II. 研究成果の刊行に関する一覧表

《H. 20年度　雑 誌》

発表者氏名 *連絡先著者	論文タイトル名	発表誌名 (最新Impact Factor)	巻号	ページ	出版年	備 考
名取雄司	電話相談から見た石綿関連肺ガンの報告	肺癌				受理印刷中
Nishikawa K, Takahashi K*, Karjalainen A, Wen C-P, Furuya S, Hoshuyama T, Todoroki M, Kiyomoto Y, Wilson D, Higashi T, Ohtaki M, Pan G, Wagner G	Recent mortality from pleural mesothelioma, historical patterns of asbestos use and adoptions of bans: a global assessment	***Environron Health Perspect*** (IF=5.64)	116(12)	1675-1680	2008	【原著】本研究費を得た成果物であることを明示
高橋 謙	諸外国でのアスベスト中皮腫	臨床検査	52(9)	1023-1027	2008	
長尾典尚, 西川晋史, 清本芳史, 轟美和子, 寶珠山務, 高橋 謙*	石綿外来・石綿健診の全国実態—実施医療機関を対象とした質問票調査結果報告—	産衛誌	50	145-151	2008	本研究費を得た成果物であることを明示
高橋 謙	「第18回世界労働安全衛生会議」参加報告	産業医学ジャーナル	31(6)	49-51	2008	
高橋 謙	世界のアスベスト疾患の実態と将来予測	衆議院調査局環境調査室編,石綿関係法施行状況調査報告書	N.A.	15-19	2008	

《DVD》

著作権者 (事務局・編集責任者)	タイトル	発表年	備考
産業医科大学(環境疫学研究室・高橋 謙)	石綿疾患対策専門家向け基礎研修用ビデオ	2008	本研究費を得た成果物であることを明示

《H.20年度 学会発表 -Proceedings・抄録等印刷を含む》

発表者氏名	発表タイトル名	学会名（開催地名）	発表年月日	備考
Takahashi K	Asia is Missing Out on Too Many Mesothelioma Cases	International Workshop on Health Effects and Safety in Use of Asbestos and MMVF (Beijing, China)	2008.10.29-31	Keynote Lecture; Proceedings, pp.50-51.
Takahashi K	Asbestos and Dust-Related Diseases in the Asia Pacific Region	The 19th Asian Conference on Occupational Health (Singapore)	2008.09.17-19	Keynote Lecture; Proceedings, pp.29-30
Takahashi K	Global Mortality of Asbestos Diseases - Implications for Asian Countries	XVIII World Congress on Safety and Health at Work(Seoul, Korea)	2008.06.29-07.02	ILO Symposium（招待）Abstracts, pp.122-123.

Ⅲ．研究成果の刊行物・別冊

電話相談から見た石綿関連肺ガンの報告

名取　雄司[1,2]

[1] 医療法人社団ひらの亀戸ひまわり診療所　呼吸器内科
[2] 中皮腫・じん肺・アスベストセンター

要旨−私達は、石綿に関する健康・建材・環境の電話相談を行うNPO「中皮腫・じん肺・アスベストセンター」を2003年に設立し、健康相談では毎年100〜500件の相談を受けてきた。石綿関連肺ガンは相談が急増しているが石綿曝露との関連が十分認識されていない疾患である。石綿関連肺ガンの診断には問診が重要で、石綿製品の知識、特に建築業での石綿含有建材の知識、世界の石綿肺ガンの規準の理解が欠かせない。そのため、国土交通省・経済産業省の建材データベースによる石綿含有建材、世界の石綿肺ガンの規準の変遷、標準的な石綿関連疾患の診断指針であるヘルシンキ・クライテリアを紹介した。石綿関連肺ガンでは石綿小体数の測定も重要で、様々な職業・家族・環境・建物・対照群の曝露に応じた石綿小体数の結果を示した。建築他の白石綿（クリソタイル）曝露を主にした石綿肺ガン事例が増加しており、石綿曝露を繊維・年数で考える典型例を示した。最後に、石綿則健診、石綿健康管理手帳、環境の石綿肺ガン対策の、意義と問題点を指摘した。

索引用語　肺ガン、石綿小体、建築、白石綿、繊維・年数

1. 初めに

私達は1985～1989年に横須賀共済病院呼吸器科に勤務、1989年～現在まで横須賀中央診療所で造船所退職者の石綿関連疾患の健診と治療を、1996年から東京の亀戸ひまわり診療所で石綿関連疾患の診察治療を行う一方、石綿粉じん軽減の安全衛生に関する産業衛生活動を推進してきた。

2000年頃から全国の石綿関連疾患の患者・家族からの電話相談が増加したため、2003年に石綿に関する健康・建材・環境の電話相談を行う民間NPO団体「中皮腫・じん肺・アスベストセンター」を亀戸で設立した。2003～2007年の間、健康相談に限定すると毎年約100～500件の相談を受けてきており、相談内容は年で異なるが、肺ガン健診との関連を考慮して述べる。

2. 年度別の相談内容の変遷

2005年以前は相談窓口自体が少なかった時期で、全国のあらゆる種類の石綿相談、のかなりの部分を担当していたと思われる。石綿製造業・造船所・建築業に勤務した本人やご家族が、中皮腫の治療の相談で泣きながら電話してくることも多く、労災補償の相談でも会社が印をおさず受けられない、監督署担当者が石綿製品自体を知らず認定されないという、現在では考えられないような基本的相談が主に年間200件前後あり、肺ガンの相談はまだ稀であった。

NPOのHPに石綿関連疾患の基本的知識と、写真で石綿製品を解説するページを開設

(http://www.asbestos-center.jp/asbestos/byphoto/index.html)、書籍でも紹介に努めた[1,2,3]。基本的相談自体で全国各地に出張せざるをえず、古くから造船所や石綿工場のあった神奈川、広島、岡山、関西と他の都道府県との間で、医療、監督署を含めた行政、相談NPOの体制の地域差を感じた時期であった。2005年以降に関連する建物、工場周囲の中皮腫の相談が見られた。

2005年のクボタショックであらゆる相談が殺到し、健康相談も500件とピークを迎えた。胸膜肥厚斑のX線診断、中皮腫の病理診断に関する相談が多かった時期であるが、肺ガンの相談が増加し始め、リスクに応じた肺ガン健診などをどうしたらよいかという相談が増加し、HPでの解説を追加した。

(http://www.asbestos-center.jp/environment/qanda.html)

報道により石綿・中皮腫・石綿関連肺ガン・胸膜肥厚斑という言葉と労災補償など制度が、多くの国民に認知されるようになったことは、長

く石綿関連疾患に取り組んできた関係者にとり大きな成果で、国民レベルでのリスク認識の転換点となったと思われる。

2006年は、2月に労災保険の中皮腫・石綿肺ガンの認定規準の変更、3月に石綿新法の施行と、労災補償分野においてじん肺法制定以降初めての大きな法的変化が起きた年であった。中皮腫の相談では胸膜肥厚斑のX線診断が皆無となり相談例数は減少し始め、内容も低濃度曝露で稀な職業や建物、環境事例が増加し始めた。肺ガンの相談は増加する傾向が見られ、労災病院、監督署、保健所などを始めとした様々な団体での相談窓口の増加を反映して基本的な相談が減少し、既にどちらかに相談した後の、対応が複雑な相談が増加した。

