additional obvious problem. This rather rare disease can only produce small absolute numbers. One single random incident can create considerable percentage differences. Moreover, in the case of Nordmann, we must take into consideration the fact that, particularly over the last few years, the high turnover of personnel in asbestos plants can give a negative value to the results, since a long period of exposure to the dust and a long dust-free interval usually must be present for the development of cancer. Now the number of workers who remain in hazardous plants for longer periods of time is very small. Dust prevention methods against dust injuries to the lungs also work against us. Nevertheless, our severe cases of asbestosis are mostly workers who are carrying the effects of dust absorbed in earlier years, when the working conditions were considerably less proper.

A second aspect of importance in the correlation between cancer and asbestosis should be mentioned here, which concerns particular conditions under which the injuries occurred and the findings made on location, conditions which describe the type of cancer and differentiate from other types of pulmonary cancer.

As keystone for the evidence, there would have to be experimental experience which would make it possible to provoke this type of cancer in animals.

Let us now turn to the statistical method. As reliable material, we can only evaluate here sections with specific anatomical examinations of the lungs, since certain errors can be made in the purely clinical diagnosis. However, purely clinical works on this subject are not available.

Case #	Age/ sex	dust expo- sure (yrs)	dust free inter- val (yrs)	asbe- tosis stage	cause of death	Author
			(yrs)			
1		2	2	III		Fahr 1943
	47 J., ♂	26		III		Borrmann-Loeschcke 1951
3	54 J., ♂	24		III		Beinecker-di Biasi 1951/53
4	♂	20		III		Beinecker Path. Inst. Munich 1954
5	37 J., ♂	20		III		Strauche-Berger 1953
6	30 J., ♂	5		II-III		Bohm 1954
7	54 J., ♂	11		III		Soupe-Letterer 1958
8	41 J., ♀	18		III		Soupe-Banicki 1958
9	38 J., ♂	13		III		Weller-Walkhoff 1959
10	45 J., ♂	15		III		Weller 1959
11	53 J., ♂	17	6	III		Weller-Koch 1959
12	63 J., ♂	10		III		Weller 1959
13	61 J., ♂	19		II	stomach ca.	Weller-Walkhoff 1959
14	53 J., ♂	7	9	II	Bronchial Ca.	Nordmann 1963
15	55 J., ♂	7	12	III	Bronchial Ca.	Nordmann 1963
16	38 J., ♂	12	7	III	lung abcess, emphysema	Nordmann 1963
17	58 J., ♂	19	5	III	Lung Ca.	Bohm-Weller 1963
18	64 J., ♂	18	1	III	Bronchial Ca.	Weller-Linzbach 1969
19	70 J., ♂	16	1	III	Oesoph. Ca.	di Biasi et al.
✓ 20	60 J., ♂	42	½	I—II	Pleura Ca.	Abeyes-Fischer-Wands
21	38 J., ♀	4	1	III		Bohme
22	54 J., ♂	27		III		Koppisch
23	50 J., ♂	4	6	III		Bohme
24	52 J., ♂	3.25	2	III		Hohn et al.
25	66 J., ♂	22	2	III	Prostata Ca.	
26	42 J., ♀	6	10	I	lung abcess amyloidosis	Weller-Pacaka
27	50 J., ♂	12	2	III	renal ins.	Weller et al.
28	55 J., ♂	5.5	6	II	lung t.b.	Weller et al.
29	45 J., ♂	1.75	0	II	lung t.b.	di Biasi et al.
✓ 30	40 J., ♂	10	2	III	Pleural tumor	Tentschlaender

[illegible] asbestos have been autopsied in Germany. [illegible] a list of these cases according to age, sex, [illegible], stage of asbestosis and cause of death if other than asbestosis, e.g. if due to cardiac insufficiency or agonal pneumonia as a result of the disease. The first 18 fatal cases have already been reported. I collected the additional 12 cases. The case of a young girl reported under No. 29 can be ignored here, since she had a very short period of exposure to the dust and did not anatomically present a case of asbestosis. Of the remaining 29 autopsies, 4 had bronchial cancer and 2 others had a malignant pleural growth. By performing the necessary calculations, we get a round percentage number of 20% for malignant tumors in the lungs of cases of asbestosis autopsied in Germany. Other malignant growths of the body were found in a total of 3 occasions, namely in the stomach, the esophagus and the prostate. Although the number of lung cancers has statistically increased considerably over the past three decades, it nevertheless remains far lower than the number of cases of cancer of the esophagus, as shown by numerous autopsy statistics. Depending on the various authors, its rate of incidence takes the second to fourth place among the cancer statistics concerning organic cancers. As shown by the above-mentioned figures, lung cancer in patients suffering from asbestosis is a primary one in Germany. The average age at death for lung tumor carriers is considerably lower than for carriers of other types of carcinoma (around 51 to 66 years of age).

These small figures do not allow us to come to any conclusions. In a breakdown by sex, there are 4 males and 2 females with lung tumors. For the sex breakdown of lung cancer in males and females, the figures, otherwise, are: 3-4:1. The number of asbestos workers suffering from lung cancer, based on sex, is of course dependent on the number of females and males working in that industry. In Germany, the females exceed by far the males employed in that industry. For the two aforementioned females, the age at death was relatively low, being 35 and 40 years. All cancer patients were suffering from chronic to severe asbestosis. Only one man with pleural carcinoma (No. 20) suffered from moderate asbestosis; the latter had had a very long, but minimal, exposure to the dust. Nordmann has already pointed out that all these cases involved prolonged employment under dust conditions. According to the above table, this applies to all cancer patients without exception. The duration of exposure was 7 years in 2 cases, 10 years in two cases, and 18 and 42 years in the last two cases, respectively. The dust-free interval prior to the development of the cancer, during which the asbestos particle deposits in the lungs was still effective, varied (6 months to 12 years). In one case, this was not exactly known (No. 30).

These figures clearly show that lung cancer is the most common complication encountered in cases of asbestosis, with the exception of agonal pneumonia and cardiac insufficiency. Even tuberculosis, whose rate of incidence is generally far higher than that of cancer, is considerably lower than for lung cancer in these cases. This constitutes conclusive evidence of the close correlation between asbestosis and lung cancer. It is suprising, to note that the current percentage values, based on large amounts of material, are in complete agreement with those of Nordmann performed

[illegible] small amounts of working material.

Abroad, the status of this question is as follows:

The English are the most experienced in this field. However, according to English documentation, this experience unfortunately does not lend itself to the study of individual observations. This is due to the fact that it is very complex, since some individual cases have been published more than once, and cannot be traced individually. For the time being, we shall have to accept the figures produced by Gloyne based on 53 autopsies of asbestosis carriers (according to Buader), during which he observed 6 cases of lung cancer (probably with pleural growth). This gives us a lung cancer incidence of 12% in asbestosis patients.

Very similar figures were obtained from the United States. I was able to collect 13 autopsy cases in U.S. literature up to 1939. This figure is probably not totally accurate, since there were a few works which I was unable to obtain. Among these autopsy cases of asbestosis, I encountered 2 cases of bronchial cancer, which we have already mentioned. This corresponds to a percentage figure of about 15%. There was no mention of any other types of organic cancer. Pneumonia was quite often reported (4 times) as the cause of death.

Absolutely no relevant data is available from France on this subject.

Other countries also reported little on the subject.

In Italy, where asbestosis is well-known, no cases of lung cancer have yet been reported (Vigliani et al.).

In world-wide literature, we therefore find 14 cases of malignant lung and pleural growths of epithelial origin out of 92 autopsies performed. The incidence of lung cancer in autopsied cases of asbestosis is therefore around 16%.

Of these 14 cases, only 11 have as yet been described in detail, so that additional statistical data still remains to be obtained (see Table 2).

