REVIEW ARTICLE

Malignant Pleural Mesothelioma

Incidence, Etiology, Diagnosis, Treatment, and Occupational Health

Volker Neumann, Stefan Löseke, Dennis Nowak, Felix J. F. Herth, and Andrea Tannapfel

SUMMARY

Background: The incidence of malignant mesothelioma in Germany is about 20 cases per million persons per year. Its association with asbestos exposure, usually occupational, has been unequivocally demonstrated. Even though the industrial use of asbestos was forbidden many years ago, new cases of mesothelioma continue to appear because of the long latency of the disease (median, 50 years). Its diagnosis and treatment still present a major challenge for ambulatory and in-hospital care and will do so for years to come.

Methods: This article is based on a selective review of the literature, along with data from the German Mesothelioma Register.

Results: 1397 people died of mesothelioma in Germany in 2010. A plateau in the incidence of the disease is predicted between 2015 and 2030. Most mesotheliomas arise from the pleura. The histological subtype and the Karnofsky score are the main prognostic factors. Only limited data are now available to guide treatment with a combination of the available methods (chemotherapy, surgery, radiotherapy). The prognosis is still poor, with a median survival time of only 12 months. Symptom control and the preservation of the patient's quality of life are the main aspects of care for patients with mesothelioma.

Conclusion: The incidence of mesothelioma is not expected to drop in the next few years. The available treatments are chemotherapy, surgery, and radiotherapy. Specialized treatment centers now increasingly provide multimodal therapy for treatment of mesothelioma.

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German Mesothelioma Register at the Institute of Pathology, Ruhr-University Bochum, Bergmannsheil University Hospital: Dipl.-Biol. Neumann, Dr. rer. nat. Löseke, Prof. Dr. med. Tannapfel

Institute of Occupational, Social and Environmental Medicine, Ludwig-Maximilians-University, Munich: Prof. Dr. med. Nowak

Pneumology and Respiratory Critical Care Medicine, Thorax Clinic at Heidelberg University Hospital: Prof. Dr. med. Herth

Institute of Pathology, Ruhr-University Bochum, Bergmannsheil University Hospital: Prof. Dr. med. Tannapfel

Malignant diffuse mesothelioma is a tumor arising from the mesothelial or submesothelial cells of the pleura, peritoneum, or pericardium. More than 80% of all mesotheliomas originate in the pleura (1), and more than 80% of patients with pleural mesothelioma are men (1, 2). This disease is much rarer than lung carcinoma: 1397 persons died of malignant mesothelioma in Germany in 2010. Mesothelioma is officially recognized as an occupational cancer and as a signal disease for occupational asbestos exposure *(Figure)*. Its incidence has been constant in recent years and is not expected to drop until some time between 2015 and 2030. Mesothelioma remains a diagnostic and therapeutic challenge for ambulatory and in-hospital care and is likely to remain one in the years to come.