2007年も同様の傾向だが、中皮腫と肺ガン合計で年間100件弱の相談が続いており、肺ガンの相談が中皮腫に近付きつつある。環境再生保全機構での中皮腫の病理診断の定着を反映して、中皮腫の病理診断に関する相談は減少し内容が複雑化した。肺ガンの相談は増加しているが、胸膜肥厚斑はなく石綿小体も少ない白石綿（クリソタイル）曝露のある産業での相談が増加してきた。

3. 中皮腫・石綿肺ガンの補償・救済率

2006年度統計では、労災補償で中皮腫1,006名、肺ガン790名、石綿新法の労災時効で中皮腫569名、肺ガン272名、生存で中皮腫627名、肺ガン172名となり、以前と比し著増で、関係者の努力の賜ものであることを感謝する。

過去の日本の中皮腫の死亡者数は、ICD10が適用された1995年以降は人口動態統計の「C45：中皮腫の死亡者数」となるが、ICD9が適用された1979～1994年の中皮腫は主に「163　胸膜のその他の悪性腫瘍」内に含有される統計のため一定の係数を乗じることがある。

古谷は、1978年以前の中皮腫の推計には過去の石綿使用170トンあたり1人と仮定、1979～1994年は「163胸膜のその他の悪性腫瘍」に係数1を乗じ、1995年以降は人口動態統計C45の死亡者数で、2006年以前の日本の中皮腫死亡者総数は12,669名と推計している。中皮腫の2倍とされる石綿肺ガンは25,338名と推計している[4]。

中皮腫の2006年までの労災補償は合計2,011名、石綿新法による労災時効救済が569名、石綿新法による救済が2,165名、合計4,745名で過去の死亡者推計12,669名の37.5%が救済・補償されたこととなる。石綿肺ガンは2006年までの労災補償は合計1,363名、石綿新法による労災時効救済が272名、石綿新法による救済が224名で、合計1,859名で過去

の死亡者推計数25,338名の7.3%のみが救済・補償されたこととなる（**表1**）[4]。中皮腫と石綿肺ガンの認識に関しては、2005年以降劇的な変化がおきているが、救済及び補償は十分進んでいない現状にあり、特に石綿肺ガンが問題となっていることを認識しておかねばならない。

4. 石綿製造業、造船業、建築業で使用した石綿の種類について

戦前から白石綿の使用が多かった石綿だが、石綿製造工場、造船所では茶石綿（アモサイト）や青石綿（クロシドライト）も使用され、過去の石綿の健康障害ではこの2つの産業の比率が高かった。

石綿製造業は、石綿紡績、石綿工業製品、石綿セメントの主要3業種からなり、年度、工場毎に使用石綿の種類は異なるが、戦中は各種の再生石綿使用が広く行われたことが知られている。大手造船所では保温材やボードに茶石綿が、1955年以降青と茶の吹き付け石綿が広範に使用されており、主に白石綿の使用は漁船などを製造する小造船所に限定されている。

建築業は戦前から白石綿の石綿スレート製品が限定的に使用され、1950年代から使用範囲が増加、1970年代以降極めて広い範囲で使用されるに到った。現在の石綿障害予防規則（略称石綿則：いしわたそく）は建築などの作業基準を厳しい順にレベルⅠからⅢと定めている。レベルⅠ作業は野丁場（のちょうば・ビルや工場など）が主で対象は吹き付け石綿（白・青・茶）、吹き付け岩綿（1961～1980年、白・青・茶）、湿式吹き付け岩綿（1970～1987年、白）、吹き付けひる石（1965～1988年，不明）、吹き付けパーライト（1971～1989年、白）などである。レベルⅡ作業も野丁場が主で煙突材（1964～1991年、白・茶）、保温材（1940～1987年、茶）、耐火被覆板（1966～1983年、白・茶）、けい酸カルシウム板第2種（1965～1990年、白・茶）が対象である。レベルⅢ作業は街場（まちば）と野丁場で珪酸カルシウム板（茶）と1970年代の一部の建材（青・茶含有で、現在製品割合調査中）を除き白石綿が主な石綿製品だった。現在の国土交通省・経済産業省の建材データベースは完成版とは言えないが、（http://www.mlit.go.jp/kisha/kisha06/07/071213_.html）最も網羅されたもので、吹き付け石綿と珪酸カルシウム板などと一部の建材を除き白石綿が主な石綿であることがわかる（**表2**）。石綿の種類で中皮腫の発症に差が生じるとされるが、肺ガンに関する石綿の種類の差は少なく、今後建設業での石綿肺ガンが問題となる。

5. 世界の石綿肺ガンの考え方の変遷

1982年に、イギリス連邦産業疾患アドバイサリ会議議会報告書は「33石綿の職業性曝露は、明確な石綿肺がなくても肺ガンを発症する」とし、その後多数の研究と文献レビューが、閾値がない累積曝露量モデルを支持、肺ガンの相対危険度＝1＋K_L（肺ガンの係数）×石綿の累積曝露量とする考え方が定着する[5]。1992年に西ドイツは職業性疾患ドイツ規定を変更、石綿関連肺ガンの規準は25繊維・年数の作業環境の石綿累積曝露量であると改変した。3つの主な石綿作業である、石綿セメント、石綿紡績、石綿断熱作業がドイツにおける職業性曝露の重要なパターンを反映、一般人口と比較し2倍の肺ガンリスクが25繊維・年数の累積曝露量と関係したからである。西ドイツの肺ガン補償患者数は1992年の223名から1994年に545名と増加し中皮腫認定を凌駕、1999年は中皮腫617名に対し石綿関連「肺ガンと喉頭癌」は776名と1.26対1の比率となった[5]。

6. ヘルシンキ・クライテリアと現在まで

1997年に石綿関連疾患の診断基準としてヘルシンキ・クライテリアが定められ[6]、職業性曝露の石綿小体数は1,000本/1g乾燥肺以上、石綿肺ガンは以下の(1)～(4)と定めた。

（1）1年の高濃度石綿曝露（石綿製品製造・石綿吹き付け・石綿製品の断熱作業・古い建築物の解体）及び5～10年の中等度石綿曝露（造船や建築）は、肺ガンの危険度を2倍以上とする。

（2）肺ガンの相対危険度は、累積曝露量（石綿繊維×曝露年数）が増加する毎に（中略）増加する。25繊維×年数の累積曝露量は肺ガンの危険度を2倍にすると予測される。

（3）2倍の肺ガンの危険度は（中略）、乾燥肺組織1gあたりほぼ5,000～15,000本の石綿小体、気管支肺胞洗浄液1mlあたり5～15本の石綿小体に匹敵する。

（4）白石綿繊維は、クリヤランス速度が速いために、アンフィボール繊維と同程度には、肺組織内に蓄積されない。ゆえに、肺内組織分析より職歴（繊維数×曝露年数）の聴取が、白石綿による肺ガンの危険度のよい指標となる。

2000年10月オーストラリアが定めたAWARD (Adelaide Workshop on Asbestos-Related Diseases)規準も一部異なるが同等の考えによる[5]。2004年にヘルシンキ・クライテリア以降の推移をまとめたAFTER HELSINKI論文[5]がだされ、現在、ドイツ、オーストリア、ベルギ゛ー、ス