A breakdown by sex gives us 7 males and 4 females.

The ages lie between 35 and 71 years of age.

Only 4 are between the relatively young ages of 35 and 41.

The period between employment and the development of cancer is always relatively long (between 12-42 years). Short term exposure to the dust is generally followed by a long dust-free interval, which would tend to indicate that the action of the dust, if there be such, gradually leads to the development of cancer.

Table 2 (continued)

Case #	Age(yrs)/ Sex	Dust exposure (years)	Dust-free interval (years)	Asbestosis stage	Type of growth	Localization	Metastases	Author
9	40/F	10	?	III	pseudo-alveolar mesothelium	right pleura	peritoneum	Teutschla
10	60/M	42	1/2	I-II	adenomatous pleural cancer	left pleura	generalized	Albert-Fischer-Wasels
11	59/M	21	?	--	non-differentiated carcinoma	left lower lobe	?	Gloyne

[redacted] of the patients who died suffered from severe asbes-[redacted] necessarily have to be in this form.

There were 9 cases of pulmonary growth and 2 cases of pleural growth. [redacted] cases of lung cancer (as much as can be determined at this time) originated from the bronchial epithelium. No specific observation of alveolar [redacted] could be observed here.

From a histological point of view, there was a definite majority of cornified carcinomas of the pavement epithelium. Out of 8 histologically diagnosed cases of lung cancer, there were 5 cases of cornified carcinoma of the pavement epithelium; one additional case of cancer of the pavement epithelium was not cornified. One additional cancer case belonged to the group of non-differentiated growths, and the last case grew acinose.

The three pleural growths were described as "pseudo-alveolar mesothelium", "adenomatous pleural carcinoma" and "squamous carcinoma".

In 4 of the plumonary growth cases, in a strict sense of the word, there were no metastases to be found.

In 7 cases, the localization of the primary lung cancer was in the lower lobes, where the asbestosis is always most severe. In 4 cases, the growth is localized in the left lower lobe; in 3 cases in the right lower lobe. In contrast, there was only 1 case of growth in the right center lobe, and another in the right upper lobe.

The concordance between the localization of the growth and the most severe asbestosis-related tissue changes in the lower lung is evident.

The statistical incidence of lung cancer in asbestosis carrier autopsies is the first conclusive evidence obtained in our efforts to determine the correlation of these two diseases at their origin. The percentage figure of 16% for lung and pleural cancer exceeds by far the incidence rate to be expected in other autopsies based on statistical data. Although the incidence of lung cancer has certainly increased considerably over the last decades, on the average, it has not increased by more than 2-6%, based on statistics of autopsies performed. Although, as we were able to show, the absolute asbestosis figures are still relatively low, they are nevertheless convincing, since approximately similar values were obtained from totally different countries (Germany, England, U.S.).

Based on the afore-mentioned conclusions, the purely statistical figures present an even more positive aspect, since such data had already been mentioned by Nordmann, although in smaller numbers.

We shall now mention the age groups of the cancer patients. Only four of the latter were between the ages of 35-41. Although younger people are sometimes afflicted by lung cancer, the highest incidence is found primarily in the age group 50-60. Within our study, 6 patients belonged to that age group.

[illegible] breakdown is concerned, the females here are at [illegible] of 11 cases, we found 6 women. For lung cancer, large [illegible] otherwise offer a sex breakdown of 3:1 for males and [illegible]. However, we must keep in mind that in comparison to the U.S., the number of women employed in asbestos plants far exceeds the number of males employed, both in Germany and in England.

As we have already mentioned, one important consideration is the [illegible] of coincidence of growth localization with the most severe changes caused by asbestosis in the lower part of the lung.

Moreover, the histological nature of pulmonary growth is evident. Statistically, the incidence of mostly cornified carcinoma of the pavement epithelium is by far the highest. Out of 8 diagnosed cases of bronchial cancer, we found 6 such cases. The general lung cancer statistics for various types of growths thus become one-sided to the advantage of cancer of the pavement epithelium. If we perform a histological breakdown of lung cancer into three large groups, namely non-differentiated cells, carcinoma of the pavement epithelium and carcinoma of the columnar epithelium, the first will have the highest statistics with a total allotment of about 2/3 of all cases.' Since cancer of the pavement epithelium has the lowest tendency towards metastasizing, it would be understandable that, of the above observations, four were found to be without metastases. The histological nature of lung cancer itself, as well as the above-mentioned highest incidence of cancer of the pavement epithelium, explains its classification under lung cancer.

Cancer was only observed following a relatively long period of latency following exposure to the dust. Could this be due to the fact that the period of employment under asbestos dust conditions was very long, or that a short period of employment with considerable exposure resulted in a longer interval during which the effect of the dust continued to progress? A series of thorough observations, which were partly performed by the author himself, showed that, particularly in the case of asbestosis patients, dust intoxication often appeared during this first interval, and often led to progressive fibrosis. Among all the lung cancer cases observed in asbestosis patients, there is not one single case in which a long period of action of asbestos particles was not reported. This agrees very well with other observations made of other types of occupational cancer.

Other histological findings in the lungs of asbestosis carriers allow us to better understand the above-mentioned correlations. In the small bronchi of lungs affected by asbestos particles, we mostly find generalized epithelial metaplasia, considered as a per-cancerous stage. It is very probable that the carcinomatous regeneration originates here. In one case, Nordmann even made the observation that, in a severe case of carcinoma in the left lower lobe, a smaller cancer was beginning to develop on the other side, which was not to be considered as metastasis, but rather as a cell-developing cancer originating from the metaplastic bronchial epithelium. For that reason, he considers the multilocular development of cancer in asbestosis patients to be particularly significant. Here we find parallels to the Schaeberger lung cancer.

[illegible] asbestosis, it appears as though other histological [illegible] in the lungs could contribute to the development of cancer. One [illegible] indication of this is the increased tendency toward growth in the tissues. To name a few, we can speak of extensive epithelial desquamation with alteration of the shapes of epithelial cells, formation of numerous macrophages and giant foreign body cells, as well as proliferation of the connective tissue. Thereupon, as mentioned by Linzbach, the various tissues are released from their normal condition without the injury to the tissue being extensive enough for the cell to collapse. This increased tendency toward regeneration and the disorder of normal tissue conditions can probably be considered as promoting factors in the development of cancer.

These theories also apply to pleural growth. The pleura is involved in the decomposition process. Here we find epithelial desquamation, fibrin deposits, regeneration of the connective tissue, cornification and accumulation of asbestos crystals and asbestos particles (Gloyne, et al.).

All these theories are based on statistical figures and constitute valid arguments in support of the inner correlation between asbestosis and lung cancer.

In addition to the increased incidence of cancer in asbestosis patients, we also require proof of the reproducibility of the conditions through animal experimentation. As yet, this point could not be proven in the case of asbestosis. This, however, is not based on negative results of experiments performed, but rather simply due to the fact that this question has not as yet been addressed to any significant degree. The first experiments were performed by Nordmann and Sorge, who obtained astoundingly similar results. These were already mentioned in the previous paragraphs. For more certainty, however, it will be necessary to obtain further confirmation and recognition of this complex correlation from other specialists.

Nevertheless, all the observations made up to now tend to indicate with all probability that Nordmann's theory on occupational cancer in asbestos workers is a valid one. Other authors such as Gloyne, Lynch and Smith, Egbert and Geiger, as well as Linzbach, also tend to take a correlation of the cause into consideration. No attempt has yet been made from any side to deny this assumption.