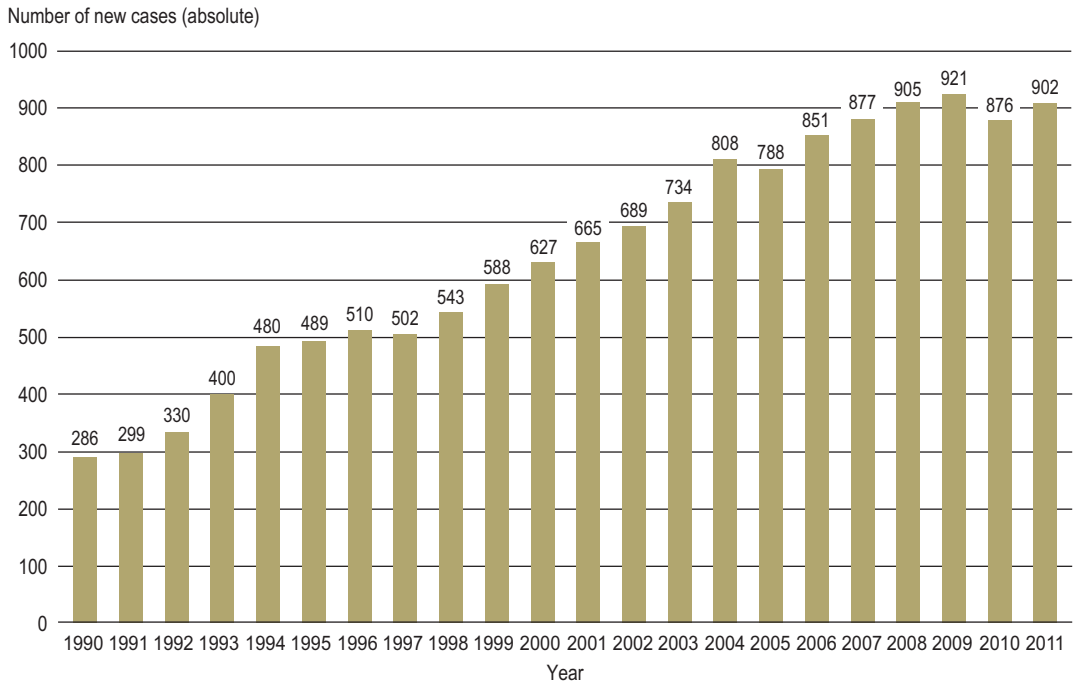
Methods

The publications reviewed for this article were retrieved by a selective search of the Medline database with the same search terms that were used in the creation of the S2 guideline (3) of the European Respiratory Society and the European Society of Thoracic Surgeons. Further quantitative data on mesothelioma as an occupational disease according to No. 4105 of the German Regulation Concerning Occupational Diseases (*Berufskrankheitenverordnung*, BKV) were obtained from the database of the German Mesothelioma Register.

Mesothelioma and asbestos

In 1960, a path-breaking study revealed the association of mesothelioma with crocidolite asbestos (4). In 1965, mesothelioma was first designated a "signal tumor" of asbestos exposure (5). As many as 90% of cases of mesothelioma are due to asbestos exposure, and there is a clear correlation between a country's asbestos consumption and the incidence of mesothelioma there (6) *(eBox)*. There are no official data on the number of people occupationally exposed to asbestos in Germany; estimates range from 1.5 to 2.5 million workers since the Second World War. In 2011, the database of the Preventive Care Division (*Gesundheitsvorsorge,* GVS) of the German legally mandated casualty insurance carriers contained data on 561 277 persons who had handled asbestos-containing materials on the job. These data, however, do not permit any statistically

FIGURE



New cases of mesothelioma classified as occupational disease according to No. 4105 of the Regulation Concerning Occupational Diseases (*Berufskrankheitenverordnung*, BKV). Source: German Social Accident Insurance (*Deutsche Gesetzliche Unfallversicherung*, DGUV)

valid inferences about the number of persons in this group who have mesothelioma.

Aside from occupational exposure, persons can be exposed to asbestos in any of the following ways (7):

- private activities
- proximity to factories where asbestos is used
- living in areas where asbestos occurs naturally
- faulty removal of construction elements that contain asbestos from old buildings.

Incidence and latency

Mesothelioma arises in 1 to 2 per million of the general population per year (6); its incidence among occupationally exposed persons is more than 40 times as high (1). Although asbestos processing is forbidden in many industrialized countries, the incidence of the disease is expected to rise further. A person's risk of developing mesothelioma is age-dependent (ten times higher in persons over age 60 than in persons under age 40) and continues to rise decades after exposure (6). The incidence is currently rising *(Table 1)* in Europe, Japan, and Australia and falling in the United States (1). The reason for this discrepancy is currently unclear. The average latency of mesothelioma after asbestos exposure was once thought to be 30 years, but more recent data have led this figure to be revised upward to 50 years (1, 8).

Diagnostic assessment and clinical manifestations

Because the clinical manifestations of mesothelioma are usually nonspecific, the diagnosis is often not made immediately. Diagnostic delays of up to six months are common (9).

Dyspnea is the first symptom of pleural mesothelioma in 90% of cases (3). Pleural mesothelioma can cause pain by irritating intercostal nerves or by infiltrating into the chest wall. Rarer manifestations include phrenic nerve palsy, irritative cough, paraneoplastic phenomena, and spontaneous pneumothorax (10). Symptomatic metastases are unusual.

The diagnosis of mesothelioma should be considered in any patient with a unilateral pleural effusion or thickening, especially if chest pain is present (11). The differential diagnosis includes pleural effusion of inflammatory or infectious origin (e.g., due to tuberculosis, pneumonia, or chest trauma) and pleural effusion due to venous congestion.

