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Respiratory health effects from occupational exposure to wood dusts

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GOLDSMITH DF, SHY CM. Respiratory health effects from occupational exposure to wood dusts. *Scand J Work Environ Health* 14 (1988) 1—15. Occupational exposure to wood dusts has been well established as a cause of nasal cancer, dermatitis, and pneumonites from molds growing in wood chips. With the exception of studies on western red cedar asthma, there is a dearth of information on the respiratory toxicity of wood dust exposure. This paper reviews the clinical and epidemiologic literature and identifies the specific woods (with botanical names) and their respiratory disease correlates, including pulmonary function declines, chronic and acute symptoms, and impaired mucociliary transport.

Key terms: nasal clearance, pulmonary function, respiratory symptoms, western red cedar asthma, woodworker's asthma.

Hardwood dusts produced in the manufacture of furniture are well established as the cause of excess nasal adenocarcinoma (1, 49). Many species of wood, especially exotic hardwoods, have been linked to a variety of dermatoses (44, 75). There are also case reports of pneumonitis due to molds found in maple bark (34, 42), suberosis (5, 62, 74), "wood trimmer's disease" (alveolitis) in Scandinavia (8, 67), pneumonitis due to molds in wood chips used for fuel (70), and redwood pneumonitis (28). However, with the exception of a chapter in Hausen's monograph (44) and the recently published review (68) by the National Institute for Occupational Safety and Health (NIOSH) there has been no assessment of the clinical and epidemiologic literature of nonmalignant respiratory diseases related to exposure to wood dust.

The lung disease thought to be caused by exposure to wood dust is woodworker's asthma, which, without a thorough work history, may be considered idiopathic by the treating physician. Clinically, this ailment is characterized as an immediate or delayed hypersensitivity reaction among workers exposed to wood dust, usually hardwoods or exotic timbers. The hypersensitivity response should not be confused with pneumonites due to mold found in tree barks or moldy wood dusts. The clinical literature on woodworker's asthma has focused on a description of the symptoms produced by different types of woods. Most epidemiologic research has concentrated on estimating the prevalence of respiratory symptoms and describing changes in pulmonary function among workers exposed to western red cedar *(Thuja plicata)*. There have been case reports linking woodworker's asthma to common woods such as oak *(Quercus species)* and California redwood *(Sequoia sempervirens)* and to exotic varieties such as teak *(Tectonia grandis)*, cedar of Lebanon *(Cedrus libani)*, iroko *(Chlorophora excelsa)*, ramin *(Gonystylus bancanus)*, American mahogany *(Swietenia macrophylla)*, and abiruana *(Lucuma species)*. Oak, mahogany, abiruana, teak, ramin, and other exotic hardwoods are used in the European and American furniture industry.

This paper describes the extent of risk of nonmalignant respiratory disease from exposure to wood dust. It presents case studies and epidemiologic evidence and a discussion of confounding and bias.

Case studies of woods other than western red cedar

Table 1 summarizes and provides additional details on the case studies presented in this section. Ordman described a bronchial asthma patient with symptoms of sneezing, runny nose, chest tightness, and wheezing that coincided with the change in types of wood at the plant where the patient worked (59). A skin patch test produced marked reactions to extracts of kejatt, "Congo hardwood" [later identified as *Lovoa klaineana* (64)], and western red cedar.

Chan-Yeung & Abboud (20) and doPico (31) described three asthma patients (ex-smokers) who reacted to redwood *(Sequoia sempervirens)* dust exposure, but who lacked serum antibodies to the wood. Bronchial challenge tests produced immediate and delayed declines in forced expiratory volume in 1 s ($FEV_{1.0}$) (20); however, doPico (31) induced a delayed response only.

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Table 1. Respiratory health effects from case studies of exposure to wood dusts. ($FEV_{1.0}$ = forced expiratory volume in 1 s, FVC = forced vital capacity, RAST = radioallergosorbent test)

Author(s)	Types of wood exposure[a]	Number of cases	Length of exposure prior to symptoms	Observed effects	Comments
Ordman (59)	Kejatt *(Pterocarpus angolenis DC)*, iroko *(Chlorophora excelsa)*, partridge or panga-panga *(Milletia stuhlmannii)*, western red cedar *(Thuja plicata)*, congo hardwood *(Lovoa klaineana)*	1	3 months	Asthma including rhinitis and dyspnea; confirmed by positive skin patch tests	No smoking data
Chan-Yeung & Abboud (20)	California redwood *(Sequoia sempervirens)*[b]	2	2—3 years	Asthma with dyspnea and wheezing; confirmed by immediate, delayed, and dual decline in $FEV_{1.0}$	Both ex-smokers; negative skin patch tests and serum antibody; chalk and western red cedar produced no effects
doPico (31)	California redwood *(Sequoia sempervirens)*[b]	1	~3 months	Nocturnal tight chestedness with dyspnea, cough, and wheeze; confirmed by delayed decline in $FEV_{1.0}$	Ex-smoker; negative skin patch tests and serum antibody; pine dust produced no response
Sosman et al (66)	Oak Mahogany Cedar	1 1 2	12 years 16 years 17—18 years	Asthma with cough, rhinitis, and dyspnea; confirmed by a decline in $FEV_{1.0}$ and FVC (immediate for oak, dual for mahogany, delayed for cedar) and positive serum antibodies for all dusts	No smoking data; negative skin patch tests; botanical names missing
Greenberg (41)	Cedar of Lebanon *(Cedrus libani)*	6	3 months	Asthma with chest tightness and rhinitis	Smoking data incomplete; negative skin patch and serum antibody tests
Pickering et al (61)	Iroko *(Chlorophora excelsa)* Western red cedar *(Thuja plicata)*	1 1	1 year Unknown	Asthma with dyspnea; confirmed by a positive gradient for the skin patch tests and positive serum antibody for iroko only and a decline in $FEV_{1.0}$ for both woods	No smoking data; negative serum antibody and skin patch tests for cedar
Eaton (32)	Cocabolla *(Dalbergia retusa)*[c]	3	Days to 18 months	Upper respiratory irritation; confirmed by positive skin patch test in two subjects only	No smoking data or serum antibody tests
Booth et al (11)	Abiruana *(Lucuma species)*	2	Days to 1 year	Asthma with nocturnal dyspnea and cough; confirmed by a decline in $FEV_{1.0}$, FVC, and maximal midexpiratory flow	Smoking data for only one subject; positive serum antibody
Howie et al (48)	Ramin *(Gonystylus bancanus)*	1	Not stated	Hypersensitivity with dyspnea, cough, and sweating; confirmed by a decline in $FEV_{1.0}$ and positive serum antibody	Nonsmoker; negative skin patch tests; by contrast positive serum antibody not found in eight asymptomatic co-workers
Bush et al (16)	Zebrawood *(Microberlinia species)*	1	5 months	Asthma with cough and dyspnea; confirmed by a dual decline in $FEV_{1.0}$ and positive skin patch, serum antibody, and RAST tests	No response to control wood dusts; unexposed referents showed no reaction to zebrawood
Girard et al (39)	Plywood Mahogany (species unspecified) Teak *(Tectonia grandis)* Okume *(Aucoumea klaineana)*	1 1 1 1	18 months 4 years 7 months 14 years	Asthma or pneumonitis with cough, dyspnea, and bronchitis; confirmed by a decline in $FEV_{1.0}$ and positive skin patch and serum antibody tests	Last two cases heavy smokers; smoking data missing on first two; prevalence survey indicated 56 % of 96 woodworkers with rhinitis and 17 % with conjunctivitis
Paggiaro et al (60)	Tanganyika aningre *(Aningeria species)*	3	Days to 3 months	Asthma with dyspnea, cough, and rhinitis; confirmed by positive skin patch tests and a decline in $FEV_{1.0}$ in two of three cases	All three smokers; negative serum antibody and RAST
Bush & Clayton (15)	Central American walnut *(Juglans olanchana)*	1	Not stated	Rhinorrhea, cough, wheezing, and dyspnea; confirmed by a decline in $FEV_{1.0}$	No smoking data; negative skin patch test and RAST
Innocenti & Angotzi (50)	African maple, samba, obeche *(Triplochiton scleroxylon)*	1	6 years	Fever, rhinorrhea, dyspnea; confirmed by an immediate decline in $FEV_{1.0}$	Ex-smoker
Hinojosa et al (47)	African maple, samba, obeche *(Triplochiton scleroxylon)*	2	2 months	Sneezing, rhinitis, wheezing, dyspnea, and nasal itching; confirmed by positive skin patch tests and immunoglobulin E and an immediate decline in $FEV_{1.0}$ when provoked	Both heavy smokers
Hinojosa et al (46)	African maple, samba, obeche *(Triplochiton scleroxylon)*	4	1 to 7 years	Sneezing, rhinitis, wheezing, dyspnea, and nasal itching; confirmed by positive skin patch tests and immunoglobulin E and an immediate decline in $FEV_{1.0}$ when provoked	Negative skin patch tests; two smokers and two nonsmokers; no response from six referents