If we now attempt to determine the origin of the carcinogenic effect of asbestos particles, we must differentiate between general and local promoting factors. We can generally assume that the occurrence of cancer is usually due to an inclination (predisposition) toward this disease. Just where we should look for the answer for this is difficult to say. We know from general human experimental pathology that predisposition toward cancer is dependent upon systemic factors. This is particularly evident by the fact that under identical experimental conditions and fairly similar exposure to carcinogenic hazards, only a number of the endangered persons do actually suffer from cancer. The available asbestosis-related observation material is not sufficient to allow us to perform an analysis of familiar carcinogenic conditions.

[illegible] and the way in which asbestos particle injuries can [illegible] general predisposition to cancer is not known. Our theory [illegible] in this regard is still only a hypothesis. However, it would seem that [illegible] general predisposition is not strong enough to promote cancer in [illegible] organs. Each of the afore-mentioned figures would tend to indicate this. The carrying localization would seem to be of primary importance here. Its morphological effects on the modified tissue reactions of the lungs have already been mentioned. Since the chemical definition of asbestos is fairly simple, the conditions in this case are easily understood. Right from the start, we can state that noe of the elements from the group of well-known carcinogenic agents can be taken into consideration here. The effects of asbestos particles on the lungs are probably the result of chemical and mechanical injuries. The chemical effects can probably be traced to silicic acid released from the somewhat vulnerable serpentine asbestos. Based on experience in the field of human pathology and numerous animal experiments, it is very impractical and unlikely that the latter would have any carcinogenic effects. We must keep in mind that the tissue changes which it causes, and which are different in their localization and extent in the case of asbestosis, would therefore present different conditions than silicosis. This different type and form of tissue regeneration can thus cause different biological reactions in the tissue. In addition to this, however, the mechanical repercussions of the many tips of asbestos needles and particles, most likely are characteristic of horablende asbestos with its solid and hardly soluble properties. These probably play a significant role in the typical tissue reactions resulting from constant mechanical irritation.

We must finally remenber that, particularly in the bronchi, there can be inflammatory reactions in severe cases of asbestosis. These are partly accompanied by the formation of bronchiectases, which can also be promoting factors for the development of cancer.

Based on our current knowledge of the subject, it is in these general, and, more particularly, regional, factors that we shall have to look for an explanation of cancer development in asbestosis patients. By definition, many of the injuries do not come under the group of chronic irritations. The fact that we are still far from completely understanding the finer factors involved here also applies to cancer development in asbestosis patients.

Let us now turn to the clinical diagnosing of cancer in lungs affected by asbestos particles: basically, all diagnostic aspects taken into consideration in the case of cancer detection in the lungs and the pleura can be used and are valid here. However, since this type of cancer originates from another primary disease, we shall have to take special characteristics of the clinical image as well as known elements with regard to the symptomatology of asbestosis into consideration.

For the past history, it is important to first do an occupational anamnesis, and keep in mind the fact that lung cancer in asbestosis patients generally appears only following year-long exposure to the particles, but

[illegible] of such exposure, [illegible] partly be caused and for [illegible] asbestosis. There is only one case in which the duration of [illegible] under dust conditions was only 1 1/2 years; in all other cases, [illegible] at least 7 years or more. In the case of short-term, intensive [illegible] to the particles, it appears that there is always a longer dust-[illegible] interval before the appearance of cancer. As yet there has been no case in which the period of time from the date of employment in dust-filled environment up to the confirmation of the presence of cancer was less than 12 years. Generally, we can expect that cancer only occurs in particularly pronounced, if not always the most severe, forms of asbestosis. The above examples are support of this.

The first symptoms of developing lung cancer, which are mostly not characteristic or pathopneumonic, will not be as evident as they might be in a previously healthy person, since shortness of breath, coughing, expectoration and certain discomforts in the thoracic area are already experienced by persons suffering from asbestosis. A certain loss of general strength, which is sometimes not present at all in the early stages of cancer, loss of weight and loss of appetite, are also frequent symptoms of severe forms of asbestosis. Acute worsening of the general condition, including local lung disorders, often indicates accompanying infections which are more difficult to overcome. In general, the rule in the case of cases of pure asbestosis is that the development of the disease occurs very gradually over the years, sometimes over decades. If there is evident local and general worsening of the condition during the course of such development, the possible occurrence of cancer must then be taken into consideration. In addition to cancer, infections which are most frequently non-specific are also encountered with bronchitis, pneumonia or abscesses. According to our experience, complex tuberculosis only played a minor role here. It is also much too often diagnosed. Of course, it is normal that it should be considered within the realm of possibilities. Nothing has yet been published on possible accompanying pulmonary lues or fungus diseases.

Of the general symptoms, quick loss of weight can be an indication, but it is not a conclusive factor. This, as we previously said, also applies to the lack of appetite, unhealthy appearance of the skin, and night sweats. If all of these are related to the progress of asbestosis, they will generally be accompanied by increased shortness of breath, cyanosis, possibly drumstick fingers and other local lung discomforts; however, we must keep in mind that a lung tumor would also promote an increase of such disorders. Generally, however, the status of the disease cannot be determined based on the case history alone.

There is little additional information that can be obtained from local disorders. Since severe asbestosis generally causes considerable irritation through coughing, little can be achieved from this symptom of the disease. This also applies to shortness of breath. Sputum observations would appear to be more important, as far as I am concerned. In the case of non-complicated asbestosis, the latter is mostly sparse and glutinous; in the case of more acute bronchitis and bronchiectasis, it is more considerable and purulent. It rarely contains blood. More frequent

[illegible] also indicate a specific disease. [illegible] blood in expectoration, consist of raspberry jelly in case [illegible] lung tumor. In [illegible] documentation, there are very few references [illegible] even for cases of simple asbestosis. Tumor cells [illegible] present in the sputum. Hornig mentions having seen considerable amounts of epithelial cells in the sputum of one asbestosis patient with tumor. If there is collapse of the lung tissue, this can easily be identified through the alteration of the sputum. This was a very significant factor in my observation. The patient suddenly began to throw up large quantities of core-shaped necrotic masses. Perhaps we can find here the "asbestosis bodies in clumps" symptom as mentioned by the English. These are rosette-shaped accumulations of asbestos particles which always appear in the sputum whenever lung tissues collapse (abcess, tuberculosis, tumor). Their diagnostic value is similar to that of flexible fibers observed in the sputum. We have already mentioned the significance of shortness of breath. In widespread tumors or bronchial obstructions, this is directly related to the latter. On the other hand, I find chest pains to be highly significant. For patients suffering from asbestosis alone, these are generally minimal and non-specific. In our tumor case, these progressed parallel to the development of the tumor; they were characteristically neuralgic. The documentation contains similar observations. These are due to an attack by the growth on the parietal pleura and possibly the intercostal nerves, if not actually on metastases.

These indications of the general and local disorders which can mostly be obtained from the case history should be sufficient.

As far as other objective findings are concerned, please note the following: asbestosis affects the lungs bilaterally. Exclusive unilateral processes, which generally indicate a tumor, do not occur here. The alterations which occur are generally very symmetrical. However, it must be noted that fibrosis can normally affect the right lung to a higher degree. General suppressions are never found above the upper part of the lungs. The respiratory sounds here are mostly hoarse, but rarely weak. The sounds of related pulmonary parts are mostly slightly to moderately weakened, and if not totally symmetrical, at least always bilateral. Only induration or specific as well as non-specific complications can cause exceptions here. The respiratory sounds are weaker in the lower part than in the upper part. The opposite is rarely the case. Accompanying sounds are more considerable and frequent in the bottom part than in the upper part; lateral differences are not significant. If definite symptoms of atelectasis are observed unilaterally, this could indicate the highest degree of tumor. Of course, this symptom is not always present in the case of lung tumor. Effusions, particularly hemorrhagic effusions, are hardly ever observed in normal cases of asbestosis. The tumor can show signs of fusion with the abcess and tuberculosis. Bronchiectasis in the form of cylindrical tracheal expansion is frequent in severe cases of asbestosis. Their differentiation with fusions can sometimes cause problems during the clinical examination.