カンジナビア4国、フランス、オランダ、オーストラリア、スイスが25繊維・年数の考え方で肺ガンの労災認定を行っている[5]。ヘルシンキ・クライテリア以降の考え方が今後日本で普及することになると思われる。

7. 様々な曝露による石綿小体数

1985～2007年の間実施してきた、様々な石綿曝露形態での石綿小体数の結果を示した(**図1**)[7]。青石綿・茶石綿曝露も多い、大造船所のあらゆる疾患の連続剖検例 72 名の職業性曝露群(図 1－⑫)の石綿小体数は1,000本/1g乾燥肺以上で、石綿曝露(職業及び工場周囲などの環境曝露)のないコントロール群20名（図1-①）は35±44本／乾燥肺1gであった[8]。白石綿主体の職業性曝露の肺ガン（同⑨）と中皮腫（同．⑧）、造船所の家族曝露中皮腫2名（同⑥）、青石綿工場周囲の環境曝露の中皮腫8名（同③＋④）、青石綿の建物曝露の中皮腫 2 名（同②）の石綿小体は両群の中間であった[9-12]。ヘルシンキ・クライテリアは、職業性曝露の石綿小体数は1,000本/1g乾燥肺以上とし、また白石綿繊維はクリヤランス速度が速く肺組織内に蓄積されず、肺内組織分析より職歴（繊維数×曝露年数）の聴取が肺ガンの危険度のよい指標としているが、今回の結果も同様で、世界の石綿肺ガンの考え方と一致している。

8. 石綿肺ガンの典型的な事例

私達が相談に応じてきた石綿肺ガンの典型的なケースを紹介する[12]。

59歳の男性、左上葉の肺小細胞癌で発症時T2N2M0にて化学療法と放射線療法を受けたが2003年に永眠、剖検されたが石綿肺や胸膜肥厚斑は認めなかった。職歴は18～59歳の間で、元々板金工だが屋根工やサイディング工の作業比率が増加、I社製サイディング(通常白石綿だが不明)、K社製サイディング（白石綿）、K社製屋根材（白石綿）、S社製屋根材「X－U」（白石綿が主で一部茶石綿の時期あり）、石綿煙突（白石綿）を使用してきた。喫煙歴は40本／日×37年だった。光学顕微鏡の石綿小体は33本／乾燥肺1g（定量下限11本／1g）で、電子顕微鏡の石綿線維数は0.55×百万本／乾燥肺1gで全て白石綿であった。

建築肺ガンの事例で白石綿が主の曝露の場合、石綿小体も胸膜肥厚斑もともにない場合も多くみられ、詳細な職業性曝露の聴取が重要とされ[14]、当事例も詳細な職業歴聴取後に労災として認定された。問診などを元に、作業年を同種作業の論文[15-19]から石綿濃度を求め、石綿繊維・年数を算定し25繊維・年数を超えた結果を(**表3**)に示した。石綿肺ガンでは、胸膜肥厚斑、石綿小体の確認も重要だが、今後は産業医学的な考え

方が重要となる典型的な事例と思われる。

9. 臨床での石綿肺ガンの診察の際に

石綿の製品と産業を知る目的で、中皮腫肺ガンの臨床医・産業医向けに作成されたもので、**厚生労働省「石綿ばく露歴把握のための手引ー石綿ばく露歴調査票を使用するに当たってー」**[20]が知られている。（http://www.mhlw.go.jp/new-info/kobetu/roudou/sekimen/roudousya2/index.html）石綿関連産業と職種を全て網羅している訳ではないが、豊富な写真と作業が提示され臨床に1冊必要な内容と思われる。

過去の石綿曝露は、胸膜肥厚斑・肺ガン患者から学ぶことが必要で、中皮腫はもちろん肺ガン患者に職歴や家族歴や居住歴を必ず実施していくことが重要である。特に石綿曝露が不明の場合の胸膜肥厚斑の十分な調査は必須で、新たな曝露を知る最もよい機会でもあり、これをルーチンにしていくだけで問診の力量が飛躍的に上昇する。それでも不明の際は詳しい機関へ相談し解決することが望ましい。中皮腫や胸膜肥厚斑のある同僚や近隣住民がいないか問診で確認することも、今後石綿肺ガンを考える場合に重要な参考となる。

胸膜肥厚斑の出現率は、X 線レベル、CT レベル、手術剖検レベルで異なるが、石綿曝露がある者に必ず出現する疾患ではなく、石綿曝露があっても胸膜肥厚斑が手術や剖検でないことはしばしば認められている[7]。

10. 就業者対策の石綿則と同健診

石綿作業に労働者を勤務させている企業は、原則として年2回の石綿則健診を実施しなければならない。石綿則健診を実施していない産業や企業は現在も数多くあり、健診を実施する産業と企業が今後拡大することが望まれる。2005 年以前は石綿則でなく特定化学物質等障害予防規則（略称特化則）が石綿作業を法律的にカバーしていたが、その時期にも特に石綿製造業以外の産業で特化則健診がほとんど実施されなかった苦い過去がある。監督署は石綿則健診の実施産業と企業の確認を行い、未実施企業に対し十分な監督を実施することが望まれる。

石綿則健診は、現在 10～20 代及び石綿作業従事歴 10 年以内の人を含め、作業従事者全員に毎年 2 回実施されている。X 線被爆の問題と潜伏期を考慮すると、今後就業時健診は全員に施行し、その後は 40 歳以上かつ曝露 10～20 年以上の者を対象として、年2回実施するよう規則の変更が望まれる。

中皮腫の腫瘍マーカーは、開発状況に応じ石綿則健診・手帳で利用す

ることが必要となる。石綿則従事者講習は現在講義を聞く座学のみで作業につけるが、実地を知らない業者の参入が飛散事故時の問題となっており、今後実地講習の追加も必要である。

11．退職者対策の石綿健康管理手帳

2007年10月、石綿健康管理手帳の交付対象が変更され、医療機関も認可制から届け出制に変更された。石綿肺・胸膜肥厚斑という医学所見でなく石綿曝露年数で手帳を支給する考え方は、発癌物質への対策として適切で、医療機関届け出制への変更も適切であった。今後は手帳を交付する産業と曝露年数などで、過去の石綿曝露に応じた柔軟かつ適切な運用が望まれる。

12．環境などにおける石綿肺ガン対策

尼崎での十分な石綿肺ガン調査の実施が重要だが、環境省委員会は肺ガン調査の中止を決定したとされ今後の禍根として懸念される。環境肺ガンの確実な調査の実施が日本で必要で、工場周囲の環境石綿肺ガンと一般大気中の石綿繊維による肺ガン発症への寄与の２つが想定される。今後環境石綿健康管理手帳の交付が本来必要で、建物や家族による石綿肺ガンとその適切な健康管理は今後の課題である。

13．まとめ

１）石綿関連肺ガンの診断には曝露歴聴取が重要で、「石綿ばく露歴の把握のための手引」が参考となる。

２）石綿肺ガンの診断には、石綿小体、繊維、胸膜肥厚斑が現在も重要だが、白石綿曝露の石綿肺ガンの場合は補助的な役割になる。曝露歴中心主義への転換が欧米同様必要で、産業医学的発想が今後重要となる。

３）石綿則健診は今後実施企業の拡大とともに、石綿肺ガン健診のエビデンス、中皮腫腫瘍マーカーの開発と利用が望まれる。

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Recent Mortality from Pleural Mesothelioma, Historical Patterns of Asbestos Use, and Adoption of Bans: A Global Assessment

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BACKGROUND: In response to the health risks posed by asbestos exposure, some countries have imposed strict regulations and adopted bans, whereas other countries have intervened less and continue to use varying quantities of asbestos.