[a] Botanical names in parentheses.
[b] Possible reactant: low molecular-weight compounds such as hydroxysugiresinol, sugiresinol, or isoequiric acid.
[c] Possible reactant: quinones in *Dalbergia species?*

Sosman et al (66) described the clinical features of four cases of hypersensitivity to oak, mahogany, or cedar dusts. The patients demonstrated immediate, delayed, and dual responses to the inhalation of dusts (or alcohol extracts) with losses of 20 to 50 % of base-line forced vital capacity (FVC) and $FEV_{1.0}$.

Greenberg reported on six cases of asthma among workers exposed to dust from cedar of Lebanon *(Cedrus libani)* (41). The cases presented similar symptoms (chest tightness and cough with occasional sneezing and nasal obstruction), but no antigen-antibody precipitations were observed.

Pickering et al (61) reported on a patient with asthma from exposure to iroko *(Chlorophora excelsa)*. Bronchial challenge produced a delayed reaction with a loss of 50 % of the base-line $FEV_{1.0}$ after 6 h. From skin patch tests, the patient appeared to show a gradient in wheal diameter (from 0.5 to 3.5 mm) based on three concentrations of iroko extract.

Eaton (32) presented three cases of respiratory and nasal irritation from exposure to cocabolla *(Dalbergia retusa)*, a tropical hardwood used in England to make pool cues. Two subjects had positive skin patch tests, but pulmonary function and immunologic tests were not done.

Booth et al (11) reported acute pulmonary hypersensitivity with positive skin tests for two workers exposed to abiruana *(Lucuma species)*. When challenged with a 1 % dilution of abiruana dust, an immediate drop in FVC, $FEV_{1.0}$, and maximum midexpiratory flow (MMF) was observed.

Howie et al (48) presented a case of asthma in which a challenge by ramin dust *(Gonystylus bancanus)* produced significant losses in $FEV_{1.0}$.

Bush et al (16) described an asthma patient whose skin patch test, immunoglobulin E (IgE) binding test, and radioallergosorbent test (RAST) were positive for zebrawood *(Microberlinia species)*. After challenge with 1 % zebrawood extract, the patient had a dual response, but no reaction occurred among referents.

Girard et al (39) reported on four asthmatic sanders who responded to dusts from plywood, mahogany, teak *(Tectonia grandis)*, and okume *(Aucoumea klaineana)*. In this prevalence survey of 96 Swiss woodworkers, 56 % had symptoms of rhinitis, 17 % had conjunctivitis, 9 % reported dermatitis, and only 2 % had symptoms of asthma.

Paggiaro et al (60) described three cases of bronchial asthma from exposure to tanganyika aningre *(Aningeria species)*, an African hardwood used in the Italian furniture industry. Intradermal skin tests were positive, and bronchial provocation with tanganyika aningre produced an immediate decline in $FEV_{1.0}$ in two of the men.

A woodworker handling Central American walnut *(Juglans olanchana)* developed asthma characterized by rhinitis, wheezing, cough, and dyspnea (15). This reaction was confirmed with an early and late decline in $FEV_{1.0}$, but the skin patch testing and RAST were both negative.

A case of occupational asthma was reported for an Italian furniture worker exposed to many types of timber (50). Bronchoprovocation with obeche or African maple *(Triplochiton scleroxylon)* produced an immediate 35 % loss in $FEV_{1.0}$.

Two Spanish patients developed asthmatic responses to African maple *(Triplochiton scleroxylon)* dust characterized by cough, sneezing, rhinitis, severe nasal itching, and dyspnea (47), which was confirmed with positive skin patch tests and a positive IgE determination. Four additional asthmatics who worked with obeche and exhibited the same symptoms were examined with the use of skin patch tests, IgE determinations, and bronchial provocation (46). Because two of the four were concomitantly exposed to ramin *(Gonystylus bancanus)*, all four subjects received bronchoprovocation with extracts of both woods. African maple produced an immediate fall in $FEV_{1.0}$ ranging from 12 to 54 %, while ramin produced a decline in $FEV_{1.0}$ of 11 to 25 % at 100 times the concentration of African maple.

Case studies of western red cedar *(Thuja plicata)*

Bridge (13) observed severe nasal symptoms in one woodworker and possible bronchitis in two others exposed to "Canadian red cedar" sawdust. Doig (30) is credited by many investigators with reporting the first case study, in 1940, specifically linking western red cedar *(Thuja plicata)* with symptoms of asthma. Ordman's patient (59) had a positive intradermal skin test to western red cedar *(Thuja plicata)*. Several Japanese reports from 1960 to 1968 described occupational asthma due to *Thuja plicata* and *Thuja standiski*, a Japanese cedar called nezuko (76). They included a case of asthma in a 33-year-old female furniture worker exposed to western red cedar who died after continual attacks of bronchial asthma.

The first thorough description of asthmatic symptoms and diagnostic procedures related to western red cedar exposure (see table 2) was reported in 1970 by three Australian researchers, Gandevia, Milne and Mitchell. In the discussion of their papers (38, 54, 55), these authors summarized the results of observations on 13 patients. Men without a personal or familial history of allergy or asthma suffered from symptoms in connection with the machining of western red cedar, but they worked problem-free with other woods. Initial complaints were of eye and nasal irritation, advancing to nasal obstruction and cough. The condition increased in severity with loss of exercise tolerance, development of wheezing, breathlessness, and nocturnal cough with phlegm production. The symptoms progressed to chronic asthma and occasionally persisted for several weeks after exposure ended. Smokers

Table 2. Respiratory health effects from case studies of exposure to western red cedar *(Thuja plicata)*. ($FEV_{1.0}$ = forced expiratory volume in 1 s, FVC = forced vital capacity)