An uneven asymmetry of the thorax, as well as distortion of the mediastinal organs and diaphragm, requires special analysis.

[illegible] would result in the most important examination [illegible] confirming the presence of a tumor. It must be remembered here [illegible] types of asbestosis do not always result in a purely symmetrical [illegible] region of the lung tissues (as claimed in the documentation). In addition to certain asymmetries, there can also be superficial descriptive [illegible] in the lower fields, particularly in the medial area. These [illegible] shadows, however, are usually not so compact and tumorous, but rather are in the form of somewhat hazy stripes. Solid or tomographic [illegible] often show the bronchial system as being open and sometimes even [illegible]. Bronchial stenosis, which sometimes follows infection, has not [illegible] been observed in cases of asbestosis. Compact, unilateral and superficial opacities in the lungs, possibly with bronchial obstruction, are practically almost indicative of a tumor. This also includes mediastinal displacements which are either constant or vary with the respiration, with paralysis of the diaphragm and recurrence with upper lobe processes, mostly accompanied by a Horner syndrome. Circumscribing opacities in the upper fields never indicate asbestosis. These conditions, in this case, are much clearer and simpler than in the case of silicosis. In the case of asbestosis, coarse shadow formations primarily indicate nonspecific infections. Tuberculosis is far from being as frequent as is generally assumed. Based on previous observations, its appearance rarely originates in the lower fields of patients suffering from asbestosis. For purposes of completeness, we must add here that, within the scope of useful diagnostic methods, tomography and bronchography can give different results as far as tumor detection is concerned, and are to be interpreted according to the standard rules that apply. The same applies to bronchoscopy. Other than for a few experiments, there is little knowledge available on diagnostic lung punctures performed to detect asbestos particles in the lung fluids. With primary pleural tumors or metastases, the detection of tumorous cells in the punctate greatly elucidates the situation. This was also observed by Alwen.

In the case of metastases, the diagnosis can always be made quickly.

The fact that persistent tumors can create fever is diagnostically non-significant, since infections also cause this symptom.

As far as blood count and the erythrocytic sedimentation rate are concerned, please note that anemia is not a symptom of asbestosis. On the contrary, high color and cellular values are signs of compensation. Accompanying infections could cause exceptions to this rule. Increasing anemia, with the exclusion of complicating causes, could be indicative of a tumor. A differential blood count should also not be considered as diagnostic evidence of the presence of a tumor. In cases of uncomplicated asbestosis, the blood sedimentation rate does not increase in itself. Nevertheless, it is often found to be significantly higher in group examinations of a large number of asbestosis patients. This is probably due to the fact that infections of the bronchial system are more often encountered in these patients. A higher and increasing sedimentation rate must always be observed and evaluated according to the standard clinical standards.

[illegible] the most important clinical aspects of lung tumor [illegible] asbestosis patients. The accurate interpretation of the latter [illegible] the purely clinical general symptomatology and thorough analysis of the individual symptoms. The important thing, as far as this is concerned, is to be able to recognize the clinical picture of asbestosis and always keep in mind that there can be complications with tumors, which are detected in the lungs of asbestosis patients almost as frequently as active tuberculosis. In Germany, only 10 cases of active tuberculosis have been reported for asbestosis patients as compared to 6 cases of tumor.

If the incidence of cancer in the lungs of asbestosis patients is as frequent as we have just stated, and if other conclusive evidence exists to support the theory that there is a close correlation between the two diseases at their origin, we must, even excluding animal experiments, already consider extending legal insurance protection to include this ailment. In previous compensation cases, trade associations have recognized this correlation, based on the uniform attitude of specialists on this matter. In the files which I personally studied on this subject, no specialist in Germany has ever adopted a different stand on the matter.

SUMMARY

The present document contains a report on case histories which have been reported and discussed concerning malignant lung and pleural tumors in patients suffering from asbestosis, based on worldwide literature. The reasons behind the original correlation between the two diseases are given. The report contains a description of the clinical picture of lung tumors in asbestosis patients and a recommendation that insurance coverage be extended to include this ailment.

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ABOUT THE LUNG CANCER WITH ASBESTOSIS !

by

Dr. H. W. Wedler (1943)

In the past 12 to 15 years a so voluminous experience of the asbestosis ha been put down (established) in the German and foreign literature, that we have a far-reaching knowledge of the danger to the asbestos workers, the clinical picture of their occupational disease and also its progress (cour With regard to the pathogenesis, however, there are still a number of ques tions remaining for which further enlightenment is to be expected, especia from the animal-experimental and chemical-physical workings (revisions, adaptions). Contrary to that, our knowledge of its complications and simul taneous phenomenons is built on a much less broad and certain basis. Here, the author was recently able to make a voluminous contribution concerning the behavior of the pulmonary tuberculosis with this coniosis. Equally in formative as well as important is the inquiry after the relation to lung cancer, whose increase with asbestosis has been repeatedly brought to atte tion over the past years. This interest is not merely confined to the soci medical territory or that of insurance's legality (judicialness), but rath reaches much beyond that into the general medicine, because with that a ne example of an exogenous cancer origin would be set. The number of observa- tions belonging in this place is, in itself, but small, yet in proportion the rarity of this ailment so considerable that a summarizing presentatio seems to be permitted. It is also welcome for the reason that, from the c nical side, there is no such work at all existing as yet in medical liter ture.

Firstly, we begin by repeating the observations of lung cancer with asbest sis as hitherto known in the world literature, then we are going to add t that the newest experiences, and point out the pecularities of this pictu of disease as well as its clinical diagnosis.

GLOYNE makes in 1933 the first mention of a carcinomatous tumor in the as- bestos dust-lung in a treatise dealing with pathological anatomy and histo logy of the asbestosis. There he discussds the complications of the asbest sis which are said to be in causal connection with it (purulent bronchiti broncho-pneumonia, tuberculosis, emphesema, bronciectases) and the simult neous diseases which, according to the knowledge of that time, had nothin to do with the influence of dust. Among the latter, he mentions an observa which he dismisses as follows : "There has also been one case of squamous carcinoma of the bleura. There is no evidence at the moment that this was any way related to the asbestosis."

In 1935 GLOYNE could contribute 2 further cases of lung cancer with asbes sis, but he blieved that an etiological connection of both diseases could not be asserted as yet. Certain histological points of view, however, see to make it quite obvious.

The first of these 2 observations concerned a woman, 35 who had been an a bestos spinner for 8 years, and who, after that, continued to live still nother 9 years without being exposed to asbestos dust. As the autopsy sho she died of a moderate asbestosis, a clot in the right heart, spleen infa and a meningeal bleeding (hemorrhage). A clinically not recognized swelli (tumor) of walnut size was found on the base of the right upper lobe of t lung, extending up to the apex and the thickened pleura. There were no me stases present. The horny plate-epithelium carcinoma had its starting poi at a small bronchus.

The second observation by way of autopsy also concerned a woman, 71. Firt years prior to her death she had once worked for 6 months, and then again 13 months in an asbestos factory, and that, according to experience, in t

extremely dust-laden department of mattresses and overhauling (or preparatio
Anatomically, GLOYNE found a medium grave (advanced) asbestosis with a part
ly disintegrated tumor in the right lower lobe of the lung, ascites and thr
bosis of the vein of the left leg. There were likewise no metastases. Histo
logically, this was also a horny plate-epithelium carcinoma.
In both cases the cancer wasn't this much spread and thus didn't seem to be
the sole cause of death. The same could be said of the asbestosis.