OBJECTIVES: This study was designed to assess, on a global scale, national experiences of recent mortality from pleural mesothelioma, historical trends in asbestos use, adoption of bans, and their possible interrelationships.

METHODS: For 31 countries with available data, we analyzed recent pleural mesothelioma (*International Classification of Diseases, 10th Revision*) mortality rates (MRs) using age-adjusted period MRs (deaths/million/year) from 1996 to 2005. We calculated annual percent changes (APCs) in age-adjusted MRs to characterize trends during the period. We characterized historical patterns of asbestos use by per capita asbestos use (kilograms per capita/year) and the status of national bans.

RESULTS: Period MRs increased with statistical significance in five countries, with marginal significance in two countries, and were equivocal in 24 countries (five countries in Northern and Western Europe recorded negative APC values). Countries adopting asbestos bans reduced use rates about twice as fast as those not adopting bans. Turning points in use preceded bans. Change in asbestos use during 1970–1985 was a significant predictor of APC in mortality for pleural mesothelioma, with an adjusted R^2 value of 0.47 ($p < 0.0001$).

CONCLUSIONS: The observed disparities in global mesothelioma trends likely relate to country-to-country disparities in asbestos use trends.

KEY WORDS: asbestos, asbestos-related diseases, ban, epidemiology, lung cancer, mesothelioma, mortality, occupational cancer, pleural mesothelioma. *Environ Health Perspect* 116:1675–1680 (2008). doi:10.1289/ehp.11272 available via *http://dx.doi.org/* [Online 14 August 2008]

The world is steadily retreating from dependence on asbestos. In 2006 the International Labour Organization (ILO 2006) and World Health Organization (WHO 2006a) jointly declared that the most efficient way to eliminate asbestos-related diseases is to stop using all types of asbestos. Nevertheless, current use varies widely. Some countries have imposed strict regulations to limit exposure, others have adopted bans, and yet others have intervened less and have continued to use varying quantities of asbestos. The global burden of asbestos diseases over time will be uneven, reflecting the extent and patterns of asbestos use.

Globally, each year, an estimated 125 million people are occupationally exposed to asbestos, and 90,000 die from asbestos diseases (WHO 2006a). Around the time of peak use in the mid-1970s, approximately 25 countries produced asbestos and 85 countries manufactured asbestos products (Virta 2005). In 1983, Iceland became the first country to ban asbestos, reflecting increasing recognition, predominantly in Western countries, of health risks associated with asbestos exposure. Subsequently, 40 or more countries have adopted bans (WHO 2006a).

Among the asbestos diseases, mesothelioma is the most sensitive and specific indicator of the disease burden in the population (Weill et al. 2004). The annual incidence of mesothelioma has been estimated at 10,000 cases in Western Europe, North America, Japan, and Australia combined (Anonymous 1997). Peto et al. (1995, 1999) predicted a dramatic increase in future mesothelioma deaths in the United Kingdom and Europe. Several statistical projections have been made since then, suggesting that deaths from mesothelioma will increase in many countries.

We recently reported that per capita asbestos use is a useful surrogate for the general asbestos exposure level of a population and may be used for estimation of health effects (Lin et al. 2007). Information is limited at the global level concerning the relationship between mesothelioma trends and trends in asbestos use, and the status of bans. Our aim in the present study was to assess, on a global scale, national experiences of recent mortality from mesothelioma, historical trends in asbestos use, adoption of bans, and their possible interrelationships. We focused specifically on pleural mesothelioma in men because a high proportion of such cases arise from asbestos exposure.

Materials and Methods

Indicators of mortality. The primary source of information on mortality was the WHO database (WHO 2006b). It registers the number of deaths by country according to the *International Classification of Diseases* (ICD). Several countries shifted from coding based on the ICD *9th Revision* (ICD-9) to that based on the *10th Revision* (ICD-10) (WHO 1992) during our 1996–2005 study period [year of change ranged from 1996 to 2002, with a median of 1998 in the countries studied; Supplemental Material, Table 1 (http://www.ehponline.org/members/2008/11272/

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suppl.pdf)]. Notably, the disease category of mesothelioma was initially introduced into ICD-10 codes comprising subcategories of pleural (C45.0), peritoneal (C45.1), pericardial (C45.2), other sites (C45.7), and unspecified (C45.9). In our study, we defined pleural mesothelioma as a composite of mesothelioma of the pleura (C45.0) and unspecified mesothelioma (C45.9) because in certain countries, including the United States, most mesothelioma was coded as C45.9 instead of C45.0. From the database, we obtained the annual numbers of male deaths for each country, based on 5-year age intervals.

We obtained national population data from the WHO (2006b), the U.S. Census Bureau (2006), the United Nations (2006), and Lahmeyer (2007), prioritized for use in that order. For each country, we calculated age-adjusted annual mortality rates (annual MRs; deaths/million/year) by dividing the number of male deaths in each year by the size of the corresponding male national population, which we age-standardized to the world standard population of the year 2000 (Ahmad et al. 2000). We similarly calculated period MRs by dividing the average annual number of male deaths from 1996 to 2005 by the average sizes of male national populations, also age-standardized.

To characterize the trend of mortality, we estimated the annual percent change (APC) of annual MRs using the Joinpoint software (version 3.0, U.S. National Cancer Institute, Bethesda, MD, USA). Briefly, the method fits a least-squares regression line to the natural logarithm of the rates using calendar year as a regressor variable. That is, $y = bx + c$, where y is the ln(rate), x is the calendar year, and c is the intercept. Hence, APC = $100 \times (e^b - 1)$ (Jemal et al. 2000; Lasithiotakis et al. 2006; Ries et al. 1997). In addition, we calculated p-values for APC = 0 and 95% confidence intervals (CIs) of APCs. Testing the hypothesis that APC = 0 is equivalent to testing the hypothesis that the regression slope parameter is equal to zero (Ries et al. 1997). We assumed a linear change of trends in log rates over time. Because trends pertained to a 10-year period, we limited analyses to countries with at least 4 years of pleural mesothelioma data under ICD-10 codes (the range was 4–9 years, with a median of 6 years).

Table 1. Recent trend in mortality from pleural mesothelioma[a] in men.

