CLINICAL ANALYSIS OF 22 CASES OF TOXIC PULMONARY EDEMA

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The pulmonary edema, caused by intoxication of irritant gases, is one of indications of severe intoxications. A violent or mild attack is depended on sorts and the concentration of the chemicals in the air. Being treated promptly, the courses would be commonly short and prognoses would be favourable. Three hundred and thirty-four cases of acute intoxication of irritant gases were treated in our institution in 1970–1987. Of these cases, 143 were the irritant reactions; 150 mild, 16 middle and 25 severe intoxication. There were 22 cases of pulmonary edema in the last group, accounting for 6.6% in all cases, 88% in the severe cases. They were 10 cases of nitrogen dioxide, 6 of chlorine, 2 of hydrogen sulfate, 1 of ammonia, 2 of dimethyl sulfate, 1 of phosgene intoxication. Twenty-one patients were recovered except a case of phosgene intoxication that died of ARDS. All patients were poisoned by breathing in high concentrations of irritant gases in a short time due to accidents. In two special cases, continuous localized rales could be found though the shadows on chest X-ray had been absorbed. The severity degrees, incubation periods, indications, X-ray showings and courses of pulmonary edema varied with the differences of sorts of poison, visiting times and treatment. Now we analyze these clinical data of 22 cases of toxic pulmonary edema by some poisons.

Cause of Poisoning

The cause of poisoning were breathing in high concentration of irritant gases in a short time period in accidents. Two pupils breathed in heavy chlorine and was poisoned in resident area in a chlorine leakage.

Clinical Data

The incubation periods were short in chlorine, dimethyl sulfate, hydrogen sulfate, ammonia. It took 30 minutes in a case of chlorine intoxication. While it was longer in nitrogen dioxide and phosgene intoxication, e.g., it took 24 hours in a case of nitrogen dioxide and 72 hours in a case of phosgene intoxication. The incubation periods of the rest 19 cases varied from 1 to 20 hours with a average of 4.3 hours. Most of the cases were between 1–7 hours (Table I).

The onset time and severity of symptoms and signs of pulmonary edema varied with different particularities (kinds) of irritant gases. For example, in pulmonary edema caused by water soluble poisonous gases, the upper respiratory tract symptoms were mild and the clinical expressions were generally the same, i.e., cough, suppressing in chest, breathlessness, white or pink sputum, hemoptysis, cyanosis, dyspnea, rales on chest (Table II).

In 10 cases of toxic pulmonary edema by nitrogen dioxide. Pulmonary signs disappeared earlier than shadows on chest X-rays. It took 13.7 days in average for the clearing of rales and 27.8 days for the shadows of pulmonary edema on chest X-rays to clear. In one special case we got reverse finding (Table III).

Treatment

After proper treatments, 21 cases were cured without any pulmonary sequela except one death with phosgene intoxication, the incubation period of which was 72 hours. In addition to symptomatic treatment, control of infection and pulmonary edema, the courses, to a great extent, were depended on whether administration of corticosteroid was given promptly or not. A short course was got when corticosteroid was given in time, otherwise, long courses were got with delayed or without such treatment (corticosteroid).

There were 3 cases in which the courses were more than 30 days and in which 2 cases were beyond 100 days without the administration of corticosteroid. It was established that pulmonary edema occurred in these 3 cases. The causes of delayed course were late visiting and no corticosteroid administration.

DISCUSSION

1. The clinical data of these 22 cases showed that incubation period of toxic pulmonary edema by irritant gases were related with the kinds, properties and concentration of poisons, e.g. the incubation periods of water-insoluble nitrogen dioxide were 5–11 hours mostly, those of water-soluble chlorine, were between 30 minutes to 1 hour. The incubation period, we should pay attention to this.