That very year (1935) a communication by LYNCH and SMITH came from the USA
about a lung cancer with asbestosis which also contained a detailed case
history (illness report). The described patient, 57, who used to be a cotto
weaver for 22 years and then, until his admission to the hospital, had been
an asbestos weaver for another 21 years, had for 5 years complained of shor
ness of breath. After having had, already 3 years prior to his death, tempo
rary pains in the back and the last 3 ribs on the right, these pains had re
appeared during the last months of his life. His physical condition started
to decline, he coughed, lost appetite, ran temperatures. Bloody sputum and
dyspnea. The clinical finding was characteristical for an asbestosis. The
breathing sound over the lung on the right was weakened. The clinical diag-
nosis purported asbestosis and chronical indurating pneumonia with ring on
lower right. Aside from the asbestosis with right-sided pleuritis and bron-
chiectases, a cavity of disintegration was pathologically-anatomically four
in the right lower lobe which was macroscopically taken for a tuberculosis
Microscopically, however, it turned out to be a plate-epithelium carcinoma.
Metastases were not present. The description of simultaneous hyaline nodule
in the lung is unusual for an asbestosis. The carcinoma had started from a
bronchus with a metaplastic epithelium. The authors thought of the chronical
irritation of the bronchia as the cause. They spoke of a "possible relatio
ship" with regard to the connection between cancer and asbestosis, and drew
parallels to other kinds of occupational lung cancer.

EGBERT and GEIGER (USA) reported in 1936 of another such observation which
they -with the exception of GLOYNE's hint (reference) in 1933- considered
be the very first of this kind. The man, 41, had been an asbestos weaver f
18 years. After 9 years of work and following a pneumonia, he had retained
a cough and shortness of breath. Eight months prior to the short hospital
treatment, he got severe, seizure-like backaches. He had grown thin, was
hardly mobile on account of his pains, had a cough, cyanosis and shortness
of breath as well as bloody-purulent sputum. Aside from the asbestosis, a
focus was roentgenologically detected in the lower part of the left lung
which resembled an atelectasis or a pneumonic process, but could be recog-
nized as a tumor, because of metastases present in the pelvis and in the s
nal column. During the autopsy not only the asbestosis, but also a 5:5:4 c
measuring acinous cancer in the left lower lobe were found which had esta-
blished metastases in the lungs, the left-sided glands of hilus and aorta,
the right adrenal gland (suprarenal body), the musculature of the abdomen,
the pelvis, the spinal column and the skull. The level of the tumor consis
ted of a big branch of the bronchus of the left lower lobe. Thus an etiolc
connection between the two illnesses seemed very obvious to them, namely :
"..that the irritating effects of the inhaled asbestos particles may in th
case have been a significant factor concerned in the development of the pr
mary lung cancer seems sufficiently plausible to be worthy of considerati

In 1936 GLOYNE was able to add a further one to his previous 3 observatior
He found a dedifferentiated carcinoma of the left lower lobe with an asbes
sis whose vector (carrier) was 51 years old and had worked for 21 years ir
the asbestos trade.

SPARKS related in 1938 without any particular details that GLOYNE had en-
countered in his autopsies 6 cancer cases with asbestosis. BAADER learned
through a letter from GLOYNE that these 6 cancer cases referred to 50 per-
formed autopsies.

Dt. Med. Woch. 1:402, 1939

NORDMANN amplified our knowledge the same year with 2 new cancer cases w
asbestosis which he could dissect in Hannover in short intervals. The fi
patient was 35 years old. From her 17th to her 26th year, exactly 7 (?)
years she had worked in the carding-, spinning-, and weaving departments
an asbestos plant. Four to 5 years prior to death she suffered of a cough
shortness of breath. Under suspicion of tuberculosis, she started to recei
medical attention 9 months before she died. HORNIG gave a probability-diagn
sis: Cancer in the left lower lobe with a marked asbestosis, because clini-
cally, there were signs of atelectasis, and tomographically, the main bron-
chus had been displaced (moved). Anatomically, it concerned a horny plate-
epithelium carcinoma with a walnut-sized deterioration-cavity which was con-
nected to the bronchus of the lower lobe. There were pleura callosity and
metastases in liver and kidneys.

The second observation concerned a man, 55, who had worked for 7 years (fro
his 36th to his 43rd year) in the preparation of an asbestos plant. Thirtee
months prior to his death he grew considerably thinner and got bloody sputu
In the beginning he was suspected of having contracted tuberculosis. There
was a muffled and weakened breathing sound (respiration) over the lower left
lung. Roentgenologically, the left lower field showed opacity. The physicia
in charge diagnosed an asbestosis with lung cancer. The autopsy confirmed
this. In the left lower lobe the cancer had, in connection with the main
bronchus, deteriorated down to walnut size, and was interrelated to the peri-
cardium, the left ventricle, the diaphragm, the peritoneum of the left upper
abdomen, the retroperitoneal tissue behind the spleen, the lymphnodes there
and the lower chest- and upper loin vertebral column. Histologically, it a-
gain concerned a horny epithelium carcinoma. A beginning bronchial carcinoma
was also found in the right lower lobe of the lung.

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

WEDLER drew attention in 1939 to another observation in Germany which origi-
natet from BOHNE, but had not been communicated (made public). The man, 58,
had worked 10 years (1925 - 1935) as master workman in an asbestos plant. On
ly a few years after having been exposed to dust, he already had trouble wit
his respiratory organs. In 1928 he was sent for 2 months to a health resort.
Several times thereafter he took other rests at sanitariums, although no my-
cobacteria tuberculosis were found. Due to an increasingly worsening conditi
he quit his job 3 months prior to his death. In the hospital he showed signs
of a general emaciation, cyanosis and a catarrh which was especially noti-
cible over the lower part of the lungs. There were numerous asbestos cor-
puscles in the sputum but no mycobacteria tuberculosis. The erythrocyte sedi
mentation was strongly accelerated (57/95). On the left, above the 9th rib e
chestnut-sized swelling which was grown together with the skin, was found ir
the enterior axillar line. It was removed and turned out to be a cancer mete
stasis. Roentgenologically, there were signs of an asbestosis as well as an
increase in markings in the right upper stories (regions). According to the
evidence at my disposal, there obviously was no diagnosis of a lung cancer
intra vitam. The patient expired of heart failure soon after the excision of
the metastasis. The findings of the postmortem examination were described as
follows: " The lungs were tightly grown together with the chest wall. The
heart was not enlarged, the musculature of a brown-reddish color and of a
somewhat flaccid consistency. The left lung was full of blood and fluid, the
lower lobe of solid (compact) consistency and of slate color. Upon removal,
the right lung tore in the area of the middle lobe. Its tissue looked yellow
reddish and completely deteriorated (decayed) and was showing extended cavit
and node formation. The upper lobe was rich in blood and fluid, of firm con-
sistency and free of air. The lower lobe was of a slatish, grey-reddish colo
and firm consistency. It was also free of air. The microscopical examinatio
of the lungs showed typical cancer tissue in the right middle lobe, whereas
the lower lobe presented all changes which are characteristic for asbestosi