Country (code)	Period MR[b] (no.[c]) (deaths/million/year)	APC[d] [%/year (95% CI)]	Trend[e]	Male population[f] (million)
Asia				
Israel (ISR)	5.5 (5)	6.6 (−14.9 to 33.4)	↔	3.1
Japan (JPN)	4.8 (9)	3.9 (2.6 to 5.2)	↑**	61.4
Eastern Europe and Southern Europe				
Croatia (HRV)	8.8 (9)	11.0 (2.7 to 20.0)	↑**	2.2
Czech Republic (CZE)	3.2 (9)	6.3 (−1.7 to 15.0)	↔	5.0
Hungary (HUN)	2.5 (8)	11.0 (3.3 to 19.3)	↑**	4.9
Poland (POL)	2.0 (6)	5.2 (−5.2 to 16.7)	↔	18.7
Romania (ROU)	1.9 (6)	1.2 (−11.2 to 15.3)	↔	10.9
Spain (ESP)	5.7 (6)	0.7 (−6.6 to 8.7)	↔	19.8
Northern Europe and Western Europe				
Austria (AUT)	7.8 (4)	−5.9 (−20.9 to 12.0)	↔	3.9
Denmark (DNK)	12.9 (6)	4.6 (−6.5 to 16.9)	↔	2.6
Finland (FIN)	12.6 (9)	−0.3 (−3.9 to 3.6)	↔	2.5
France (FRA)	12.7 (4)	−1.0 (−14.7 to 14.9)	↔	28.7
Germany (DEU)	12.0 (7)	3.3 (−0.8 to 7.6)	↑*	40.1
Iceland (ISL)	10.1 (7)	−1.4 (−28.8 to 36.5)	↔	0.1
Lithuania (LTU)	2.0 (5)	12.3 (−34.3 to 92.1)	↔	1.6
Luxembourg (LUX)	12.7 (7)	5.4 (−11.0 to 24.8)	↔	0.2
Netherlands (NLD)	30.0 (9)	0.0 (−1.5 to 1.6)	↔	7.9
Norway (NOR)	12.7 (9)	−2.7 (−7.5 to 2.3)	↔	2.2
Sweden (SWE)	12.8 (6)	3.5 (−2.0 to 9.2)	↔	4.4
United Kingdom (GBR)	31.1 (4)	0.5 (−4.0 to 5.3)	↔	29.1
Americas excluding South America				
Canada (CAN)	10.3 (4)	5.6 (−7.4 to 20.4)	↔	15.1
Cuba (CUB)	0.6 (4)	5.2 (−36.1 to 73.2)	↔	5.6
Mexico (MEX)	2.2 (6)	2.9 (−7.2 to 14.2)	↔	49.4
United States of America (USA)	9.0 (4)	0.8 (−2.4 to 4.1)	↔	135.1
South America				
Argentina (ARG)	2.5 (7)	8.9 (3.3 to 14.7)	↑**	18.6
Brazil (BRA)	0.5 (6)	9.0 (0.1 to 18.7)	↑**	87.3
Chile (CHL)	3.1 (7)	3.3 (−8.1 to 16.2)	↔	7.5
Ecuador (ECU)	0.5 (4)	16.4 (−37.5 to 116.7)	↔	6.3
Uruguay (URY)	2.3 (5)	13.6 (−43.7 to 129.2)	↔	1.6
Oceania				
Australia (AUS)	25.5 (6)	4.6 (−0.6 to 10.1)	↑*	9.5
New Zealand (NZL)	20.5 (4)	10.4 (−10.3 to 35.7)	↔	1.9

[a] See "Materials and Methods" for our definition of mesothelioma. [b] Period MR from 1996 to 2005, age-adjusted to the world population of 2000. [c] Number of years with available data. [d] APC, together with its 95% CI and p-values, were calculated with Joinpoint software. [e] Trend: ↑ when APC > 0 ($p < 0.10$); ↓ when APC < 0 ($p < 0.10$); ↔ when $p > 0.10$ for APC. [f] Average of male national population from 1996 to 2005. *Marginally significant ($0.05 < p < 0.10$). **Statistically significant ($p < 0.05$).

Indicators of asbestos use. We extracted data on new use of asbestos by country from a U.S. Geological Survey (USGS) report (Virta 2006). We defined "use" as production plus import minus export (Virta 2006). We considered negative values of use (caused by storage and the like) uninformative and excluded them from further analyses. To characterize trends, we divided use numbers by sizes of national populations for the corresponding year or period (to give use per capita, expressed as kilograms per capita/year) (Lin et al. 2007). The USGS database provides data only sparsely in 10-year intervals up to 1960, 5-year intervals from 1970–1995, and annually for 1996–2003. We classified use of ≥ 3.0 kg per capita/year as high and ≥ 4.0 as very high, and change in use during a particular period (Δ, kilograms per capita/year) as the difference between average use during the earlier and latter subperiods (halves) of the entire period (e.g., for the period 1960–1985, change is the difference between the average use of 1960 and 1970 and the average use of 1975, 1980, and 1985; for the period 1970–1985, change is the difference between the average use of 1970 and 1975 and the average use of 1980 and 1985). We calculated Δ values for all possible combinations of available data. We retrieved national ban status from the database compiled by Kazan-Allen (2005, 2006) and verified it by separate reports. To describe historical trends in asbestos use and relationships with banning status, we grouped countries according to their national ban status into early-ban (adopted by 1995), late-ban (1996–2006), and no-ban groups.

Statistical analysis. We adapted geographic grouping of countries from the U.N. Statistics Division (United Nations 2006). We performed statistical analyses using Joinpoint, SPSS version 12.0 (SPSS Inc., Chicago, IL, USA), and Excel 2003 (Microsoft Corp., Redmond, WA, USA). When we used Joinpoint, we assumed a linear change (or 0 joinpoint) during the observed period, with a maximum length of 10 years. We deemed $p < 0.05$ statistically significant and $0.05 < p < 0.10$ marginally significant. We use the terms "increase" (denoted as ↑) or "decrease" (↓) when APC was marginally or statistically significant, and "equivocal" (↔) when APC and its significance level were neither statistically nor marginally significant.

When we evaluated trends in asbestos use by groups of countries, we weighted means by the size of national populations of the corresponding periods. We analyzed data from the United States separately because of the known high degree of historical asbestos use. We regressed recent changes in pleural mesothelioma mortality (APC values) against historical changes in use of asbestos (Δ values for various periods). We weighted each regression model by the sizes of male national populations in the corresponding period.

Results

Trends in mortality. Table 1 shows the period MRs and APCs in mortality for pleural mesothelioma and male population by country. Mortality from pleural mesothelioma was highest in United Kingdom (31.1 deaths/million/year), with a global median of 7.8 deaths/million/year. Trends of mortality were as follows: statistically significant increases in five countries, marginally significant increases in two countries, and equivocal results in 24 countries. Global median APC was 4.5%/year, and negative values of APC were recorded in five countries of Northern and Western Europe. We observed increasing trends more often in countries with above-median period MR values than in those with below-median values (26.7%, or 4 of 15, vs. 20.0%, or 3 of 15).

Regionally, countries of Northern and Western Europe and Oceania showed high and stable MRs; those of Eastern and Southern Europe, South America, and Asia showed low and increasing rates.

Trends in asbestos use. Asbestos use peaks were higher and occurred earlier in the countries of Northern and Western Europe, Oceania, and the Americas (excluding South America) (Table 2). Very high (≥ 4.0 kg per capita/year) asbestos use was recorded in Australia, Canada, and several countries of Northern and Western Europe.