Whenever mesothelioma is suspected, a detailed occupational history should be taken and the patient should be referred to an experienced center for pulmonary medicine. Initially, non-invasive tests such as ultrasonography, computerized tomography (CT), and magnetic resonance imaging (MRI) can be used to obtain further support for the suspected diagnosis

TABLE 1

Predicted peak incidence years and incidence at peak for mesothelioma in various countries

Country	Incidence at peak (new cases per million per year)	Peak year(s)	Predicted deaths per year at peak	Study
Australia	40	2010	1000	Leigh 2002 (e8)
United Kingdom	38	2016	2040	Tan 2010 (e9)
Germany	20	2015–2020	1600	Pesch 2010 (e10) Peto 1999 (e11)
France	20	2020–2040	1300	Banaei 2000 (e12)
USA	15	2010	2800	Larson 2007 (e13)
Japan	15	2025–2033	1200	Azuma 2009 (e14)
Spain	11	2016	520	Pitarque 2008 (e15)
Netherlands	10	2028	900	Segura 2003 (e16)

and assess the extent of disease. The diagnosis can only be definitively established by biopsy.

Imaging methods

Transthoracic ultrasonography enables an assessment of the pleura in the presence of a pleural effusion; it is the best available means of visual guidance for pleural puncture (12).

CT is the best way to judge the extent of tumor and to detect lymph node metastases (11).

MRI is the best way to determine whether the tumor has invaded the diaphragm or the chest wall.

Positron emission tomography (PET) is now coming into wider use; its main advantage is greater sensitivity for the detection of distant metastases (11).

Pleural puncture and cytological diagnosis

Tumor cells are found in pleural effusion fluid in more than 50% of cases of pleural mesotheliomas, with the likelihood of positive cytology depending on the tumor subtype. Cytological abnormalities are found in both reactive and malignant processes, and negative cytology does not rule out mesothelioma (13). As discussed in the guidelines (3, 13), the sensitivity of cytological diagnosis is limited.

Percutaneous needle biopsy and image-guided percutaneous pleural biopsy

Studies have shown that percutaneous needle biopsy without image guidance is 7% to 47% sensitive and 100% specific (14). Malignant and benign pleural changes are unevenly distributed in the pleura; taking biopsies under image guidance (with either ultrasound or CT) raises the sensitivity to the range of 77% to 87%, still with 100% specificity (15).

Thoracoscopy and thoracotomy

In the guidelines (3), video-assisted thoracoscopic surgery (VATS) is recommended for the diagnostic assessment of pleural effusions of unclear origin. The sensitivity and specificity of VATS for the diagnosis of pleural mesothelioma are 95%–98% and 100%, respectively. VATS enables the removal of specimens under visual observation, as well as pleurodesis in the same procedure (14). The surgeon can inspect the lesion with VATS to assess its resectability (16).

Histopathological diagnosis

The histopathological appearance of mesothelioma is variable and therefore presents a diagnostic challenge. The diagnosis should be made by a specialized pulmonary pathologist (possibly in a reference center for pulmonary diseases). Close cooperation between the surgeon and the pathologist is needed (3, 13, 17).

Mesothelioma is divided into epithelioid, biphasic, and sarcomatoid subtypes on the basis of the predominant histomorphological growth pattern. Special immunohistochemical tests are obligatory (13, 17). There is no single specific marker for mesothelioma; different combinations of markers are used depending on the differential-diagnostic questions to be answered (13, 17).

Staging

The chest X-ray usually shows a unilateral pleural effusion (11). A chest CT is the best way to assess the extent of tumor and of lymph node involvement.

MRI or mediastinoscopy may be needed for the assessment of chest-wall infiltration or mediastinal involvement (affected mediastinal lymph nodes) (11). In addition, abdominal ultrasonography, bone scintigraphy, and sometimes MRI of the head may be needed to rule out distant metastases (11). The European Pneumological Society (3) recommends using the tumor-nodes-metastases (TNM) classification of the Union for International Cancer Control (UICC) (18). Mesothelioma is staged on the basis of the histopathological and intraoperative findings along with the results of clinical staging tests.