lower pole here is lower than the pelvis ridge. During the pneumothorax test nearly 3000 ccm of a yellowish-brown, thread spinning (?) fluid es- capes from the left pleura cavity. The entire mediastinum is displaced to the right. The heart is hanging drop-shaped in the mediastinum; its left r (edge) is situated in the center (middle) line. The right lung, with the e ception of minor rope-shaped concretions, is free in the pleura cavity. In the pleura costalis palm-sized (hand) solid, white, sinewy plates with single (isolated) bulb (knob) shaped equally solid, white nodules are found A big radiate scar is seen in the pleura of the right upper lobe of the lun On the pleura of the right lung one recognizes a fine, moderately tenacious grey felt-like coat. The right lung itself is of proper size and of medium air and fluid content. The pleura and scision are showing a moderately strong, black, net-shaped design (marking). The lung tissue, moreover, is c a red color. Focus illnesses cannot be proved. In the lower lobe-branch of the right lung artery a small brown-red blood plug is clinging to the inti ma. The lung arteries are empty. The left pleura is in its full extention, thick-skinned (like rind). On the inner surface one finds masses of bulbs (knobs) standing closely together apato the size of a walnut with a mulber ry-like surface which consists of a jelly-ish -white on cut- tumorous tis When cut, this tissue secretes a thread-spinning fluid. One also sees be- sides the tumor tissue some sinewy plates as on the right. The tumor tiss doesn't anywhere penetrate the base any deeper, most of all, not the lung tissue. Only in the region of the skin nodes, (as mentioned above) on the left side of the chest, there are tumor nodes in the rib musculature. The left lung is strongly atelectatic and adhers only with a rope-shaped con- cretion to the chest wall. The lung tissue is of a tough-firm consitency, grey-reddish color and is showing on scision and surface a black, net-lik design (marking) which is a bit more pronounced than the one on the right side. There is no tumor anywhere in the lung tissue itself. Trachea, bron- chia of both lungs are of proper width and of delicate wall. Tumor tissue nowhere provable. Lymphnodes of hilus on both sides are of black color and soft consistency. The heart is hardly as big as the corpse's fist. Perica dium leaves smooth and shiny. Subepicardial fatty tissue is present in mo- derate abundance. The left ventricle is small, the right one a bit enlarge The wall of the left one is 5 mm, that of the right one 2 to 3 mm thick. All heart valves delicate and capable of closing. Crown (wreath?) arteries of medium width and delicate wall. The myocardium is evenly brown-red on a cuts. Aorta in full expansion is delicate and elastic.

Microscopical findings:

Right lung: In places the lung structure is showing minor emphysematous changes. Nodule-shaped deposits of a fine-grained black pigment are found i several places in the peribronchial tissue. In this region, the peribron- chial tissue shows a distinct hyalin transformation and fibrosis. Yet besid the deposits of the anthracotic pigment one also sees partly fresh, and al- so partly degrading typical asbestosis corpuscles. These are always lying together in larger quantities with the anthracosis pigment. But they are al so found independent of that, lying alone in the lung alveoli and in the in terstitial tissue. Likewise, there are plenty of coal dust deposits and as- bestos corpuscles found under the pleura. The big bronchia are in part con- taining mucus and shed (repelled) epithelium. The bronchioles are often en- larged, but they are coated everywhere with a single-layered flimmer (glim- mer) epithelium. Epithelial metaplasis are nowhere provable. The lung tissu immediately under the pleura is showing a slight collapse of the alveoli. Here, the alveolar epithelium shows often a glandular, but nowhere atypical character. Other than that, nowhere pneumonic changes in the lung tissue.

Left lung: The tissue of the left lung reveals the finding of the collapse induration with desquamative alveolar catarrh and fibrosis of the interstic In the peribronchial tissue -just as on the right- there are plenty of an- thracosis deposits with a hyalinosis of the surrounding tissue. One finds i

is striking to note, that at hitherto made animal experiments with asbestos dust, although conducted with different viewpoints, obviously no one has made similar observations. There were also no such observations during various animal autopsies (dogs, rats) that were performed on animals which used to live in asbestos plants.

If one wishes to speak of occupational cancer in a fixed group of workers, so must, at first, the statistical proof be established that the cancer in question occurs more frequently than in other professional (occupational) or population groups, whereby the demand for a possibly similar age combination with the comparable figures (numbers) should be hard to meet. The statistical path is also holding still a further unmistakable difficulty for the asbestosis. With regard to this in itself rare disease, it can concern only small absolute numbers (figures). With that, just one single observation as a chance event can already cause quite large percentual shift. Furthermore, with regard to NORDMANN one ought to consider that, especially in recent years, the change of workers in the asbestos plants is going to injure (prejudice) the results in a negative sense, since for the cancer origin usually a long dust exposure, and perhaps a longer dust-free interval must have presented itself. Today, only few workers are staying that long in the endangered plants. Furthermore, the fight against dust most desirably counteracts the dust damage to the lung. Nevertheless, concerning severe asbestoses, today we're still dealing mostly with workers who have carried their dust damage over from earlier times when work conditions were considerably less favorable.

As second point of view, important for the question of a link between cancer and asbestosis, it ought to be discerned what special circumstances (conditions) were encountered with regard to dust damage and the findings at the place (area) of the disease which make the cancer intelligible and distinguish it from other lung cancers.

As key-stone of the proof, experimental experiences ought to ducument that the cancer production is also succeeding with animals.

Let us first turn to the statistical path. Here we can use as really reliable only the dissections with an exact anatomical examination of the lung because there exist certain possibilities of error with the purely clinica diagnoses. Furthermore, purely clinical works (dissertations) concerning this question are not available.

Thirty asbestos workers have hitherto been dissected in Germany. The added table No. 1 (pg. 197) is rendering the cases according to age, sex, time o work, stage of asbestosis or the heart weakness conditioned by it, or an agonal pneumonia. The first 18 deaths have already been published. I have collected the remaining 12. The under No.29 listed young girl can here be neglected, since she had only a short exposure to dust and, anatomically, hadn't developed an asbestosis as yet. Of the remaining 29 dissected, 4 he a bronchial cancer and 2 others a malignant pleura tumor. From this a percentage of exactly 20% can be calculated for malignant tumors of the lung with dissected asbestoses in Germany. Other malignant new-formations of th body were found altogether only 3 times, one each of the stomach, the esophagus and the prostate. Even if the lung cancer has statistically increas considerably in the past 3 decades so is it still distinctively outstrippe by the cancers of the digestive tract, according to major autopsy statisti Otherwise, depending on the different authors, its frequency puts it in th 4th to 2nd place in the cancer statistic of organ cancers. In Germany the lung cancer with asbestosis is far in the foreground, as the above figures are showing. The average age of the lung tumor vector at the time of death is also considerably lower than that of vectors of other carcinomata (roun ly 51 to 66 years). Yet, to be sure, the small numbers are not allowing as yet to come to special (particular) conclusions. According to the repartition of the sexes, for every 4 men there are 2 women with lung tumors.

Otherwise, as for the repartition of sexes concerning lung cancers among men and women, the ratio of 3-4-1 is indicated. As to sex, the quota of the asbestos workers diseased with lung cancer is also depending, naturally, on the number of women and men working in the plants. In Germany the former are outweighing the others by far. With regard to the 2 above mentioned women, the relatively young age of 35 and 40 years at time of death is st king. All cancer vectors had a marked to severe asbestosis. Only the man with the pleura carcinoma (No. 20) had a moderate asbestosis with a very long, yet probably only little dust exposure. NORDMANN has pointed out already that a longer dust exposure is a contributing factor in all cases. According to above tabl this applies without exeption to all cancer vectors. The time period of exposure is twice 7, twice 10, and once each 18 and 42 years. The dust-free interval prior to the tangibly falling ill with cancer, and during which the asbestos dust-depot can continue to be effective, varied in length from 6 months to 12 years. Once it wasn't exactly known (see table, No. 30).

These figures show unequivocally that lung cancer is the most frequent complication with asbestosis, if one disregards agonal pneumonia and heart weakness. Even the tuberculosis whose frequency usually far surpasses that of cancer, is here standing way back of the lung cancer. With this decisive proof (evidence) for the closer connection of asbestosis and lung cancer is given. It is amazing that today's percentages from the larger reference material (research) are matching exactly the figures which NORDMANN had given earlier from a smaller observation material.