Authors	Number of cases	Length of exposure prior to symptoms	Observed effects	Comments
Milne & Gandevia (54)	2	Days to 1 year	Western red cedar asthma confirmed by a decline in $FEV_{1.0}$ and FVC	Diagnosis not confirmed by any other tests; smoking data incomplete
Gandevia & Milne (38)	6 4	8 months to 8 years 3 weeks to 2 years	Western red cedar asthma confirmed by a decline in $FEV_{1.0}$ and FVC; rhinitis confirmed by three of four skin patch tests being positive	Negative skin patch tests; work histories not presented
Mitchell (55)	1	2 years	Western red cedar asthma confirmed by a decline in $FEV_{1.0}$ and positive skin patch tests	Nonsmoker
Chan-Yeung et al (22)	3	1 month to 3 years	Western red cedar asthma confirmed by a decline in $FEV_{1.0}$ (immediate and delayed) and positive skin patch tests for two of three subjects	No smoking data; negative serum antibody test
Cockcroft et al (25)	1	1 year	Western red cedar asthma confirmed by a delayed decline in $FEV_{1.0}$, a decline in FVC and maximum expiratory flow at 25 and 50 % vital capacity, an increase in closing capacity, and an increase in nitrogen washout	Ex-smoker; no effect seen for spruce dust
Hamilton et al (43)	1	Days	Western red cedar asthma confirmed by a dual decline in $FEV_{1.0}$	Ex-smoker
Blainey et al (10)	2	9 months for both patients	Western red cedar asthma confirmed by a late decline in $FEV_{1.0}$ and maximum expiratory flow at 50 % of vital capacity, and a late nasal airways resistance in one subject	No smoking information; no reactions to other wood dusts (pine, beech, obeche, deal) or lactose powder
Cockcroft et al (26)	2	Not stated	Western red cedar asthma (nocturnal) confirmed by a dual decline in $FEV_{1.0}$	Ex-smoker and nonsmoker; negative skin patch tests

and nonsmokers were affected, although smoking status was generally overlooked in these early studies.

Bronchial challenge tests with western red cedar dust and extracts of the dust showed immediate, delayed, and dual hypersensitivity response patterns. These responses were characterized by either a precipitous drop in $FEV_{1.0}$ and/or FVC within 45 min after inhalation (immediate) or a severe pulmonary function deterioration up to 24 h after exposure (delayed) or both reactions. In the authors' judgment, these severe responses were the best means to establish a diagnosis of western red cedar asthma (38, 54, 55).

Six additional papers, three from Canada (22, 25, 26), two from England (10, 61), and one from Australia (43), described ten additional cases of western red cedar asthma. When patients were challenged with aerosols of western red cedar, the reported symptoms were the same as in the Australian cases, and pulmonary function declines confirmed the diagnoses.

The effects of wood dust on lung function or on the development of asthmatic symptoms are usually described in case reports. The case reports summarized in tables 1 and 2 aid in the development of new hypotheses to be tested in epidemiologic studies. However, the lack of a comparison or reference group makes it difficult to draw conclusions on the underlying prevalence of illnesses associated with wood dust. Case studies generally provide a range of clinical impressions concerning symptoms, but they rarely address confounding effects such as smoking. Furthermore, case studies contain little exposure data other than a list of employment in a woodworking occupation and thus are uninformative regarding the extent of hazard.

Epidemiologic studies of woods other than western red cedar

The epidemiologic findings of respiratory health effects among woodworkers exposed to woods other than western red cedar have been summarized in table 3.

A 1976 NIOSH survey of a lumber mill in Washington state produced two studies examining symptom prevalence among workers exposed to Douglas fir *(Pseudotsuga menziesii)*, alder *(Alnus oregona)*, and hemlock *(Tsuga heterophylla)* (14, 33). Both studies indicated that 13.5 % of western red cedar shake-mill workers had symptoms of woodworker's asthma in comparison to 5.2 % in the lumber mill and 0 % among the office personnel (see the last entry in table 4). From the industrial hygiene survey the prevalence of woodworker's asthma showed a positive association with dustiness based on cedar concentrations but not on concentrations of other woods in the lumber mill. Occupational rhinitis and chronic bronchitis were much more prevalent among the shake-mill and lumber-mill workers than among the office personnel. Overall, the prevalence of total respiratory disease symptoms among the workers in the shake mill (40.5 %) and lumber mill (37.9 %) was over twice that among the office workers (16.0 %). Only among

Table 3. Epidemiologic studies of respiratory health effects among woodworkers exposed to woods other than western red cedar. ($FEV_{1.0}$ = forced expiratory volume in 1 s, FVC = forced vital capacity, FEV% = $(100 \times FEV_{1.0})/FVC$, K_{co} = carbon monoxide diffusion, MEF_{50} = maximum expiratory flow at 50 % of the FVC, MMF = maximum midexpiratory flow, TL_{co} = single breath lung transfer factor for carbon monoxide)

Author(s)	Types of wood exposure[a]	Number and source of case or exposed group	Number and source of reference group	Measure of effect and risk level	Comments
Brooks et al (14), Edwards et al (33)	Hemlock *(Tsuga heterophylla)*, Douglas fir *(Pseudotsuga menziesii)*, alder *(Alnus oregona)*	58 workers in a lumber mill	25 unexposed office workers; no airborne samples collected	Prevalence ratios for lumber-mill workers versus unexposed workers: rhinitis 5.6, bronchitis 2.8, all respiratory symptoms 2.4	No association with $FEV_{1.0}$ or with years employed; possible misclassification of exposure due to internal migration
Al Zuhair et al (2)	Chipboard and veneers (species unknown)	53 workers at a particle board and veneer plant (plant 1)	52 employees of inoperative power plant; no airborne samples collected	Decline in FVC over a shift ($P < 0.05$)	No difference in symptoms, but no data provided; finish workers not analyzed separately
	Limba *(Termenalia superba)*, beech *(Fagus sylvatica)*, ash *(Fraxis excelsior)*, mahogany (species not specified)	60 machine and cabinet shop workers and 11 office workers (plant 2)		Declines in base-line $FEV_{1.0}$ ($P < 0.001$) and FVC ($P < 0.01$)	
Whitehead et al (71)	Pine Hardwood (mostly hardrock maple, *Acer saccharum)*	220 pine furniture workers 354 hardwood furniture makers	Compared high, medium, and high/medium with low dust exposure levels	$FEV_{1.0}$ and MMF declined (for young males) among highly exposed smokers and nonsmokers; MMF and FVC declined ($P < 0.05$) among highly exposed smokers and nonsmokers; MMF showed log odds ratios of about 2 for hardwood and pine workers ($P < 0.02$)	No evaluation of symptoms; overused FEV_1/FVC as measure of group response
Beckman et al (7)	Pine	238 pine furniture workers [same source as in the Whitehead et al (71) investigation]	Compared subjects having symptom complex (low pulmonary function or chronic cough or chronic phlegm) with normals (using logistic regression)	Sex, age, and smoking fit the best model to symptom complex (significance $0.08 > \alpha \geq 0.001$); no effect for accumulated pine wood dust exposure	More appropriate methodology than in the Whitehead et al (71) investigation
Hedenstierna et al (45)	Pine	48 Swedish sawmill workers exposed to terpenes; assumed to be exposed to pine dust	47 workers unexposed to terpenes; both the exposed and reference groups compared to external pulmonary function values	Prevalence of mouth-throat symptoms greater among exposed smokers ($P < 0.05$); among nonsmokers greater prevalence of following symptoms: mouth-throat ($P < 0.01$), chest oppression ($P < 0.001$), morning cough ($P < 0.01$), cough during day ($P < 0.05$); among exposed workers base-line $FEV_{1.0}$ reduced ($P < 0.05$) and phase III $\%N_2$/l increased ($P < 0.01$)	Not adjusted for age or sex; did not directly compare exposed workers and referents with robust methods
Goldsmith (40)	White oak *(Quercus species)*, mahogany *(Swietenia macrophylla)*, andiroba *(Carapa species)*, poplar *(Liriodendron tulipifera)*, walnut *(Juglans nigra)*	55 sanders and cutters from a North Carolina furniture plant	23 finish workers and 16 workers unexposed to wood dust or finishing work	Frequent sneezing, odds ratio 4.0 ($P = 0.030$); eye irritation, odds ratio 4.1 ($P = 0.049$); stepwise regression for base-line peak flow and cumulative employment in dusty jobs ($P = 0.0345$); stepwise regression for postshift peak flow and fraction of particulate < 10 μm in size ($P = 0.0272$)	Overall study power low for detecting symptom differences; lack of personal exposure data (only area samples)
Carosso et al (17)	Assumed to be hardwoods	55 asymptomatic exposed workers (A), 15 exposed workers with cough and dyspnea (B_1), 20 exposed workers with dyspnea and bronchial hyperactivity (B_2)	53 laboratory employees (C)	Skin patch tests more positive for exposed workers with dyspnea and bronchial hyperactivity than for the other groups ($P < 0.0001$); analysis of covariance showed negative correlations between length of exposure and $FEV_{1.0}$ and MEF_{50} ($P < 0.01$); $FEV_{1.0}$, FEV%, MEF_{50}, TL_{co}, and K_{co} had negative correlations with length of exposure ($P < 0.01$)	Exposure levels for specific woods (or botanical names) not given; subjects assumed to be all men