Survival time and prognostic factors

Patients with malignant pleural mesothelioma have a poor prognosis, with estimated median survival times varying from 4 to 12 months (3). Only 12% of patients with negative prognostic factors live longer than one year.

The main prognostic factors are age, sex, tumor subtype, and tumor stage. Patients with epithelioid tumors have a relatively favorable prognosis, as do women and patients who are under age 75 when the diagnosis is made.

Another clinically relevant prognostic factor (3) is the Karnofsky score, a rating of the patient's symptom-related restriction of activities, ability to care for himself or herself, and autonomy, on a scale of 0 to 100.

Other prognostic factors are of use solely for the purposes of clinical research (low hemoglobin content, high LDH level, or high leukocyte and platelet count). Potential serum markers, e.g., soluble mesothelin or osteopontin, are now being studied but cannot currently be used for valid prognostication (3).

Treatment

Mesothelioma is a rare cancer that is best treated in specialized centers offering state-of-the-art care with either curative or palliative intent, as well as pain control. In such centers, oncologists, radiologists, and surgeons should closely cooperate and coordinate their patients' care in regularly scheduled meetings. Specialized centers also generally participate in clinical trials and enter their patients into disease registries.

The goals of treatment for cancer are to prolong life and to improve the quality of life. The current treatments for mesothelioma are only partly successful at meeting these goals. No cure is now available.

Palliative care is appropriate in situations where the following criteria are met:

- poor general condition and nutritional state
- biphasic or sarcomatoid mesothelioma (any stage)
- stage 3 or 4 epithelioid mesothelioma
- N2 stage and/or M1 stage.

For palliative treatment, thoracoscopy with pleurodesis can be used to control symptomatic pleural effusions and lessen pain. Recurrent pleural effusions can be treated by talcum pleurodesis with 93% efficacy (19).

Multimodal strategies for treatment with curative intent are currently being pursued. Little evidence is available to date indicating which treatment combinations are best for which types of patients (3).

Treatment with curative intent is appropriate in situations where the following criteria are met:

- the patient is under 70 years old
- no appreciable cardiopulmonary compromise
- no relevant accompanying disease
- epithelioid mesothelioma (stage 1 or 2)
- N0 situation (mediastinoscopy).

In the following sections, we will discuss only robust treatment modalities that have demonstrated their reliability and for which the available evidence from clinical trials is good enough for them to be mentioned in clinical guidelines *(Table 2)*. There is no room here for an additional discussion of little-tested or experimental approaches.

Surgery

The goal of surgery is gross total resection of the tumor. As mesotheliomas tend to grow diffusely, they are usually not totally resectable; some residual tumor tissue (often microscopic) is generally left behind. Adjuvant chemotherapy is given achieve elimination of remaining tumor cells (20).

Pleurectomy/decortication

Pleurectomy and decortication with en bloc resection of the parietal and visceral pleura is an effective method of preventing pleural effusion (20). It is a suitable means of symptom control for patients who cannot benefit from pleurodesis, in particular those with a lung that cannot expand adequately ("trapped lung syndrome") because of fibrotic changes, of either neoplastic or inflammatory origin, that restrict the mobility of the visceral pleura and can cause it to adhere to the parietal pleura. Pleurectomy/decortication has a lower mortality (1.5%–5%) than extrapleural pleuropneumectomy, and patients recover from it more rapidly. There is an increased risk of local recurrence after this procedure (2.5%–5.9%); a significant effect on median survival (10 to 17 months) has been observed, but there is no significant effect on long-term survival (21).

Extrapleural pleuropneumectomy (EPP)

This procedure involves resection of the lung, the pleura, the pericardium, and the diaphragm and should only be performed in highly specialized centers in trials of multimodal treatment. The mortality of this highly invasive procedure can be held down to 3.4%–10% in experienced centers, but its morbidity can be as high as 50%, and complications often necessitate a second procedure (20). EPP provides no advantage in terms of survival rates, even in the setting of multimodal treatment (22). The reported rates of local recurrence after EPP vary widely, from 0% to 37% (3, 23, 24).