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

The British are the most experienced in this field. Unfortunately though, according to the English medical literature, there is no possibility to list the individual cases in the same manner as above because it is poorly arranged, and some individual cases were published not once but several times, so that they can't be kept apart any more. One has to be content, for the time being, with GLOYNE's figures. In 50 dissections of asbestosis cases (according to BAADER) he came across 6 cases of lung cancer (probably including 1 pleura tumor). From this follows a lung cancer with asbestosis-frequency of 12 %.

The figures reported from the USA are quite simular. From there I collected 13 autopsy cases from medical literature up to 1939. Possibly, this figure may not be quite complete since some dissertations (medical reports) were not accessible to me. Among these dissected asbestoses I encountered 2 bronchial cancers which were mentioned above. This would correspond to a percentage of roundly 15 %. Another organ cancer was not specified there. The pneumonia has been reported relatively often (4 times) as cause of death.

Strangely, with regard to this subject there are no expedient (instrumental) statements whatsoever of her own from France.

Just as little on it was published in other countries.

In Italy, where the asbestosis is very well known, no case of lung cancer ha been seen to date (VIGLIANI, etc.).

Thus, in the medical world literature we hitherto survey (confront) 14 malignant lung-pleura tumors of epithelial origin which derived from 92 autopsies This are exactly 16 % cancer cases with dissected asbestoses.

Out of these only 11 have been described in detail so far at first that still further statistical results can be gained from them. (see table No. 2)

As to the sex proportion, the result is 7 (men) to 4 (women).

The age lies between 35 to 71 years.

Of this, 4 are standing alone in the relatively young age of 35 to 41 years.

The time span from the start of work to the development of cancer is always comparatively long (between 13 to 42 years). After a short time of dust ex-

posure a longer, dust-free interval is usually inserted which seems to pr
that the dust influence -if at all- is leading only very gradually to a ca
cer development.

The majority of the afflicted patients suffered of a very severe asbestosis
without it having to be obligatory in this form.

There were 9 times lung- and twice pleura excrescences present. All lung ca
cers -as far as this can afterwards still be decided with certainty- seem t
have gone out from a bronchial epithelium. An observation which would be ty-
pical for an alveolar cancer, is not among them.

According to the histological character, the horny plate epithelium carcino-
mata are in the majority. Of 8 histologically more closely denoted lung can-
cers, 5 were horny plate epitheliums; a further plate epithelium cancer was
not horny. Another cancer belonged to the group of indifferentiated excres-
cences, and the last one grew acinous.

The 3 pleura excrescences were described as "pseudo-alveolar metsothelioma"
as "adenomatous pleural carcinoma" and as "squamous carcinoma".

Four of the lung excrescences -in a narrower sense- had no metastases esta-
blished.

The localization of the primary lung cancers is pointing alone 7 times to th
lower lobes, where the asbestosis is always developed most strongly. The ex-
crescence is 4 times located in the left and 3 times in the right lower lob
In contrast to that, the right middle- and upper lobe are represented but
once each with a tumor.

This local agreement (conformity) of the tumor localization with the stron-
gest asbestotic tissue changes in the lower parts of the lungs is striking.

The numerical accumulation of the lung cancer in dissected asbestosis vecto
is the first clear evidence for a closer causal connection of these two di-
seases. The percentage of 16 % lung- and pleura cancers far exceeds the o-
therwise statistically to be expected frequency in other autopsies. Althoug
the frequency of lung cancer probably has increased considerably in the pas
decades, it doesn't amount to more than 2 to 6 % on the average, according
to major autopsy statistics. If the absolute figures for the asbestosis -as
we were able to show- are still quite small they appear, nevertheless, con-
vincing insofar that they were found in entirely different places with ap-
proximately equal frequency (Germany, England, USA).

To these purely numerical proportions further positive viewpoints can be ad
ded to above derivations which NORDMANN, to be sure, has partly pointed out
already with the help of lower figures.

At first, we mention here the age of the cancer vectors. Four of them were
still at the relatively young age of 35 to 41 years. Although lung cancer i
occurring already in juveniles, it can be found most frequently between the
ages of 50 to 60 years. According to our material, 6 patients belong to thi
age group.

The distribution of the sex, as in comparison with the other numerical pro-
portions, has here shifted in disfavor of the women. Among 11 cases we en-
counter 4 women. The larger statistics usually give a ratio for lung cancer
of 3-4-1 between men and women. Yet, one must keep in mind that women em-
ployees outnumber the men in asbestos plants, especially in Germany and Eng
land and in contrast to the USA.

As was mentioned above, the frequent conformity (agreement) as to the seat
(location) of the tumor with the asbestosis' severest changes in the lower
parts of the lungs seems to be very noteworthy.

Furthermore, the histological character of the lung excrescences is striki
The mostly horny plate-epithelium carcinoma is numerically in the foregrou

We counted alone 6 of them among 8 more closely denoted bronchial cancers. The otherwise with lung cancer usual proportion among the individual forms of excrescences is here broken completely in favor of the plate epithelium carcinoma and has been onesidedly shifted. If the lung cancers are divided histologically into the 3 major groups of the indifferentiated cells, the plate- and cylinder epithelium carcinomata, so constitute the former the main contingent in the major statistics with roundly 2/3 of all cases. Since the plate epithelium carcinomata are least inclined to metastasize it may seem understandable that in 4 cases of the above mentioned observations no metastases were seen. It is precisely the histological nature (condition) of the lung cancers with the unequivocal prevailing (outweighing) of the plate epithelium carcinoma that speaks for its independent status among the lung cancers.

The cancer was always observed only after a relatively long period of dust influence. Be it that the time of working in the asbestos dust was very lon or that with a short work time with usually considerable exposure a longer interval was inserted during which the dust damage could further take effec A row (series) of irreproachable observations which could partly be made by this author himself teach us that with the asbestosis the dust damage often appears precisely just in this interval and eventually leads to an increasing fibrosis. Among all cases of lung cancer with asbestosis not one singl one is found where this long time of asbestos dust-influence was not given (allowed). Herein exists a very good agreement with regard to experiences with other occupational cancers.

The other histological findings in the asbestos lung make a further understanding of the above connections possible. In the asbestos dust-lung one mostly finds extended epithelium metaplasia at the minor bronchia which can be taken to be pre-cancerous stages. The carcinomatous new-formations most probably emerge in the main from them. In one case NORDMANN even made the observation that with a large carcinoma of the left lower lobe a just beginning small cancer occurred on the other side which had to be regarded no as a metastasis, but as a cancer autochthonously springing from the metaplatic bronchial epithelium. He, therefore, regards the multiocular cancer origin with the asbestosis as especially distinctive (characteristic). We are here finding parallels to the Schneeberger lung cancer.

It appears, as if besides these metaplasis the other histological changes i the lung also have a part in the cancer origin. In the first place, they al have the strongly increased growth-tendency of the tissues in common. Here, the abundant epithelium desquamations are to be mentioned with changes in the shape of the cover cells, the formation of numerous macrophagia and foreigh body-giant cells as well as the connective tissue-excrescence. Thereb as referred to by LINZBACH, the individual tissues are freed (disengaged) from their normal relations without such a considerable damage to the tissu as to incur a cell destruction. In this increased growth-tendency and distu bance of the normal tissular relations one can most probably see contributing forces for the cancer origin.

These viewpoints also apply to the pleura excrescences. The pleura is in these re-building processes included. There one finds epithelium desquamations, fibrin layers (strata), development of connective tissue, callositie and the storing of asbestos crystals and asbestosis corpuscles (GLOYNE, etc

All these viewpoints listed are adapting well to the insights which spring from the statistical figures, and thus become supporting arguments for the inner connection between asbestosis and lung cancer.