Asbestos use fell most quickly in countries that adopted early bans, at an intermediate rate in countries with late ban adoption, and most slowly in countries without bans (Figure 1). Specifically, the early-ban group, during its period of adopting bans, recorded a reduction rate of –8.3%/year, from 2.4 kg per capita/year in 1983 (first ban) to < 0.01 kg per capita/year in 1995 (last ban). This was about twice as fast as the late-ban and no-ban groups, which recorded a reduction rate of –4.1%/year and –5.2%/year, respectively, during the same period. Similarly, the late-ban group, during its period of adopting bans, recorded a reduction rate of –10.7%/year, from 0.7 kg per capita/year in 1996 (first ban) to 0.2 kg per capita/year in 2003. During the same period, the value for the no-ban group was –4.9%/year, resulting in a 2.2-fold quicker reduction rate in the late-ban group. The historical use pattern of the United States differed from that of other countries. The United States recorded the earliest and maximal peak use at 4.2 kg per capita/year in 1950, followed by progressive reduction over four decades and approaching 0.02 kg per capita/year in 2003, equating to a reduction rate of –1.9%/year. The no-ban group had the lowest peak but currently maintains the highest level of asbestos use at 0.4 kg per capita/year. The period of 1970–1985 contained historical use peaks with a notable shift to downward trends for many but not all countries.

Interrelationships. The change in asbestos use (Δ) during 1970–1985 was the strongest predictor of APC among the many periods tried, with an adjusted R^2 value of 0.47 ($p < 0.0001$) (Table 3). Changes in asbestos use during other adjacent periods (e.g., 1960–1990, 1970–1990) also predicted APC in mortality, each with relatively high statistical significance. Figure 2 shows the positive log-linear relationships between changes in asbestos use and APCs in mortality, where increments in recent MRs are associated with increments in historical asbestos use.

Discussion

The present study identified wide differences in recent mortality from pleural mesothelioma in various countries. Recent MRs were highest in the countries of Northern and Western Europe and Oceania. Increasing

Table 2. Historical trend in per capita asbestos use and status of national ban.

Country code	Use of asbestos[a] (kg per capita/year)						Change in use (Δ) from 1970 to 1985[b]	National ban[c]
	1950s	1960s	1970s	1980s	1990s	2000s		
Asia								
ISR	3.13	2.87	1.23	0.78	0.44	0.02	–0.59	No ban
JPN	0.56	2.02	2.92	2.66	1.81	0.46	0.12	2004
Others[d] ($n = 39$)	0.06	0.15	0.25	0.27	0.30	0.31	0.05	3/39
Eastern Europe and Southern Europe								
HRV	0.39	1.13	2.56	2.36	0.95	0.65	0.49	No ban
CZE	1.62	2.36	2.91	2.73	1.30	0.14	0.21	2005
HUN	0.76	1.23	2.87	3.29	1.50	0.16	1.32	2005
POL	0.36	1.24	2.36	2.09	1.05	0.01	–0.11	1997
ROU	NA1	NA1	1.08	0.19	0.52	0.55	–1.73	2007
ESP	0.32	1.37	2.23	1.26	0.80	0.18	–1.07	2002
Others[d] ($n = 15$)	0.79	1.57	2.35	2.05	2.35	1.72	0.30	5/15
Northern Europe and Western Europe								
AUT	1.16	3.19	3.92	2.08	0.36	0.00	–1.77	1990
DNK	3.07	4.80	4.42	1.62	0.09	NA2	–2.96	1986
FIN	2.16	2.26	1.89	0.78	NA1	0	–1.53	1992
FRA	1.38	2.41	2.64	1.53	0.73	0.00	–1.06	1996
DEU	1.84	2.60	4.44	2.43	0.10	0.00	–0.30	1993
ISL	0.21	2.62	1.70	0.02	0	0.00	–2.52	1983
LTU	NA1	NA1	NA1	NA1	0.54	0.06	NA1	2005
LUX	4.02	5.54	5.30	3.23	1.61	0.00	–2.04	2002
NLD	1.29	1.70	1.82	0.72	0.21	0.00	–1.20	1994
NOR	1.38	2.00	1.16	0.03	0	0.00	–1.72	1984
SWE	1.85	2.30	1.44	0.11	0.04	NA2	–1.96	1986
GBR	2.62	2.90	2.27	0.87	0.18	0.00	–1.41	1999
Others[d] ($n = 5$)	3.05	4.32	4.05	2.40	0.93	0.05	–1.30	5/5
Americas excluding South America								
CAN	2.76	3.46	4.37	2.74	1.96	0.32	–1.66	No ban
CUB	NA1	NA1	NA1	0.15	0.36	0.74	NA1	No ban
MEX	0.28	0.57	0.97	0.77	0.39	0.26	0.04	No ban
USA	3.82	3.32	2.40	0.77	0.08	0.01	–1.73	No ban
Others[d] ($n = 12$)	0.06	0.22	0.44	0.29	0.07	0.07	–0.08	0/12
South America								
ARG	NA1	0.88	0.76	0.40	0.18	0.04	–0.26	2001
BRA	0.27	0.38	0.99	1.25	1.07	0.74	0.66	2001
CHL	0.07	0.92	0.56	0.64	0.55	0.03	0.14	2001
ECU	NA1	NA1	0.67	0.52	0.14	0.26	0.29	No ban
URY	NA1	0.74	0.75	0.54	0.47	0.08	–0.20	2002
Others[d] ($n = 6$)	0.27	0.43	0.60	0.47	0.29	0.19	–0.04	0/6
Oceania								
AUS	3.24	4.84	5.11	1.82	0.09	0.03	–2.71	2003
NZL	2.05	2.56	2.90	1.00	NA1	NA1	–2.56	No ban
Others[d] ($n = 3$)	NA1	NA1	NA1	NA1	NA1	0.22	NA1	0/3

Abbreviations: NA 1, data not available; NA 2, not applicable because of negative use data: 0.00 when the calculated data were < 0.005; 0 if there are no data after the year the ban was introduced. See Table 1 for country codes.

[a] Numbers corresponding to use of asbestos by country and region were calculated as annual use per capita averaged over the respective decade. [b] Change in use (Δ, kilograms per capita/year) during the period defined as the difference between the average of consumption during the former subperiod (1970–1975) and latter subperiod (1980–1985). [c] Year first achieved or year planned to achieve ban. When shown as fraction, the numerator is the number of countries that achieved bans and the denominator is the number of other countries in the region. [d] Data on asbestos use were available (but mortality data unavailable) for others in each region, in which case data were aggregated.

trends, as measured by APCs in mortality, were common in the countries of Eastern and Southern Europe, Asia, and South America.

We assessed mortality trends over the most recent 10-year window, using the earliest opportunity to analyze the disease under the standard code of ICD-10. However, the study period was inadequate to depict trends in many countries. National data recorded only under ICD-9 had to be precluded (e.g., Italy). For the countries shifting from ICD-9 to ICD-10 during the study period, we limited our analyses to the period when data were recorded under ICD-10.