Chemotherapy

A path-breaking publication from the year 1999 (25) and multiple studies thereafter (26, 27) showed that chemotherapy with cisplatin and pemetrexed can be effective. Randomized therapeutic trials are difficult to organize because case numbers are small. One such trial of chemotherapy versus placebo did not reveal any significant effect on survival times (28). No randomized trials of chemotherapy as a second line of treatment have been performed to date, although the available evidence to date does suggest that

TABLE 2

Overview of treatment studies for malignant pleural mesothelioma

Treatment	n	Study design	MST (months)	Type of intervention	Study
Pleurectomy/decortication (P/D)	44	retrospective cohort	17.2 8.1 6.8	P/D total, n = 10 P/D subtotal, n = 34 exploratory biopsy, n = 22	Schipper 2008 (e17)
	102	cohort	15.3 7.1	radical P/D, n = 51 non-radical decortication, n = 51	Nakas 2008 (e18)
	79	retrospective	13.9 4.2	VATS P/D, n = 51 exploratory biopsy, n = 28	Halstead 2005 (e19)
	165	prospective	13.4 14.7	P/D and CH, n = 67 EPP and CH, n = 98	Nakas 2012 (e20)
	65	retrospective cohort	17.0 13.0	P/D, n = 34 EPP, n = 31	Okada 2008 (e21)
	3,152	review (32 studies)	14.5 4.5	P/D supportive care	Maziak 2005 (e22)
	54	retrospective cohort	14.0 7.0	P/D and CH, n = 47 supportive care, n = 7	Aziz 2002 (e23)
Extrapleural pleuropneumectomy (EPP)	29	pro-/retrospective cohort	19.5	EPP and adjuvant CH, n = 29	Ambrogi 2012 (e24)
	111	retrospective cohort	13.0 14.0	EPP and CH, n = 64 P/D and CH, n = 47	Aziz 2002 (e23)
	663	retrospective	12.0 16.0	EPP, n = 385 P/D, n = 278	Flores 2008 (e25)
	49	cohort	12.5	EPP alone or with neo-/adjuvant CH, n = 49	Aigner 2008 (e26)
	70	prospective	20.0	EPP and neo-/adjuvant CH or RA, n = 70	Yan 2009 (e27)
	50	randomized multicenter	14.4 19.5	EPP with inductive CH and postop. RA, n = 24 inductive CH without EPP, n = 26	Treasure 2011 (e28)
	179	cohort	11.5 14.0	EPP, n = 112 VATS decortication, n = 67	Nakas 2008 (e29)
Chemotherapy (CH)	173	non-randomized phase II	13.0	CH with carboplatin, doxorubicin, and gemcitabin, n = 173	Hillerdal 2008 (e30)
	448	randomized phase III	9.3 12.1	CH with cisplatin, n = 222 CH with cisplatin and pemetrexed, n = 226	Vogelzang 2003 (e31)
	161	retrospective	11.3 8.0	CH with cisplatin, gemcitabin, mitomycin C, interferon alpha 2, n = 109 supportive care only, n = 52	Metintas 2007 (e32)
	250	randomized phase III	8.8 11.4	CH with cisplatin CH with cisplatin and raltitrexed	van Meerbeeck 2005 (e33)
	126	retrospective	16.7 15.3	CH with pemetrex alternative CH	Knuuttila 2012 (e34)
	273	randomized multicenter controlled study	7.6 8.5	active symptom control, n = 136 active symptom control and CH with mitomycin/ vinblastine/cisplatin, n = 137	Muers 2008 (e35)
Radiotherapy (RA)	100	retrospective	10.2 14.2	all patients with EPP, n = 100 only patients with EPP and RA (IMRT), n = 64	Rice 2007 (e36)
	16	retrospective	17.0	RA (IMRT) and inductive CH with cisplatin and pemetrexed	Rosenzweig 2012 (e37)
	57	prospective	33.8 10.0	stage I and II disease stadium III and IV disease RA after EPP (n = 54) or P/D (n = 3)	Rusch 2001 (e38)
	123	retrospective	13.5	adjuvant RA (42.5 Gy) after P/D	Gupta 2005 (e39)
Multimodal treatment	36	prospective	24.0	P/D, hyperthermic pleural lavage, CH, RA	Lang-Lazdunski 2011 (e40)
	25	prospective	12.8	neo-adjuvant CH, EPP, RA	Bille 2012 (e41)
	183	retrospective	19.0	EPP, adjuvant CH, and RA, n = 183	Sugarbaker 1999 (e42)
	40	prospective phase II	29.1	neo-adjuvant CH with pemetrexed/cisplatin, EPP, RA, n = 40	Krug 2009 (e43)
	37	prospective phase II	33.0	inductive CH with cisplatin, pemetrexed, EPP, adjuvant RA, n = 37	van Schil 2010 (e44)
	36	prospective multicenter	23.0	neo-adjuvant CH with cisplatin, gemcitabin, EPP, RA, n = 36	Weder 2007 (e45)
	21	retrospective	23.2	CH, EPP, RA (IMRT), n = 21	Patel 2012 (e46)
	33	retrospective	30.0	pleurectomy, CH with cisplatin, pemetrexed, RA, n = 33	Bölükbas 2011 (e47)