2. In 22 cases of toxic pulmonary edema, rale disappeared earlier than shadow on chest X-ray.

   On occasions when roentgenoscopy is not available, disappearance of rales should not be regarded as the criterion for the healing of pulmonary edema. In special cases continuous localized rales could be found though the shadows on chest X-ray had been absorbed. This may be due to the accumulation of secretions in the narrowed and deformed bronchioles damaged by poisons.

3. The course of pulmonary edema by irritant gases are closely related with administration of corticosteroid besides visiting in time, symptomatic treatment, prevention and control of infection. In cases with prompt

Table I
Incubation Periods of Various Poison Intoxications

Kinds	Cases	Incubation period (hours) 0.5	1	1.5	2	3	4	5	6	7	8	9	10	11	20	24	72
Chlorine	6	1	3		2												
Hydrogen Sulfate	2				2												
Ammonia	1					1											
Dimethyl Sulfate	2			1		1											
Nitrogen Dioxide	10							3		1	1	1		2	1	1	
Phosgene	1																1

Table II
Cases of Toxic Pulmonary Edema by Irritant Gases

Symptoms & Signs	Number of Case
Photophobia	1
Lacrimation	7
Ophthal Malgia	1
Coma	3
Headache	2
Dizziness	9
Nausea	8
Vomiting	4
Cough	18
Suppressing on Chest	16
Breathlessness	20
Chest Pain	3
Fever	8
Conjunctiva Congestion	8
Pharyngeal Congestion	6
Cyanosis	17
Dyspnea	17
Hemoptysis	4
Foamy sputum	11
Dry and Crepitant Rale	22

administration of corticosteroid after poisoning, the time of shadow absorption on chest X-ray were 7.4 days in average, while they were 98 days in cases without administration of corticosteroid and were 30 days in cases with delayed administration. There were 3 cases that their courses were more than 30 days and there were 2 cases their courses were beyond 90 days. These cases were believed that pulmonary edema occurred in initial poisoning.

The chronicity of these cases might be: (1) The chronicity of pulmonary edema, especially interstitial pulmonary edema state due to improper treatment; (2) The rebound phenomenon because the damaged epthelial cells had not completely recovered, even the minor infection would ignite recurrence of the edema state; (3) There might be obstructive bronchiolar alveolitis. There were reports that irreversible bronchiolar fibrosis might occur in the very rare untreated cases. What-

Table III

Comparison of Time for Rale and Chext X-ray Shadows Disappearance

Case	the Time of Rales (days) Clearing	the Time of Chest X-ray Shadow Disappearance (days)
1	5	8
2	6	9
3	7	7
4	3	6
5	10	10
6	7	4
7	6	8
8	15	95
9	19	30
10	19	101
Average	13.7	27.8

Table IV

In Influence of Administration of Corticosteroid on the Courses
(Disappearance of Shadow on Chest X-ray as the Criterion)

Groups	Number of Cases	Courses (days)
Prompt Steroid	7	7.4 (4-10)
Delayed Steroid	1	30
No Steroid	2	98 (95-101)

ever the causes, it can be completely cured without any symptoms left if corticosteroid is administered early.

In summary, the authors hold that in irritant gas intoxication, prompt treatment should be given and in the severe cases, especially if the symptoms of pulmonary edema appear, early and adequate administration of corticosteroid for a short course should be given.

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RESULTS OF A STUDY ON THE CHEMICAL COMPOSITION OF WOOD DUST AND THE ETIOLOGY OF BRONCHIAL ASTHMA IN WOODWORKERS

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The possible biological actions of wood dust are of an irritant, allergic, toxic, and carcinogenic nature. Besides the cutaneous disturbances, the most common pathologies found in workers at risk are respiratory and oculo-rhinitic; specifically, in the respiratory system wood dust can cause bronchial asthma, either of an allergic or pharmacoirritant nature. Therefore, studies have developed concerning: 1) the chemical composition of the type of wood, 2) *in vivo* and *in vitro* experiments regarding the toxicity of wood dust or its extracts and derivatives, 3) clinical and epidemiological observations of subjects at risk, and 4) environmental investigations in lumber workshops and yards.