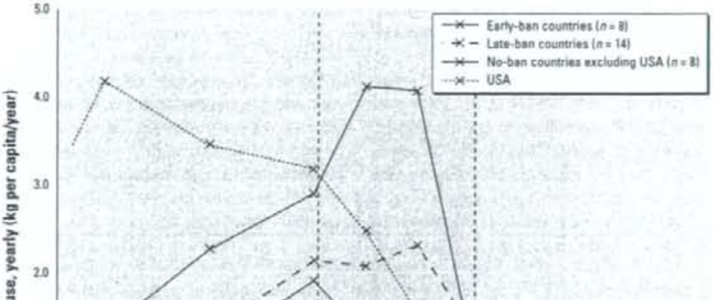

Figure 1. Historical trends in use of asbestos from 1950 to 2003 grouped by status of national bans. Early-ban countries are countries that adopted bans in 1995 or before ($n = 8$); late-ban countries adopted bans from 1996 to 2006 ($n = 14$); no-ban countries, excluding the United States, did not adopt bans until 2007 ($n = 8$). Asbestos use (*y*-axis) is per capita yearly use (averages weighted by the sizes of national populations). The USGS (Virta 2006) database provides data only sparsely in 10-year intervals up to 1960, 5-year intervals from 1970–1995, and annually for 1996–2003. Straight lines connect available data.

Table 3. Relation between recent change in pleural mesothelioma mortality and historical change in use of asbestos based on regression analyses.[a]

Period for use of asbestos	No. of countries	Adjusted R^2	*p*-Value
1950			
1960	23	−0.035	0.615
1970	24	−0.038	0.689
1975	25	0.000	0.325
1980	25	0.073	0.102
1985	25	0.182	0.019
1990	27	0.277	0.003
1960			
1970	24	−0.044	0.857
1975	23	0.052	0.151
1980	27	0.201	0.011
1985	27	0.300	0.002
1990	29	0.415	< 0.001
1970			
1975	26	0.121	0.046
1980	26	0.348	0.001
1985	29	0.466	< 0.001
1990	29	0.366	< 0.001
1975			
1980	27	0.328	0.001
1985	28	0.267	0.003
1990	29	0.091	0.062
1980			
1985	28	−0.031	0.675
1990	26	−0.006	0.368
1985			
1990	27	0.037	0.170

[a] APC of the age-adjusted annual MRs from 1996 to 2005 (dependent variable) versus change in use during the corresponding period (independent variable).

Further, data may lack comparability, especially because mesothelioma is rare and difficult to diagnose. A major concern is that increasing trends recorded in countries with low mortality levels could be explained by improved disease recognition (Peto et al. 1995; Weill et al. 2004), and such secular trends in diagnosis would be statistically indistinguishable from real increases (Peto et al. 1995). Our study revealed increasing mortality trends in the group that recorded above-median values for the period MR (group 1) than the group that recorded below-median values for the period MR (group 2). Such bias is likely to be less serious in group 1 than group 2. Thus, although increases in disease recognition are probable, this factor alone does not explain the increasing trends. The proportionality with which recent mortality trends were related to historical trends of asbestos use offers a more compelling explanation.

Pleural mesothelioma is the predominant type of mesothelioma and is strongly related to asbestos exposure. However, in certain countries, most mesothelioma was coded into the subcategory of unspecified mesothelioma (C45.9) instead of the subcategory of pleural mesothelioma (C45.0): the ratio of C45.0 to C45.0 + C45.9 ranged from 0.08 (Israel), 0.11 (United States), and 0.12 (Canada) to 0.94 (New Zealand) and 0.98 (Finland), with a median of 0.63. We therefore created a composite category of C45.0 and C45.9 to ensure comparability, which we deemed more reasonable than the alternative choices of analyzing only C45.0 or mixing C45.0 with other subcategories—for example, peritoneal (C45.1) or pericardial (C45.2) or other sites (C45.7).

Our findings on mortality trends are comparable with trends reported earlier for individual countries, including the Netherlands (Segura et al. 2003), Sweden (Burdorf et al. 2005), Finland (Karjalainen et al. 1997), and Denmark (Kjaergaard and Andersson 2000), as well as overall Europe (Montanaro et al. 2003). However, methods and indices employed to evaluate trends are unique to each study, and comparisons cannot exceed the general trend characteristics. For the United States, we recorded equivocal trends (i.e., APC = 0.8%). Similarly, Price (1997) first observed that the annual growth rate during 1973–1992 was declining, and Price and Ware (2004) reported "no substantive changes in time pattern of mesothelioma incidence since 1992." Furthermore, surveillance information in United States does not show an apparent trend from 1999 to 2002 (National Institute for Occupational Safety and Health 2005).

Regarding historical trends in asbestos use, we identified several distinctive patterns:

a) a very early (1950) and very high (≥ 4.0 kg per capita/year) peak followed by a progressive decline (in the United States); *b*) a midterm (1960s-1980s) very high peak, followed by an abrupt decline (Australia and several Northern and Western European countries); and *c*) a late (≥ 1980) and relatively moderate peak followed by a moderate decline (Hungary and Japan).

In the United States, a "bubble" in asbestos use occurred in the mid-20th century because of early manufacturing research, industrial demand, and ready supply from Canada (Virta 2006). However, the United States was also the first to experience the burst of the bubble due to growing health concerns and liability issues (Virta 2006). In 1989, the U.S. Environmental Protection Agency (EPA) banned most asbestos-containing products, but this regulation was overturned by the U.S. Court of Appeals in 1991 (U.S. EPA 1989). Nevertheless, use fell to 4,600 tons in 2003 (0.7% of peak use). In many other countries, increasing use of asbestos paralleled the growth curves of industrialization.

Generally, countries recording early and high levels of asbestos use displayed peaks by 1980 followed by downward trends. The turning points preceded the earliest bans and are thus not direct outcomes of bans. Rather, paths leading to bans likely entailed regulatory restrictions and economic incentives and disincentives, which furthered reduction of use. Virta (2005, 2006) attributed maturation of the asbestos market superimposed on health issues as the main reason for the decline in use since 1980. Several relevant events with international impact coincided with this period. The International Agency for Research on Cancer (IARC), after acknowledging the carcinogenicity of asbestos in 1973 (IARC 1973), classified asbestos as a human carcinogen in 1977 (IARC 1977). The ILO added lung cancer and mesothelioma caused by asbestos to its list of occupational diseases in 1980 (ILO 1980) and adopted the Asbestos Convention in 1986 (ILO 1986). It was also around this period that the landmark studies by Selikoff and colleagues (Nicholson et al. 1982; Selikoff et al. 1984a, 1984b) gained wide recognition.

The adoption of bans by Northern European countries in the 1980s set a precedent for other countries, but the particular restrictions imposed by a "ban" vary by country, and the rates at which the absolute zero use levels were reached also vary. Collectively, countries adopting bans reduced use about twice as fast as those with lesser interventions. Notably, the countries of Eastern and Southern Europe (grouped here as "other" countries in Table 2) have continued to use asbestos, approaching high levels even after the turn of the century. The recent per capita use for the "other" Asian countries is low but shows little sign of decreasing. This is largely attributable to sustained use in China and India. Hence, our findings reinforce the widely held concern that the center of asbestos use is shifting to industrializing countries (Kazan-Allen 2005; LaDou 2004; Takahashi and Karjalainen 2003). Moreover, if the ecologic relationship reported here holds true for the future, corresponding risks should be anticipated in these countries.