Aside from the increased rate of cancer vectors with asbestosis, the animal experimental reproductibility (reproductiveness) must be demanded as a further convincing proof of these ratios (conditions). Regarding the asbestosi this point cannot be considered ascertained as yet. Yet this isn't on account of experiments that turned out negatively but simply because this mat

er (question) has not yet been looked into to a larger extent. The firs
experiments were made by NORDMANN and SORGE with a seemingly striking re-
sult of agreement (conformity). We have already discussed it above. For
reasons of precaution, however, one will have to wait for further confir-
mations by other experts (ratifications) and acknowledgment of these com-
plicated conditions.

At any rate, all hitherto known facts are with great probability leading t
the belief that NORDMANN's opinion (view) of the occupational cancer of ti
asbestos workers is justified. The other authors, such as GLOYNE, LYNCH
and SMITH, EGBERT and GEIGER, as well as LINZBACH are showing the tendency
to assume here a closer causal connection. The attempt to refute this as-
sumption has, as of now, not been undertaken by any one.

If we're now asking ourselves where to look for the cancerogenous effect
of the asbestos dust, we have to separate the general and local disposing
factors. It is everywhere assumed that for the occurrence (beginning) of a
cancer a general cancer disposition (proneness) is to be presupposed. It
is hard to say, though, where to look for it. From the general human and
experimental pathology is known that the readiness for cancer depends on
factors of constitution (disposition). This expresses itself in such a
manner that under the same experimental conditions and with nearly equal
exposure for cancerogenous damages in man the quota of cancer patients al-
ways constitutes just a part (fraction) of the endangered. The material of
observation regarding the asbestosis and available to us doesn't suffi-
ciently allow an analysis from familiar cancer affliction (?) (disposition?)

How far and in what manner the asbestos dust damage is creating such a ge-
neral cancer disposition, we don't know. Its assumption remains a hypothe-
sis. Yet it doesn't seem that this general disposition is so strongly ef-
fective that it might, perhaps, be also favoring (helping) the origin of
cancer of other organs. The presented figures don't speak for that. Of de-
cisive importance seems to be, most of all, the local transposition (chang
Its morphological expression in the altered (changed) tissue reactions of
the lung were already more closely specified above. Mainly chemical and
mechanical factors have to be taken into account as their cause. Since the
asbestos can be chemically simply defined, the proportions here are mo-
derately surveyable. One can indeed say from the first that substances fro
the group of the known cancerogenous agents are out of the question. The
influence of the asbestos dust on the lung is probably carried out via
(over) chemical and mechanical defects. We are trying to find the chemical
effect in the silicic acid which ought to detach itself from the more vul-
nerable serpentine-asbestos. That it might have a cancerogenous effect is,
according to the experiences of the human pathology and the abundant anima
experiments, very improbable and has been practically sufficiently refuted
Yet one must keep in mind that in the tissue changes, caused (established)
by them, and which are for the asbestosis locally differently arranged and
emphasized (marked), different situations (proportions) are given here tha
with the silicosis. This dissimilar arrangement and shape of the new-for-
mation of tissue can cause (unleash), nevertheless, other biological modes
of reaction of the tissue. But above that, one will have to consider just
these mechanical retroactions of the many pointed asbestos needles and cor
puscles which are special particulars of the hornblende-asbestos with its
stiff, hard to solve quality (nature). On account of the strange tissue
reaction caused by the permanent mechanical irritation, they certainly are
of great significance.

Finally, there is a reminder that with a severe asbestosis inflammable re-
actions -partly with formations of bronchiectases- occur foremost at the
bronchia which, on their part, can be of assistance to the cancer origin.

Using today's knowledge, we must look for the explanation for the cancer
origin in connection with asbestosis to these general and, most of all,

what greater importance seems to me the consideration of the sputum. Wit
the uncomplicated asbestosis it is mostly scant, tough and mucous, yet w
stronger bronchitis and bronchiectases also more ample and purulent. Bloo
is only very rarely in it. More frequent and even scant blood depletions
require a special explanation. I, personally, have seen blood in the sputu
in form of the rasberry jelly sputum just once with a complicating lung tu
mor. Also for the plain asbestosis, there are only isolated, scant stateme
of this sort existing in medical literature. Tumor cells in the sputum oug
to be very rare. HORNIG claims to have seen abundant epithelium cells in the
sputum in his case of tumor with asbestosis. If a disintegration of the
lung tissue sets in, it will be easily recognizable by the change in the
sputum. This was very impressive in the case of my observation. The patien
suddenly brought up large amounts of granulous conglobated necrotic masses
Perhaps it would be possible to find on one of such occasions the symptom
of the British, namely the "asbestosis bodies in clumps". It concerns ro-
sette-shaped piles (heaps) of asbestos corpuscles which can always appear
in the sputum when lung tissue disintegrates (abscess, tuberculosis, tumor)
Diagnostically, they are equivalent to the elastic fibers in the sputum. Th
significance of the shortness of breath has already been discussed above.
It will solely refer to it only in case of a larger expansion of the tumor
or bronchial occlusion, etc. Contrary to that it seems to me, as if the
chest pains are of greater significance. With asbestosis alone, they are
usually trifling and undefined. In our case they came fully to the fore, to-
gether with the advancing of the tumor, they took on a typical neuralgiform
character. There are similar references to it in the medical literature.
The cause of it can probably be attributed to the spreading of the tumor to
the parietal pleura and, eventually, to the intercostal nerves, if not even
to metastases.

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

As to the other objective findings, the following may be noted: The asbesto-
sis is attacking both sides of the lungs. Strongly onesided processes, as
in most tumor cases, do not occur. Usually, there is also a far reaching
(sweeping) symmetry of the change predominant. One must know, however, that
the right side of the lung can also normally be assailed more strongly by
the fibrosis. We never find any grosser dulnesses over the upper lung re-
gions. The sound of respiration is here mostly harsh, only seldom muted
(diminished). The dependent lung parts present mostly a moderate to medium
strong weakening of sound which is, if not fully symmetrical, so almost
always doublesided. Only grosser (stronger, thicker) rinds or specific and
unspecific complications can account for exeptions. The sound of respiratio
is weaker at the bottom than at the top. This is very rarely reversed. There
are more numerous and more frequent additional noises found at the bottom
than at the top; sides matter little. If onesided (unilateral) unequivocal
signs (symptoms) of an atelectasis are found, so is this, to the highest
degree, suspicious of tumor. Yet, of course, this symptom of lung tumor
doesn't have to be obligatory. Effusions, especially those of a hemorrhagic
nature, practically don't occur with the common asbestosis. The tumor can
have signs of colliquation in common with the abscess and the tuberculosis.
Bronchiectases in form of cylindrical dilations of the trachea are not rare
in cases of severe asbestosis. Occasionally, they could make their demarca-
tion against colliquations difficult during the clinical examination.

Grosser asymmetries of the thorax, distortions of the pleura organs and
diaphragm are always requiring a separate explanation.

The X-ray finding might be the most important examination method of a tumo:
One must consider thereby that the grave asbestosis doesn't always lead on
to fine symmetrical concretions of the lung tissue, as could be assumed ac-
cording to the medical literature. Aside from certain asymmetries, areal
opacities of a circumscribed nature in the lower fields especially medial

edged (recognized) the connection. According to documents, relating to this matter, and which I have examined, no medical expert in Germany ha challenged or rejected this viewpoint (opinion).

Summary.

This is a report on the hitherto known and expanded casuistics of malignar lung- and pleura excrescences with asbestosis in the medical world lite- rature. The reasons which are making a causal connection between both di- seases obvious are shown. The clinical picture of the lung tumor with as- bestosis is discussed, and the extension of insurance protection to in- clude this complication is recommended.