This present work is related to the first group of research investigations in that it studies the chemical composition of the different types of wood through the use of TLC (thin layer chromatography); in relationship to the third group of studies it is related to clinical observations carried out in our occupational allergology out-patient clinic.

METHODS USED IN THE STUDY OF THE WOOD CHEMICAL COMPOSITION

Woods examined were chosen on the basis of information obtained from wood workers who came under our observation for respiratory disturbances, choosing those types of wood that were most often used or most often thought by the patients themselves to be responsible for their problems.

Before carrying out TLC, samples of the different types of wood were pulverized manually by rasping. Approximately 2 grams of finely ground and well dried wood dust were added to a solution of 95% ethanol and allowed to stand for 24 hours, to obtain an extract; an aqueous 1% HCl solution was added for the determination of alkaloids. We carried out chromatographic studies on these wood extracts, adapting a method recently proposed by the W.H.O. for phytopharmacological research,[6,7] which employs TLC. We used, for the TLC, plates of silica gel (Merk HF 254). For the elution of compounds containing different charges, a system of solvents analogous to that found in the literature[9] was used, according to the degree of polarity. After elution and subsequent drying in an oven, the plates were sprayed with several reagents in order to determine the main classes of compounds: Polyphenols, Terpenoids, Cardenolids, Alkaloids, Anthranoids and Coumarins. The eluents and the reagents used are listed in Table I. Furthermore, in lieu of specific reagents, the plates were sprayed with 2N H_2SO_4 to detect eventual organic compounds different from those studied above and which we shall call "non identified compounds"; at the moment, these shall not be taken into consideration.

It is noteworthy that TLC represents one of the most sensitive analytical techniques, capable of detecting quantities of substances on the order of a few micrograms (whereas the detection of compounds present in still smaller quantities requires a concentration of the extract). It reveals information not only regarding the categories of the substances extracted (polyphenols, alkaloids, etc.), but also their numbers (number of spots). At first, TLC can orient us as to the type of substance under examination, on the basis of its differential motion due to a difference of polarity (for example, if a terpene compound can be eluted with a low polar solvent, then it will be identified as a steroid terpene, while a saponine will be eluted with more polar solvents). Therefore, TLC analysis can be considered a preliminary step for deeper subsequent examinations.

The classes of compounds that we considered make up the major part of the secondary metabolites of woody plants that can be considered harmful for the organism: in fact, Polyphenols have irritative and sensitizing properties; Cardenolids have cardioactive effects; Alkaloids have systemic toxic effects and can bring about the liberation of histamine; Terpenoids have irritative and sensitizing effects and, in particular, saponins have hemolytic properties; some Coumarins have photosensitizing effects.[4]

RESULTS OF THE CHROMATOGRAPHIC ANALYSIS OF THE DIFFERENT TYPES OF WOOD AND COMMENTS

The results of the chromatographic examinations are contained in Table II and III. The woods tested are indicated with their commercial names followed by their scientific names and, in parenthesis, their family names. The results are expressed as the number of significant spots revealed in the nonconcentrated extracts; these spots are marked with an "x".

We grouped the woods into exotic and domestic and further distinguished the softwoods (conifers) from the hardwoods (latifolia). In general, exotic woods contain a moderate amount of Polyphenols and Cardenolids as well as Terpenoids, while the Alkaloids are present only in Asian Rosewood, Mansonian Walnut and Teak, and the Anthranoids only in Mansonian Walnut. Among the domestic woods there was a widespread presence of Polyphenols and

Table I

Eluents and Reagents Used for the Study of the Chemical Composition of Wood Dust Through the Use of TLC