[a] Botanical names in parentheses.

shake-mill workers exposed to western red cedar was a significant ($P < 0.001$) decline in $FEV_{1.0}$ detected during a shift (14), a finding not unexpected given the known effects of *Thuja plicata*. However, assuming migration between mills, one cannot attribute chronic symptom effects to each wood dust exposure or type of mill. Furthermore, the prevalence data were unadjusted for possible confounding by age, smoking, prior exposures, and social class.

Al Zuhair et al (2) compared pulmonary function during the workshift among British workers from two furniture plants with employees of an inoperative power station (referents). The workers were exposed to dusts from chipboard, unspecified veneers, limba *(Terminalia superba)*, beech *(Fagus sylvatica)*, ash *(Fraxinus excelsior)*, mahogany (species unspecified), oak *(Quercus species)*, and ramin *(Gonystylus bancanus)*. The authors reported that no differences in respiratory symptoms were found; however, no symptom data were provided. The level of $FEV_{1.0}$ and FVC among the machine and cabinet shop workers (including 11 office workers) in the second furniture plant showed greater mean declines in pulmonary function than the power-plant employees although the utility workers were older by 8 to 10 years. No dose-response associations were observed between loss of pulmonary function and dust level, although workers exposed to the highest dust levels in the second plant tended to show the greatest decline in $FEV_{1.0}$ and FVC. However, exposure to finishes was not analyzed separately, base-line pulmonary function values were not provided or analyzed, no dust samples were obtained at the power plant (reference), and no details were provided on the symptom prevalence among the woodworkers.

Whitehead et al (71) conducted a prevalence study of respiratory function among 354 hardwood (mostly *Acer saccharum* maple) and 220 pine furniture workers. The average dust exposure in the department where the subjects worked was multiplied by the number of years employed in that work area and summed to provide low, medium, and high categories of life-time dust exposure. The authors sought trends in mean pulmonary function levels categorizing their findings by smoking status, age, sex, and type of wood. Overall, no clear correlations were seen for the hardwood workers, although the FVC, $FEV_{1.0}$, and MMF rate[3] declined for current smokers at higher exposure levels among those older than 35 years of age.

The investigators next developed prediction equations for the pulmonary function values based on age, height, and sex. Among the workers exposed to hardwood dust, FVC showed inverse associations (lowest ratio of pulmonary function compared to predicted in the highest exposure category) for smokers and nonsmokers. Similar results were observed for MMF among the smokers and ex-smokers. Among the present smokers and ex-smokers exposed to pine, inverse associations were observed for $FEV_{1.0}$. MMF produced a clearer trend among ex-smokers and never smokers than among current smokers (71).

The authors classified the subjects as low or normal on whether their observed pulmonary function value fell below the lower fifth percentile of healthy nonsmokers. Among both types of woodworkers, only MMF showed statistically significant odds ratios of about 2.1 ($P < 0.02$), smoking having been adjusted for. Whitehead et al have suggested that measurable effects exist for wood dust exposure among pine and hardwood furniture makers. However, given the large number of comparisons, the small numbers of subjects in the low pulmonary function categories, and the lack of responses among nonsmokers, the authors' interpretations are difficult to accept.

Beckman et al (7) examined 238 pine furniture workers from Whitehead et al's study using logistic regression with maximum likelihood estimation. The outcome variable, respiratory dysfunction, was defined as decreased $FEV_{1.0}$ (less than the fifth percentile of normals) or positive response to questions about chronic cough or chronic phlegm on a questionnaire. Sex, age, and smoking were significantly correlated with respiratory dysfunction, but no effect was discerned for years of exposure to pine wood dust. These results are contrary to Whitehead et al's (71) for pine workers. However, the findings seem more plausible because the methodology used by Beckman et al appears to be more appropriate and robust for the continuous data than the categorical stratified approach used by Whitehead et al (71).

Hedenstierna and his colleagues (45) examined the pulmonary symptoms, spirometry and nitrogen (N_2) washout of 48 Swedish sawmill workers exposed to pine (terpenes) and 46 unexposed sawmill workers. The dust concentrations averaged 0.85 mg/m^3, while the mean terpene level was 254 mg/m^3. (Terpene levels had increased two- to threefold during the previous five years; historical dust concentrations were not presented.) Among the smokers only mouth-throat symptoms were significantly greater among the exposed workers than among the referents. Among the nonsmoking workers, those exposed to terpenes had significantly greater risk of the following symptoms: mouth-throat irritation, chest oppression (tightness), morning cough, and cough during the day, although there was no adjustment for age or sex. Among 24 exposed nonsmokers, there was a significant base-line decrement of 0.31 l in $FEV_{1.0}$ compared to external reference values when adjusted for age, sex, and height; closing volume and phase III % N_2/l were significantly higher in the exposed nonsmokers. These risks were not found among the referents, regardless of smoking status. When duration of employment was examined with linear regression, only phase III was sig-

[3] The authors reported that the MMF rate was reduced among the ex-smokers only (and omitted mention of FVC and $FEV_{1.0}$), but the published data are as described here.

nificant among the exposed smokers, whereas among the nonsmoking exposed millworkers there was no significant correlation between lung function and duration of employment. There were no acute changes in pulmonary function in a comparison of Monday morning (base line) values with Wednesday or Thursday afternoon values. It is unclear why the authors did not compare exposed workers directly with referents and did not use more robust methods such as multivariate regression. Although the current mean pine dust levels were low, it may be possible that base-line pulmonary function could have been a function of historically higher wood dust concentrations. However, because the research was on current terpene exposure, and not on wood dust per se, the relevance to pine dust exposure may be limited.

In 1984 Goldsmith (40) presented the first epidemiologic study of the hardwood furniture industry in southeastern United States. The author compared symptom responses and pulmonary function among the following three groups of furniture workers: those exposed to wood dust [55 sanders and cutters working mostly with oak *(Quercus species)*, mahogany *(Swietenia macrophylla)*, andiroba *(Carapa species)*, poplar *(Liriodendron tulipifera)*, and walnut *(Juglans nigra)*]; those exposed to finishes (23 workers); and those exposed to neither wood dust nor finishes (16 workers). With the use of logistic regression and adjustment for age, sex, and pack-years, none of the chronic pulmonary disease symptoms or asthma conditions were significantly correlated with exposure to wood dust; the only exceptions were positive responses to acute symptom questions asking if subjects had eye irritation or frequent sneezing while at work. These two replies were significantly ($P < 0.05$) correlated with wood dust exposure with odds ratios of 4.0. Using multivariate regression analysis, the author found no significant associations between base-line pulmonary function and dust or finish variables after adjusting for age, sex, height, and smoking (factors that explained 50 to 70 % of the variance). The exception was peak flow, which had a significant correlation ($P < 0.05$) with cumulative employment in wood dust jobs. Change in FVC over the workshift was correlated with finishing jobs after adjustment for age, daily smoking level, mass median particle diameter, and geometric mean ($P = 0.0203$). Difference in peak flow was significantly correlated with the fraction of particulates < 10 μm in size, after adjustment for age, daily smoking habit, and mean dust levels ($P = 0.0272$). Except for the correlation between change in peak flow and dust concentrations (particulates < 10 μm), there were no significant associations between wood dust levels and pulmonary function measured in the base-line examination or during the workshift. There were no interactions between smoking and either dust or finish exposure, and both may have been a result of the lack of personal dust sampling data or of low study power for the analysis of symptoms.