Regression analyses showed the strongest relationship between recent APC in mortality from pleural mesothelioma and change in asbestos use during 1970–1985 (adjusted $R^2 = 0.47$, $p < 0.0001$). The same analyses incorporating countries with six or more data points produced similar results (data not shown). The strong relationship is largely attributable to countries recording recent mortality trends in the same direction as historical use trends (lower-left and upper-right quadrants in Figure 2). The positive correlations found for change indicators of a number of periods in the present study reinforce the notion that per capita asbestos use is related to subsequent mortality level at the national level, as we reported earlier using absolute-level indicators (Lin et al. 2007). However, the time difference (i.e., latency) for the best predictive model was only 22.5 years (from mid-1977 to 2000), and thus the observed relationship may have reflected only early effects. In this connection, recent mortality trends of the eight early-ban countries are noteworthy: Seven countries recorded had equivocal MR trends, and only Germany had an increase in MR trend (Table 1). Germany actually recorded a historical use peak in 1980, trailing other early-ban countries by 5–10 years (detailed data not shown) and presumably delaying favorable changes in mortality trend. Continuing use of asbestos results in the accumulation of asbestos in the environment, thus creating possibilities for ongoing exposure due to maintenance, repair, and demolition during the entire life span of asbestos products. Given the long latency time, the mortality data available did not allow us to analyze the full consequences of such effects after the new use in longer term. Nevertheless, we observed significant (albeit weaker) relationships for changes in use during other close periods with longer latencies [e.g., 1950–1985 (latency 32.5 years) and 1950–1990 (30 years)].

In this study, we took advantage of the earliest opportunity to analyze mortality trends in a range of countries. Limitations included our dependence on a crude indicator of exposure (i.e., asbestos use per capita for sparse years with limited data), "bans" entailing varying restrictions on use that could not be measured, and no distinctions available

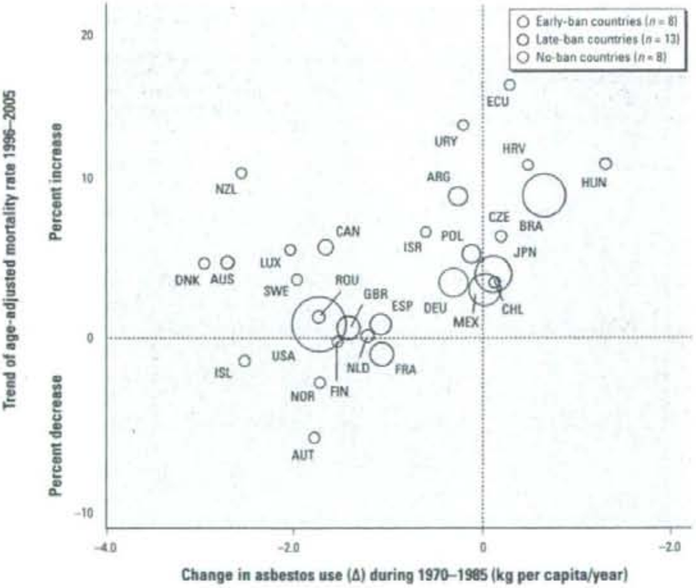

Figure 2. Trend of MRs for male pleural mesothelioma in relation to change in asbestos use. See Table 1 for country codes. Circles have areas proportional to the sizes of male national populations; the smaller equal sizes indicate male national populations < 5,000,000. We defined the trend of MRs (y-axis) as APC, as calculated by the Joinpoint software. Bivariate relationships were examined by linear regression, weighted by the sizes of male national populations, and produced the following model: $y = 0.011x + 2.022$ (adjusted $R^2 = 0.47$, $p < 0.0001$).

between asbestos fiber types. Mortality data were limited to 31 countries, with developing countries likely lacking well-developed surveillance systems to assure quality of data. Moreover, the observed relationships are ecologic at the national level only, so all findings should be cautiously interpreted.

Because there is no safe threshold of exposure to asbestos, any degree of contact will involve some risk. On the other hand, the degree of risk is related to exposure. The experience of many countries suggests that attempts to reduce exposure without a concurrent reduction in overall use are insufficient to control risk. Countries implementing bans recorded reductions in asbestos use about twice as fast as those not adopting bans, for which our study period was probably too early to observe their full effects. However, the observed disparities in global mesothelioma trends are likely to relate to country-to-country disparities in asbestos use trends.

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今月の主題　アスベストと中皮腫

話題

諸外国でのアスベスト中皮腫

高橋　謙

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諸外国でのアスベスト中皮腫

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〔KEYWORDS〕 アスベスト，中皮腫，国際比較

中皮腫は，二十世紀前半まで未知も同然の疾患であった．中皮腫に関する最初の報告は1940年前後になされているが，Wagnerが1960年に南アフリカの鉱山労働者と近隣住民の石綿曝露と中皮腫の関係を報告[1]するまで，本疾患に対する認識は乏しかった．さらに1964年，米北東部の建設断熱工の間で肺と胸膜の癌死亡が増加するとしたSelikoffらの研究報告[2]をきっかけに，世界的に石綿疾患が注目されるようになった．

世界的視点に立てば，現在なお，中皮腫は稀で診断の難しい疾患と言える．このため，中皮腫に関してグローバルな実態を俯瞰できるような信頼性の高い報告は見当たらない．最近の総説[3]では，中皮腫の罹患に関するデータを有する国は少数であるが，報告されている中ではオーストラリア・ベルギー・英国が最も高い罹患率を示し，百万人年当たり約30人(粗罹患率)とされている．これがどれくらいかというと，日本の人口を1.3億人とすると年間約3,900人の罹患を意味する．わが国の中皮腫死亡者数は2006年に1,050名[4]であったから，いかに大きな数字であるかがわかる．周知のように中皮腫は進行が速く致死率が極めて高いため，罹患率と死亡率はほぼ等しい．また，わが国においては，中皮腫に限らずほとんどの疾患で全国レベルの罹患数は把握されていない(疾患別死亡数は正確で網羅的な統計がある)．

中皮腫の80%は石綿が起因しているとのコンセンサスがある[5]．一方，石綿に曝露した人のうち中皮腫になるのはごく一部であると考えられる．石綿以外の原因によっても中皮腫が起きるという可能性は否定できないが，8割が特定原因によって説明できる(「(人口)寄与割合」)という特徴は，様々な癌の中で際立っている．ちなみに日本人の肺癌に対する喫煙の寄与割合は男性68%，女性18%というデータ[6]があり，これと対比できるが，中皮腫の場合は男女を区別していない．「中皮腫は石綿曝露によって特異的に発生する」とか，「中皮腫は石綿曝露と特異的関係がある」という言い方は，この高い寄与割合が背景にある．したがって本稿では，『中皮腫』と『アスベスト中皮腫』は同義という立場をとる．

おおよその推定値ということであれば，全世界の中皮腫による年間の死亡数として，西ヨーロッパ，北米(米加)，日本とオーストラリアを合わせた数が約10,000人と見積もられている[5]．また，世界保健機関(WHO)は，年間90,000人が石綿関連疾患により死亡していると推定したうえで根絶に取り組むべきとの宣言を出している[7]．

1. 方法

諸外国での中皮腫を独自に評価するため，当研究室で行った解析結果[8]を紹介したい．WHOは，加盟国の報告を基に国別・疾病別の死亡数のデータベース(WHO Mortality Database；以下WHO-DBと略)を維持・公開しており，これを活用した．WHO-DBに登録された死因としての疾病は国際疾病分類(International Classification of Diseases；ICD)に基づいている．ただしICD

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