ELUENTS (v:v) :	
E1	Toluene : Ethyl Acetate (1:1)
E2	Chloroform : Ethyl Acetate (1:1)
E3	Chloroform : Methanol (9:1)
E4	Chloroform : Acetic Acid : Water (50:45:5)
E5	1-Butanol : Acetic Acid : Water (4:1:5)
E6	Methyl Ethyl Ketone : Toluene : Methanol : Acetic Acid : Water (80:10:5:2:6)
E7	Toluene : Ethyl Acetate : Diethylamine (5:4:1)
REAGENTS :	
R1	Potassium Ferricyanide : Ferric Chloride (for Polyphenols: phenols, phenolic acids, flavonoids, tannins, catechins, coumarins, quinones, and stilbenes)
R2	Acetic Anhydride : Sulfuric Acid (for Terpenoids: terpenes, steroids, sterols, and saponins)
R3	Phosphomolybdic Acid (for reducing compounds: mainly appropriate for terpenes if associated with R2)
R4	3,5-Dinitrobenzoic Acid : Potassium Hydroxide (for Cardenolids)
R5	Basic Bismuth Nitrate : Acetic Acid : Potassium Iodide (for Alkaloids)
R6	Sulfuric Anisaldehyde (for Coumarins and Anthranoids, especially if associated with R1)

Terpenoids and a constant lack of Cardenolids, Alkaloids, and Anthranoids, that is, those classes of compounds having potential systemic pharmacological activity. In general, the larger amount of active substances contained in exotic woods with respect to domestic woods seems to account for the fact, at the present, that the former have a greater toxicity. Nevertheless, on the one hand, the presence of large amounts of accessory components in some domestic woods, such as Cherry, and, on the other hand, the scarcity of these components in some exotic woods, such as Obeche, make it unwise to generalize.

Instead, differences are less marked when comparing the presence of Polyphenols or Terpenoids; these were found in all examined except Mahogany, Obeche and Elm. It may be surprising that some softwoods (conifers), both domestic and foreign, examined by us contain no Terpenoids which are the most characteristic substances found in the Pine family; however, it is necessary to bear in mind that the analysis was carried out on well seasoned wood dust and, therefore, free of resins, and that some volatile terpene fractions can be lost during the initial phases of the techniques involved in chromatography. Furthermore, more work must be done on the "nonidentified substances" found in 3 of the 5 softwoods examined.

In the hardwoods (latifolia), in addition to the Terpenoids contained in Beech, Walnut, and Linden, large amounts of Polyphenols are present especially in Cherry, Walnut, and Olive. Because of the characteristics of such compounds chemical analysis allows us to confirm that these woods have a greater capacity for causing irritative and allergic reactions. Moreover, Colophony, contained in conifers, is a Terpene, and Plicatic Acid, found in Red Cedar, is a Polyphenol.[1,2] Such an observation, together with the results of clinical data, allows us to conclude that even domestic woods, rich in such substances, are to be considered as a potential cause of asthma, no less than exotic woods; in Italy, insurance protection exists only for the latter.

A first consideration that can arise from our study is a

Table II

Results of the Chromatographic Analysis of the Different Types of Wood (Exotic Woods)

Woods (commercial and scientific names)	Polyphenols	Terpenoids	Cardenolids	Alkaloids	Anthranoids & Coumarins	Non identified compounds
SOFTWOODS						
Douglas Fir Pseudotsuga douglasii Carr.	xxx	x	-	-	-	xxx
Pitch Pine Pinus spp	xx	-	-	-	-	x
HARDWOODS						
Afrormosia Afrormosia elata Harms.	-	xx	-	-	-	-
Asian Rosewood Dalbergia latifolia Roxb.	xxx	-	x	xx	-	-
Iroko Chlorophora excelsa Benth.	xxx	-	xx	-	-	-
Mahogany Shorea spp	-	-	-	-	-	-
Mahogany Entandrophragma utile Sprag.	-	-	x	-	-	-
Mansonian Walnut Mansonia altissima A. Chév.	xxxxx	x	xx	xx	x	-
Obeche Triplochiton scleroxylon K.	-	-	-	-	-	-
Padouk, Kejatt Pterocarpus spp	xx	x	-	-	-	xx
Ramin Gonystylus bancanus Kurz	-	xxx	-	-	-	-
Tanganyika Aniegré Aningeria altissima Aubr. P.	-	xx	-	-	-	-
Teak Tectona grandis L.f.	xxx	xx	-	x	-	-