Carosso et al (17) compared pulmonary function and skin patch tests in three groups of Italian furniture workers and a reference group of laboratory workers. The woodworkers were administered symptom questionnaires, and on this basis were grouped as follows: group A — 55 exposed asymptomatic workers; group B_1 — 15 exposed workers with chronic cough and dyspnea on exertion; and group B_2 — 20 workers with dyspnea and bronchial hyperreactivity. Group C consisted of 52 employees from the investigators' laboratory staff. Group B_2 showed greater skin reaction than the other groups, although reactivity to specific woods was presented unclearly. After adjusting for age, height, weight, and smoking habits in a multivariate regression, the authors found that $FEV_{1.0}$, FVC, FEV % [$(100 \times FEV_{1.0})/FVC$], and maximum expiratory flow at 50 % of the FVC (MEF_{50}) were significantly ($P < 0.05$) lower in the B_1 group than in the other groups. The same results were observed for the single breath lung transfer factor for carbon monoxide (TL_{CO}) and carbon monoxide diffusion (K_{CO}), but not for alveolar volume. In addition, the means for FEV %, MEF_{50}, and K_{CO} were in the opposite direction, and $FEV_{1.0}$ showed the following trend: $B_1 < B_2 < A < C$. The means for TL_{CO} were in the opposite direction. The authors examined duration of exposure to wood dust using the analysis of covariance and showed a significant ($P < 0.01$) negative correlation for length of exposure versus $FEV_{1.0}$ and MEF_{50}. The findings for $FEV_{1.0}$, FEV %, MEF_{50}, TL_{CO}, and K_{CO} were significant for the duration of wood dust exposure and for the square of the duration of exposure. Although this paper has some drawbacks (lack of exposure data and types of woods), it suggests that wood dust exposure is strongly correlated with chronic obstructive lung disease among asthmatics. Furthermore, impaired pulmonary function was demonstrated in both symptomatic and asymptomatic woodworkers in a comparison with referents. The authors also showed that there was a significant reduction in K_{CO}, the K_{CO} of the asthmatics being lower than that of the healthy exposed workers and that of the healthy exposed workers being lower than that of the referents. Carosso et al ascribed the findings either to reduced capillary blood volume due to vasoconstrictive extractives in the wood dust or to a thickening of alveolar capillaries as a result of allergic responses.

Epidemiologic studies of western red cedar

Table 4 provides a summary of the epidemiologic studies of western red cedar asthma. Gandevia (37) studied 30 men highly exposed to western red cedar and 17 men with minimal or no exposure to the dust in the same Australian plant from which two cases of asthma came (38, 54). An association was found

Table 4. Epidemiologic studies of respiratory health effects among woodworkers exposed to western red cedar *(Thuja plicata)*. ($FEV_{1.0}$ = forced expiratory volume in 1 s, Gaw/Vtg = ratio of the reciprocal of airway resistance to thoracic gas volume, FVC = forced vital capacity, MMF = maximum midexpiratory flow, V60 % TLC = 60 % of the maximum total lung capacity)

Author(s)	Number and source of case or exposed group	Number and source of reference group[a]	Measure of effect and risk level	Comments
Gandevia (37)	30 highly exposed workers	17 workers with low or no exposure	Mean daily decline in $FEV_{1.0}$ and FVC greater in highly exposed workers, regardless of smoking status ($P < 0.025$)	Unadjusted for height and age; misclassification of exposure and pulmonary function tracings lessen confidence in results
Ishizaki et al (51)	1 320 Japanese furniture workers, 25 asthmatic responders skin patch tested with 10 % western red cedar extract	20 asthmatic nonresponders [spruce *(Picea species)*, lauan *(Sharea species)*]	Overall prevalence of asthma 4.5 %, rhinitis 9.5 %, hives 3.6 %, dermatitis 4.6 %, and conjunctivitis 9.5 %; highest prevalence in processing area	Pulmonary function not reported; no healthy referents examined; dermal responses only at a 10 % concentration of western red cedar; no effects for reference dusts
Mue et al (58)	17 woodworkers identified from a questionnaire and confirmed by clinical examination	22 asthma patients, 22 healthy referents	Odds ratio for positive skin patch tests 13.8 in comparison of woodworkers with both reference groups combined; 50 % of woodworkers had a greater than 20 % decline in $FEV_{1.0}$ and maximum expiratory flow at 50 % of vital capacity versus 0 % among 25 referents	No smoking data collected; also positive response in 13 of 16 cases using Prausnitz-Kustner test
Chang-Yeung et al (23)	22 patients with asthma from western red cedar	2 healthy volunteers, 4 bronchitics, 4 asthmatics	82 and 0 % of cases and referents, respectively, reacted to bronchial challenge with a decline in $FEV_{1.0}$	No serum antibodies found; skin patch tests produced mild responses to plicatic acid; no response to reference wood; validated response to plicatic acid; greatest response seen in V60 % TLC and Gaw/Vtg
Chang-Yeung (18)	16 responders to western red cedar	10 referents [Douglas fir *(Pseudotsuga menziesii)*]	100 and 0 % of the cases and referents, respectively, responded to plicatic acid	No serum antibodies found; skin patch tests produced mild responses to plicatic acid; no response to reference wood; validated response to plicatic acid; greatest response seen in V60 % TLC and Gaw/Vtg
Chang-Yeung (21), Ashley et al (4)	405 cedar mill workers	220 mill workers unexposed to western red cedar, 82 ex-cedar mill workers	Prevalence ratios for western red cedar workers versus unexposed workers (adjusted for age and smoking): breathlessness 2.3 ($P = 0.0002$), rhinitis 1.6 ($P = 0.04$), cough 2.0 ($P = 0.005$), phlegm 2.4 ($P = 0.002$), wheeze 1.8 ($P = 0.07$), conjunctivitis 1.8 ($P = 0.11$); overall prevalence of western red cedar asthma 1.1 to 4.9 %; MMF greater among workers exposed to western red cedar than among the referents ($P < 0.0001$)	Nonparticipants in study not surveyed to determine if they differed from the volunteers; no evidence of deterioration in pulmonary function over a week; data suggest possible synergy between exposure to western red cedar and smoking
Brooks et al (14), Edwards et al (33)	74 workers in a red cedar shake mill	25 unexposed office workers	Asthma associated with dustiness; prevalence for western red cedar exposure versus nonexposure: rhinitis 12.8, bronchitis 2.4, and all respiratory symptoms 2.5; decline in $FEV_{1.0}$ over shift ($P < 0.001$)	Likely to have been other wood dust exposures due to internal migration; results unadjusted for age, smoking, or social class

[a] Type of reference wood in brackets.

between rhinitis and asthma (all among nonsmokers) and work in jobs with high exposure to western red cedar (table 4). Among highly exposed red cedar workers, there was a decline in $FEV_{1.0}$ and FVC regardless of smoking status ($P < 0.025$), although the author noted that interobserver errors may have occurred in the grading of pulmonary function tracings. Gandevia expected greater declines in the heavily exposed workers, and he concluded that western red cedar is not a general bronchoconstrictor, such as was observed in the case studies of Gandevia & Milne (38), Milne & Gandevia (54), and Mitchell (55).