CH, chemotherapy; RA, radiotherapy; EPP, extrapleural pleuropneumectomy; P/D, pleurectomy/decortication; n, number of patients; MST, median survival time in months; VATS, video-assisted thoracoscopy; IMRT, intensity-modulated radiotherapy

second-line treatment can prolong survival more than symptom control alone (29). Decisions about chemotherapy should be made individually for each patient after the physician has discussed the matter thoroughly with the patient and his or her family, who must be clearly told that the efficacy of treatment is limited. Only patients with a Karnofsky performance status above 60% are candidates for chemotherapy. Palliative chemotherapy may be indicated for patients with rapid tumor progression or severely limiting symptoms (30).

Radiotherapy

Patients with mesothelioma are given prophylactic radiotherapy at puncture sites and after surgical interventions to prevent local recurrence and to relieve pain in palliative care. Radical radiotherapy of the entire tumor is not currently feasible, because these tumors tend to grow in a complex geometrical configuration, and the resultingly high radiation load of treatment would be likely to cause collateral damage to the heart and lungs (24).

Prophylactic radiotherapy after decortication/pleurectomy is not recommended in the guidelines (3), which do, however, state that radiotherapy can be given after EPP in a clinical-trial setting. Radiotherapy for pain relief should be discussed with patients who have chest pain and infiltration of the chest wall (3).

Multimodal approaches

Multimodal treatments involve surgery combined with chemotherapy and, in some cases, radiotherapy. In one trial, neo-adjuvant chemotherapy combined with pleuropneumectomy and followed by radiotherapy led to a higher average 3-year survival rate than unimodal treatment (76 %) (31) and prolonged the median survival time (22 months for stage I) in another study (32).

Clinical trials are now underway to assess the possible benefit of combining cytoreductive pleurectomy with intraoperative hyperthermic chemotherapy, a procedure in which the temperature is raised to 42°C to increase the tissue penetration of chemotherapeutic drugs and thereby potentiate their effect.

Screening methods

Attempts to detect mesothelioma early with serum markers (33), high-resolution CT (HRCT), or PET have not yielded any clinical breakthroughs to date (34, 35). Pleural ultrasonography is less sensitive than CT and is thus unlikely to be of additional use for early detection (11, 36). Because of the low prevalence and poor prognosis of mesothelioma and the limited therapeutic options for it, as well as the less than ideal sensitivity of the putative screening methods proposed to date, there is as yet no validated method for the early detection of this disease, even if performed repeatedly at close intervals (3).

A more detailed discussion of the diagnosis and treatment of mesothelioma and of the pertinent insurance aspects can be found in the international guidelines of the ERS/EST Task Force (3) and the Mesothelioma Interest Group (37), as well as the Falkenstein recommendations of the German Social Accident Insurance (DGUV) (38) and the S2 guideline of the Association of Scientific Medical Societies in Germany (AWMF) (39).

Mesothelioma from the viewpoint of occupational health

The diagnosis of mesothelioma must always arouse the suspicion of an occupational disease. According to German law (§202 SGB VII), the physician is required to report a suspected occupational disease in such cases, even if the patient has no recollection of being exposed to asbestos in the workplace. In view of the fact that the latency of disease can be as long as 60 years, the patient's occupational history must be taken by an appropriately trained person in a qualified and comprehensive manner. It must be borne in mind that mesothelioma can also be caused by short-term, low-level exposure (40, e1) *(eBox)*.