deeper examination aimed at both woods with greater reactivity (Mansonia, Rosewood, Teak, Cherry, Larch, etc.), as well as woods that resulted in practically no reactivity (Such as Obeche), but which were reported in the literature as being responsible for pathological effects.[5] Another consideration that seems to derive from our study is the use of TLC methods in preliminary hygienic and sanitary investigations of work environments where lumber is employed for which adequate bibliographical references are lacking. A third line of development involves the chromatographic separation of the compounds through the use of TLC and the subsequent employment of the various fractions for pharmacological tests on animals, or for allergometric tests or bronchial challenge tests on workers at risk and symptomatic. For example, it is possible, using patch tests, to apply the single spots cut out from the chromatographic plates, and subsequently carry out skin tests or tests involving bronchial exposure with the same preliminary chromatographic fractions, dried and redisolved in controlled solutions. Furthermore, the analysis of different samples of the same wood did not always give rise to identical results (such as the Douglas Fir), and this can be explained, at least in part, by the different origin of the trees: and this is another reason for using, in the etiological research of the disturbances attributed to wood dust, the components extracted directly from the material supposed to be responsible.

CLINICAL CASES

We now report case history data regarding 86 wood workers observed during the past 5 years at the Institute of Occupational Health of the Catholic University of Rome for respiratory pathology problems. Table IV contains a summary of clinical history data concerning the subjects observed. The subjects were all of the male sex with an average age of 43 years and average work seniority of 18 years at that type of job. On the basis of the type of employment, they were divided into 2 groups: those exposed only to wood and those who were also exposed to paints (in this latter group we should take into consideration isocyanates and other components of paints as possible contributers to the genesis of the respiratory symptomology). All the subjects underwent a specialistic examination by an otorhinolaryngologist, a cranial radiography to evaluate the paranasal sinuses, a radiography of the chest, a spirometric examination, and

Table III

Results of the Chromatographic Analysis of the Different Types of Wood (Domestic Woods)

Woods (commercial and scientific names)	Polyphenols	Terpenoids	Cardenolids	Alkaloids	Anthranoids & Coumarins	Non identified compounds
SOFTWOODS						
Larch Larix decidua Mill.	xxx	-	-	-	x	x
Northern Redwood Pinus silvestris L.	-	xxx	-	-	-	-
Spruce Picea abies Karst	xx	x	-	-	-	-
HARDWOODS						
Ash Fraxis excelsior L.	xx	-	-	-	x	-
Beech Fagus sylvatica L.	-	xx	-	-	-	-
Cherry Prunus avium L.	xxxxxxx	-	-	-	-	-
Chestnut Castanea sativa Mill.	xx	-	-	-	-	x
Elm Ulmus campestris L.	-	-	-	-	-	xx
Linden Tilia cordata Mill.	-	xx	-	-	-	-
Maple Acer campestre L.	x	-	-	-	-	xx
Oak Quercus petraea Liebl.	x	-	-	-	-	-
Olive Olea europea L.	xxx	-	-	-	-	-
Walnut Juglans regia L.	xx	xxx	-	-	-	-

allergometric tests carried out by pick or i.d. test with allergens provided by the Lofarma Company and containing "Pollens," "Mycophytes," and "Inhalants" which include also 30 extracts of wood dust both from exotic as well as domestic woods. Furthermore, some of these subjects (chosen on the basis of history criteria, type of exposure, and type of referred pathology, and, moreover, excluding those that presented with serious impairment of respiratory functions of the obstructive type even at rest) underwent bronchial challenge tests which were both aspecific (with ultrasonic mist or methacoline) and specific with the more commonly used and suspected wood dust or with toluene diisocyanate (TDI) or both, depending on the circumstances. A reduction of at least 20% of the FEV_1 was considered as a positive result. In the meantime, it was not possible for us to carry out a skin test with TDI conjugated to human albumin. The more significant group of subjects with positive results for wooddust, that is, those 3 that responded to Tanganyika Aniegre both with the skin test as well as the bronchial exposure test, underwent a RAST for this type of wood.