Ishizaki et al (51) conducted a study of red cedar asthma among 1 320 furniture workers in Kanuma, Tochigi Prefecture, Japan. The prevalence of asthma and rhinitis was highest in the processing work area (exposure assumed to be sanding and assembly), and conjunctivitis symptoms were greatest in sawing. Of the 60 identified asthma patients, 42 % were sensitive to cedar dust in intradermal tests. This paper is difficult to interpret because attention is so heavily focused on the 60 asthma patients, only 26 of whom reacted positively to the inhalation of red cedar dust, and there was no adjustment for atopic status. Inhalation of cedar dust produced inconsistent pulmonary function findings and, given the lack of healthy referents, the authors' interpretation that the skin test results confirm atopic response to western red cedar is not supported. There was no discussion of the confounding effects of age, sex, and smoking on symptoms, and

some computational errors hampered the interpretation of the results.

Mue et al (58) studied 17 asthmatic framemakers, 12 asthma patients, and 22 healthy referents and contrasted their dermatologic and respiratory responses to red cedar extracts. The cedar fraction saturated 30 to 60 % with ammonium sulfate was the most sensitive. Sixteen of 17 patients had positive skin reactions compared with only three of 44 referents; 50 % of the cedar asthma patients had a greater than 20 % loss of $FEV_{1.0}$ and a decline in MEF_{50} in comparison to none of the referents. The researchers also induced 100 % mortality from anaphylatic shock among guinea pigs sensitized to the same fraction of western red cedar. It was unclear why the extract required the ammonium sulfate, why only half of the original patients were studied, and why smoking was not controlled.

Chan-Yeung and her colleagues (18, 23) presented a pair of benchmark papers on western red cedar asthma. (See the fourth entry in table 4.) The authors studied 22 British Columbian woodworkers who had respiratory symptoms and were occupationally exposed to red cedar. The subjects' responses were compared to those of a reference group, none of whom gave a history of exposure to western red cedar. Eighteen of the 22 (82 %) woodworkers reacted to the red cedar extract with an immediate, late, or dual loss of $FEV_{1.0}$ or FVC, while none of the referents responded to the bronchial challenge. Douglas fir *(Pseudotsuga manziessii)* extract (used as a control dust) produced an insignificant decline in $FEV_{1.0}$ after provocation.

To analyze further the components of asthmatic responses produced by western red cedar, the authors prepared a dialyzed extract of cedar dust (23). This extract contained high molecular-weight substances and was administered to three responders without reaction. A second fraction, containing the nonvolatile components of cedar extract, was tested on two woodworkers and produced parallel declines in pulmonary function. Since plicatic acid is the largest proportion of the nonvolatile fraction, it alone was tested at half strength on 16 patients and on all the referents. Four immediate reactions, five late responses, and seven dual reactions were recorded along with the expected symptoms; no referents reacted to the nonvolatile extract. After recovery, four woodworkers were challenged again with the same dose of plicatic acid. The late asthmatic responses occurred earlier, and symptoms were more severe and more prolonged (23).

Chan-Yeung and her colleagues concluded that skin tests were of no value in diagnosis; bronchial challenge yielding early, late, or dual declines in $FEV_{1.0}$ was judged to be the best method of diagnosing western red cedar asthma (23). Plicatic acid, the major nonvolatile component of red cedar extract (40 % by weight) was judged to be the etiologic agent causing the western red cedar asthma syndrome. The authors concluded that the asthmatic responders were allergic to plicatic acid although the immunologic mechanisms remained to be determined. [Evans & Nicholls (35) subsequently demonstrated that red cedar has the same capacity as cotton dust to trigger histamine release in pig and human lung in vitro.] The paper of Chan-Yeung et al is important because of its demonstration of etiologic activity by plicatic acid in responders but not in referents (23).

In a companion article, Chan-Yeung (18) determined which measurements of airway response provided the best indicators of bronchoconstriction. She reported that the greatest response was seen in 60 % of the maximum total lung capacity (V60 % TLC), declining 60 and 80 % during initial and delayed reactions, respectively. The ratio of Gaw/Vtg[4] also declined precipitously in both immediate and late responders. The levels of reduction in the maximal expiratory flow volume curves depended on the severity of the bronchoconstriction.

Chan-Yeung and her colleagues (21) next conducted a prevalence study comparing 405 red cedar workers with two groups of reference workers, 220 sawmill workers never exposed to western red cedar, and 82 ex-cedar sawmill workers now working in British Columbian mills cutting other timbers (21). Adjusting for age and smoking, the authors reported prevalence ratios of about 2.0 for breathlessness, rhinitis, cough, phlegm, wheeze, and conjunctivitis when the western red cedar workers were compared to the noncedar exposed referents. Respiratory symptoms were greater among the ever-smoking exposed workers than among the nonsmoking exposed men, a finding suggesting synergism between the two factors. Although the prevalence of western red cedar asthma was 1.1 % among the exposed workers, the authors estimated the prevalence for ever-exposed workers to be about 4 to 5 % on the basis of the 4.9 % prevalence among ex-cedar workers. The higher symptom prevalence in the former group in comparison to that of currently exposed workers suggests that sensitized individuals tend to migrate to jobs where there is no exposure to irritating cedar dust. Thus, it is logical that workers remaining in cedar mills are a selected group that tolerates cedar dust exposure.

A companion article reported that there was little daily change in lung function and no evidence of deterioration in pulmonary function over the week (4). When the data were stratified on duration of dust exposure, greater lung function decline was observed among current smokers when the cedar workers were compared to referents. With the use of linear regression and stratification on duration of employment, the decline in MMF was greater in cedar workers than in unexposed workers among both the smokers and nonsmokers (4).

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[4] These measures are obtained on a body plethysmograph that determines airway resistance (Raw), its reciprocal (Gaw), and thoracic gas volume (Vtg).

Table 5. Epidemiologic studies of nasal symptoms among woodworkers. ($FEV_{1.0}$ = forced expiratory volume in 1 s)