Taking an occupational history from an elderly and (often) multimorbid patient can be difficult but may be facilitated by the use of a catalogue of photographs of workplaces in which workers historically received intense exposure to asbestos (Questionnaire of the Munich Tumor Center, [e2]).

Asbestos is still being used commercially in the newly industrialized countries of Asia, and the incidence of mesothelioma there can be expected to rise. Only a worldwide prohibition of asbestos use (e3) can prevent a further rise in the number of victims.

Countries that produce asbestos and/or use it for industrial purposes should be compelled by international pressure to cease these activities. In particular, attempts by industry lobbyists to cast doubt on the carcinogenicity of white asbestos (chrysotyle)—particularly with respect to lung cancer—should be contradicted in the scientific discussion (e4).

Conflict of interest statement

Dipl.-Biol. Neumann, Dr. Löseke, Prof. Nowak, and Prof. Tannapfel have served as paid medicolegal consultants for casualty insurance carriers for the pathological diagnosis of mesothelioma and the determination of a causal link to asbestos exposure in individual cases.

Prof. Herth states that he has no conflict of interest.

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KEY MESSAGES

- Malignant diffuse mesothelioma—a reportable occupational illness—can be induced by relatively brief and low-level exposure to asbestos.
- A pertinent occupational history should be obtained from the patient by a person who has been appropriately trained to do this in accordance with expert recommendations.
- The diagnosis of mesothelioma is best confirmed by biopsy. Tissue samples are best obtained either in a CT-guided semi-invasive procedure or by open surgery.
- The gold standard for the diagnosis of mesothelioma is histopathology combined with immunohistochemical analysis.
- This disease still confers a poor prognosis. The currently available multimodal treatments should be performed only in specialized centers.

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Corresponding author
Dipl.-Biol. Volker Neumann
Deutsches Mesotheliomregister am Institut für Pathologie
der Ruhr-Universität Bochum am Berufsgenossenschaftlichen
Universitätsklinikum Bergmannsheil
Bürkle-de-la-Camp-Platz 1
44789 Bochum, Germany
Volker.Neumann@ruhr-uni-bochum.de

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REVIEW ARTICLE

Malignant Pleural Mesothelioma

Incidence, Etiology, Diagnosis, Treatment, and Occupational Health

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eBOX

The use of asbestos in Germany

"Asbestos" is a commercial term referring to different types of naturally occurring mineral fibers (chrysotile ["white asbestos"] and various types of amphibole asbestos [crocidolite, amosite, anthophyllite, actinolite, tremolite]) that share certain physical properties: non-inflammability, high resistance to heat, flexibility, suitability for weaving, and other properties. This combination of special properties led to asbestos being called, in the past, "a mineral of a thousand uses"—a designation that can only be used ironically today in view of the carcinogenicity and fibrogenicity of these substances, which have led to millions of cases of fatal disease.

In Germany, the commercial use of asbestos reached a peak from 1968 and 1977 (200 000 tons per year) and has been forbidden since 1993. It has been forbidden in the European Union since 2005. Around the world, however, asbestos is still extensively used in industry, and 2 million tons of it are produced every year.

Is there an asbestos dose threshold for mesothelioma?

Ongoing debate surrounds the issue of a putative threshold value that needs to be exceeded for a mesothelioma to be induced. Even though the risk of mesothelioma is thought to be dose-dependent (e5), there is nonetheless no borderline value below which the risk of mesothelioma can be considered to be zero.

Despite the reduction of exposure in Germany (500 fibers per cm^3 inhaled air in the 1950s, compared with less than 1 fiber per cm^3 since the definitive prohibition of asbestos in 1993) and the resulting reduction of the pulmonary asbestos load (8), the continuing rise in the incidence of, and mortality from, mesothelioma has not yet been stopped.

Non-asbestos-related mesothelioma

The percentage of mesotheliomas that are not associated with asbestos varies widely from study to study but is generally estimated at 10% to 20% (e5). Other than by asbestos, mesotheliomas can also be induced by zeolite (erionite), another type of asbestos-like mineral fiber. Moreover, research findings suggest a role for further mesothelioma-inducing factors (SV-40 viruses, recurrent infection, genetic predisposition) (e6). Current research also focuses on the question whether innovative nanomaterials (nanotubes) might also be carcinogenic and induce mesotheliomas (e7).