Author(s)	Types of wood exposure[a]	Number and source of case or exposed group	Number and source of reference group	Measure of effect and risk level	Comments
Black et al (9)	Assumed to be hardwoods such as beech, oak, and mahogany	9 furniture workers from High Wycombe in the United Kingdom	12 nonwoodworkers, mostly researchers from an atomic energy plant	Referents' nasal clearance 6.8 (range 1.9—18.5) mm/min; only two exposed subjects had measurable clearance; rest classified as having mucociliary stasis	One snuff user from exposed group should have been excluded; some dysplasia observed in the cytologic examinations of the woodworkers' nasal mucosa
Andersen et al (3)	In order of quantity used: teak *(Tectonia grandis)*, oak *(Quercus species)*, chipboard, rosewood *(Dalbergia nigra)*, mahogany (species unspecified), jakoranda *(Machaerium species)*, beech *(Fagus sylvatica)*, ramin *(Gonystylus bancanus)*, motine *(Guibourtia arnoldiana)*, masonite, pine (species unspecified)	43 furniture workers exposed to wood dust concentrations of > 5 mg/m³	25 furniture workers exposed to wood dust concentrations of < 5 mg/m³	Higher exposed workers had excess symptoms of middle ear inflammation, sinusitis, prolonged colds, asthma, bloody nose, and rhinitis (significant but no P-value given); proportion of mucostatics increased as dust level (over five levels) increased (significant, but no P-value given)	Over a weekend two-thirds of a sample recovered normal nasal clearance; $FEV_{1.0}$ or forced expiratory flow at 25—75 % of the forced vital capacity did not correlate with the dust levels
Boysen & Solberg (12)	Teak *(Tectonia grandis)*, mahogany (species unspecified), bibo, ramin *(Gonystylus bancanus)*, koto *(Pterygota macrocarpa)*, oak *(Quercus species)*, beech *(Fagus sylvatica)*, chipboard (from pine and spruce)	113 Norwegian furniture workers from five well-established plants and employed at least six years	54 nonfurniture workers employed in chemical industry, 12 otolaryngological patients, and 18 workers from a hospital	Prevalence ratios for symptoms: nasal obstruction 4.0 ($P < 0.05$), allergy 2.0, and rhinitis 3.7 ($P < 0.05$); histological score of nasal dysplasia correlated ($R^2 = 0.16$) with nasal stenosis ($P < 0.001$) and number of years from first job ($P < 0.001$)	Exposure to hard and soft woods significant ($P < 0.05$) only in simple correlation
Wilhemsson & Lundh (73)	Assumed to be hardwoods	45 Swedish furniture and flooring workers from six plants; employed average of 15 years with wood dust exposure of 2.0 mg/m³	17 staff members from Department of Otolaryngology at the University Hospital of Huddinge	Prevalence ratios: columnar epithelium 0.76 ($P < 0.05$), ciliated columnar epithelium 0.57 ($P < 0.05$), goblet cell hyperplasia 5.50, metaplastic epithelium 1.60, and metaplastic cuboidal epithelium 2.42 ($P < 0.05$)	No association between rhinoscopic and histologic findings; identification of wood species could have aided specificity
Wilhemsson et al (72)	Assumed to be hardwoods	22 cases of ethmoidal adenocarcinoma among Swedish wood workers employed from 18 to 55 years	None	86 % (19 of 22) had cuboidal metaplasia; 69 % (16 of 22) had dysplasia	A reference group needed; tobacco habits not reported

[a] Botanical names in parentheses.

In 1977, Chan-Yeung conducted a follow-up study of 38 patients who had western red cedar asthma and had been unexposed for an average of 1.5 years (19). Of the group, 27 (71 %) became asymptomatic and 11 (29 %) had continued pulmonary symptoms. Of the latter subgroup, eight patients had recurrent bouts of asthma that coincided with upper respiratory infections or exposure to auto exhaust, cigarette smoke, or cold weather. The author could not determine whether bronchial hyperreactivity is the predisposing factor in western red cedar asthma or the result of the condition (19).

Ten years later Chan-Yeung and her colleagues (24) extended the follow-up to include 232 patients diagnosed with western red cedar asthma and traced their clinical status over an average of four years. There were four groups of patients studied: group 1 unexposed to red cedar and asymptomatic, group 2 unexposed to cedar and with symptoms, group 3 working with red cedar daily, and group 4 working with cedar intermittently. There were no significant differences in age, height, sex, or smoking habits between the groups. Atopic individuals were more likely to be in the exposed groups than in the unexposed ones. When examined, the patients in group 1 had significantly higher $FEV_{1.0}$, FVC, and forced expiratory flow at 25—75 % of the forced vital capacity (FEF_{25-75}) than the subjects in group 2. The provocative concentration of methacholine was higher among the asymptomatic patients than among those with symptoms of asthma and thus indicated that the asymptomatic group was diagnosed at an earlier stage. The authors suggested that early diagnosis and removal from exposure will benefit occupational asthma patients, particularly those with a confirmed diagnosis of western red cedar asthma.

Studies of sinonasal health effects

To examine early precursors of nasal cancer, investigations of nasal clearance and examinations of nasal mucosa were carried out in Great Britain, Denmark, Norway, and Sweden. The results of these investigations have been summarized in table 5. Black et al (9) studied mucociliary clearance in British furniture workers by blowing a microdrop of ^{99m}Tc-labeled styrene particles in saline into the subjects' nasal mucosa. The nasal clearance of 12 referents, mostly researchers at an atomic energy facility, was compared to that of nine furniture workers from High Wycombe. The referents' clearance was much faster than that of the furniture workers, whose clearance rates were so slow that a group rate could not be derived. Cytologic examinations of nasal mucosa from the furniture workers suggested some abnormalities, including squamous and metaplastic cells in four of the subjects. The referents' nasal cytology was not examined (9).

Andersen et al (3) studied mucociliary transport, respiratory function, and symptomology in 68 Danish hardwood furniture workers from eight plants. Nasal clearance was measured by the placement of a blue-stained particle (0.5 mm) of saccharin on the surface of the inferior turbinate. The subjects were instructed to report when a sweet taste occurred, and this occurrence was verified by the appearance of blue-colored mucus in the oropharynx. On the basis of the levels of wood dust in the breathing zones of the workers, the group was divided into those exposed to dust concentrations of > 5 mg/m^3 and those exposed to < 5 mg/m^3. Middle-ear inflammation, sinusitis, prolonged colds, asthma attacks, bloody noses, and rhinitis were more prevalent among those exposed to dust concentrations of > 5 mg/m^3. There were two modal points in the distribution of nasal transit time, at 14 min and at 40 or more minutes, the latter group being defined as mucostatic. The authors examined five mean levels of wood dust ranging from 2.2 to 25.5 mg/m^3, and there was a striking dose-response gradient observed for the proportion with mucostasis. At the highest level, 63 %, compared to 11 % at the lowest level, had mucostasis (3).

Boysen & Solberg (12) collected nasal biopsies from 113 Norwegian furniture workers and 54 referents. Histological samples were scored blindly for levels of dysplasia and analyzed with linear regression. Hyperplastic rhinitis, nasal stenosis, and allergies were two to four times more common among the furniture workers. Sixteen percent of the variance in the histological scores was explained by the presence of nasal stenosis and the number of years employed in the furniture industry ($P < 0.001$).

The nasal histology of woodworkers with and without nasal cancer was studied in two related studies (72, 73) from Sweden. Forty-five veteran furniture workers and 17 staff members from a department of otolaryngology received a histological examination of the mucosa of the middle nasal turbinate [the site where nasal tumors arise in exposed furniture workers (1)]. The workers had been employed an average of 15 years, and they had a mean wood dust exposure level of 2.0 mg/m^3. (Species of woods were not given.) The exposed workers had increased cuboidal metaplasia ($P < 0.05$), and the referents had greater columnar and ciliated epithelia than the exposed subjects ($P < 0.05$); but there was no correlation between the rhinoscopic and histological findings (73). Wilhelmsson et al (72) reviewed 22 patients who had ethmoidal adenocarcinoma and who had been exposed to wood dust for 18 to 55 years. They determined whether or not the adjacent nonmalignant tissues contained cuboidal metaplasia (72). The results indicated that 19 of 22 (80 %) cases had cuboidal metaplasia and 16 of 22 (69 %) cases also had dysplasia, although contrast with a reference group (such as chronic pharyngitis patients) would have made the findings more compelling. On the basis of these two studies, the investigators hypothesized that wood dust produces the following sequence of histological changes paralleling mucostasis: loss of cilia and hyperplasia of the goblet cells, initiation of cuboidal cell metaplasia, followed (after a quiescent period) by squamous cell metaplasia. After decades, cellular aplasia leads to adenocarcinoma of the nasal sinuses (73).

All five of the reviewed studies suggest that rhinitis and nasal dysplasia are common among veteran European furniture workers. Given the dose-response association for dust levels (3) and the relation between cuboidal metaplasia and ethmoidal adenocarcinoma (72, 73), nasal symptoms and cytological examinations (especially for those with mucostasis) need to be included in any comprehensive health survey of woodworkers.

Discussion of confounding and other biases

In any evaluation of the association between exposure to wood dust and the risk of respiratory disease, confounding factors must be addressed. Confounding factors are variables that, in a given study, are associated with both the exposure and the disease and also pose an independent risk of disease. Confounding should not be confused with effect modification where the presence of a third factor alters the association between exposure and disease but not at all the exposure strata. (An example might be slowed particle clearance from the nasal mucosa of heavy smokers but not from that of light or nonsmokers.) Leaving confounding variables unadjusted will lead to a spurious assessment of the strength of any association between wood dust exposure and respiratory disease. For end points such as reduced pulmonary function ($FEV_{1.0}$, FVC, and MMF), symptoms of respiratory illness (cough, phlegm, rhinitis, shortness of breath), and effects on normal respiration (impaired nasal clearance

or asthmatic attacks), confounding variables may include age, sex, and smoking (40, 53). Height may also be a confounder for pulmonary function, but sex is a surrogate for this factor, and, because most of the findings in this literature review have been reported for men, they are unlikely to have been confounded by gender.

Age is highly correlated with the amount of work experience and thus with the level and duration of exposure to wood dust. Advancing age also increases the risk of respiratory disease (57). Many of the case studies focused on veteran workers, but their responses occurred after many disease-free years of work with wood dust. Veteran workers must be viewed as a selected, resistant, and surviving population. That is, their reactivity appears only after other more sensitive workers leave employment because they could not tolerate the work conditions [as shown by the asthma prevalence among ex-cedar workers (21)] or because wood dust affected their health or because economic rewards were higher elsewhere. Thus reported risks in cross-sectional studies are likely to be underestimates of the respiratory hazards from current exposure to wood dusts.

Cigarette smoking is a powerful confounding factor because it affects not only the whole respiratory tract, but also other organs and tissues as well (27, 69), and has been shown in some studies of byssinosis (52) to be highly correlated with employment in dusty jobs. Cigarette smoking was overlooked in some early case studies, but later epidemiologic research appeared to be cognizant of its influence. Smoking also has the capability to interact synergistically with occupational dust exposures to produce a greater disease effect than two exposures separately (36, 52). It is worth noting that woodworkers, like workers in other occupations characterized by high levels of particulate exposure such as coal mining and grain handling, are forbidden to smoke on the job because of the fire and explosion hazard. Thus smoking woodworkers may consume fewer cigarettes than other industrial workers[5] (29), and therefore confounding or effect modification by smoking may not be as great as for other hazardous occupations such as the installation of asbestos insulation (65).

Acute health effects such as change in pulmonary function during a shift are less affected by confounding from sex, lifetime smoking histories, or other factors; however current smoking must be evaluated (40).

There are other possible sources of confounding, including current or past exposure to hazardous materials (such as asbestos, silica, cotton dust, and coal dust), personal or familial history of allergies, drinking of alcoholic beverages (6) (which is often closely linked to smoking), and additional exposures during work and leisure time (formaldehyde glues, radiation, refinishing work as a hobby). All of these factors may affect respiratory symptoms and pulmonary response to wood dust but may not be strong enough to bias the results. Furthermore, these possible confounders may not have been measurable or were not surveyed in the reviewed studies.

Biases in the measurement of either wood dust exposure or the classification of respiratory disease may also influence the estimation of risk. Sackett (63) presented an inventory of potential biases that led to either an under- or overestimate of the true risk of disease. Possible biases that might be relevant to studies of wood dust and respiratory disease include selection bias in the reference or exposure group (recall that, in reference 21, 82 of 203 or 27 % of the reference group of noncedar-mill workers were actually ex-cedar workers); interviewer bias (a possible problem in reference 3, where symptoms were elicited by the interviewers without a standardized questionnaire); diagnostic bias (reference 51 seemed to draw conclusions on skin testing from 60 asthma patients, more that half of whom did not have occupational responses); and misclassification of exposure [reference 2 assumed inappropriately that all furniture workers were exposed to wood dust (some worked in finishing) and that the referents were unexposed to particulates at an idle power plant]. Misclassification was also likely in references 14 and 33, in which in-plant migration between the planing and shake mills was not examined. Gandevia (37) thought there was misclassification of both exposure and impaired pulmonary function. Because the biases (such as misclassification of exposure) are unlikely to be equal between case and comparison groups, the direction of the risk measures (towards or away from the null value) is unknown; however, lack of a complete follow-up of worker cohorts due to selection is likely to underestimate the real risk of respiratory conditions (63).

Low study power hampers the interpretation of both reference 40 and reference 71, and all case studies lacking a reference group inhibit the drawing of unbiased conclusions regarding the respiratory toxicity of many types of wood. Identification of type of wood by botanical name was not done in some studies (17, 62, 66), nor were there adequate dust samples obtained in reference 40.

In conclusion case studies of many rare and exotic woods (abiruana, cedar of Lebanon, "Congo hardwood", kejatt, mahogany, ramin) suggest that exposed workers respond with eye, nose, and chest irritation. Extracts of some of these woods have also produced positive wheals when skin patch tests were done, but no response was seen for mahogany, oak, or cedar of Lebanon. Despite the variety of woods producing dermatoses (75), positive correlations

[5] Smoking prohibition on the job may also increase oral tobacco use and heavier smoking during leisure time to "make up" for the lack of nicotine intake during work-hours; these habits are liable to differ between cultures.

between respiratory effects and skin patch testing need to be better established.

Extensive studies have been done on a clearly defined asthma syndrome produced by exposure to western red cedar *(Thuja plicata)*. Plicatic acid was discovered by Chan-Yeung and her co-workers (18, 23) to be the etiologic agent in this syndrome. The western red cedar asthma syndrome includes rhinitis, conjunctivitis, wheezing, cough, and nocturnal attacks of breathlessness characterized by a precipitous decline in $FEV_{1.0}$ (the measure used in most studies) regardless of smoking status. Skin patch tests are not effective in the clinical diagnosis of the response to this wood dust.

Other commonly used woods such as oak, beech, redwood, pine, teak, alder, and hemlock produce pulmonary effects that are less well-described than the asthmatic responses to western red cedar. These symptoms include bronchitis, loss of pulmonary function during the workday or when exposed, and nasal mucociliary stasis. Nasal obstruction showed exposure-related findings for concentrations of wood dust in a Danish study of the furniture industry (3) and cuboidal metaplasia may be a precursor lesion for adenocarcinoma of the nasal turbinates (72, 73). There appears to be some evidence that smoking may exacerbate the risk of respiratory disease among woodworkers and that those exposed to high concentrations of wood dust have an increased risk of several pulmonary symptoms.

Wood dusts are composed mostly of lignin, hemicellulose, and cellulose, which by themselves and in small quantities (such as that produced by hobbyists) are not mutagenic or toxic (56). The presence of alkaloids, acids, and other natural constituents (which give color and grain to the timber) produces the pulmonary sensitivity. However, it is also likely that decades of exposure to fine wood dust also produces tissue injury that eventually initiates mucostasis and metaplasia and leads to adenocarcinoma of the nasal sinuses. In the light of respiratory cancer excesses among some woodworkers (1, 40, 49), pulmonary injury or symptoms should be examined as predictors of neoplasia. New surveys of woodworkers need to be done to estimate the prevalence of these health effects in active *and* retired workers. Because of existing risks for asthma, nasal cancer, and other respiratory conditions, there is need to improve the toxicity testing of woods and their constituents to elucidate the toxic properties better; particularly needed is improved hygienic sampling to examine dose-related responses and to assess interactive effects of combinations of dusts and finishes or adhesives.

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