RESULTS AND COMMENTS

After examining the results of our clinical case studies we can observe that the type of respiratory pathology found in the workers studied was made up of recurrent asthma crises in 45.3% of the cases, less than half of which also had oculorhinitic symptoms; in the remaining 54.7%, the symptoms were mainly bronchial. Among the clinical and functional findings observed in the 86 subjects, we noted: 1) the presence of chronic rhinopharyngitis in 58.2% of the cases; 2) radiological alterations of the paranasal sinuses in 46.7%; 3) an increase in the bronchovasal lung tissue in 73.3% of the cases and hyperdiaphany in 30%; 4) obstructive ventilatory deficit in 50% of the cases; and 5) mixed ventilatory deficit in 15% of the cases.

The cutaneous allergometric tests (Table V) were positive only in 13 subjects, amongst which 7 were positive for nonwork related allergens, 2 were positive for both work and nonwork related allergens, and 4 were positive only for work related allergens. The woods that resulted in a positive skin

Table IV
Clinical Data of Subjects Studied

Number	86	
Age (yr, mean and range)	43	(31-62)
Work seniority (yr, mean and range)	18	(5-38)
Current smokers	49	(56.9%)
Exposed only to wood	21	(24.4%)
Also exposed to paints	65	(75.6%)
Duration of symptoms at diagnosis (yr, mean and range)	4.6	(0.6-15)
Prevalence of symptoms (No. and %):		
Chronic cough and phlegm	47	(54.7%)
Asthma	39	(45.3%)
Work related:		
asthma	35	(40.7%)
eye symptoms	16	(18.6%)
nasal symptoms	23	(26.7%)
Clinical and functional findings (No. and %):		
Chronic rhinopharyngitis	50	(58.2%)
Radiological alterations of the paranasal sinuses	41	(46.7%)
Radiographic increase in bronchovascular marking	63	(73.3%)
Obstructive ventilatory deficit (in baseline FEV_1)	43	(50.0%)

Table V
Prevalence of Skin Reactivity to Common Allergens and Wood Dust Extracts (Prick or Intradermal Tests)

Subjects examined (No.)	86	
Positive for work related allergens	4(*)	(4.6%)
Positive for both work and non-work related allergens	2(°)	(2.3%)
Positive for non-work related allergens	7	(8.1%)
Negative	72	(84.8%)

(*) 2 positive to Tanganyika; 2 positive to Cherry
(°) 1 positive to Pine, Oak, Dermatophagoides pt., and some Mycophytes; 1 positive to Tanganyika and Graminaceous pollen

test in the 4 workers were the Tanganyika Aniegre (in 2 cases) and the Cherry (in 2 cases); in the two with mixed positive results, one case reacted positively to the Tanganyika Aniegre together with Graminaceous pollen, while the other reacted positively to Pine and Oak together with Dermatophagoides and some Mycophytes.

Table VI indicates those subjects who were positive only to the specific bronchial challenge test, both with woods and TDI; those subjects positive only to the aspecific bronchial challenge test, both with mist and methacoline; and those positive to both. The number of subjects who underwent the specific test was 25, of which 6 both for woods and TDI. Seven out of 13 subjects examined resulted positive to wood dust, and of these 7, 2 were also positive to ultrasonic mist. There were 10 out of 18 positive results to TDI; of these, 4 were also positive to mist and 1, in addition to mist, was also positive to Mansonian Walnut.

Table VI

Results of Bronchial Challenge Tests Both Specific (Wood Dust and TDI) and Aspecific (Metacholine or Ultrasonic Mist)

Subject examined (No.)	25 (of which 6 both for woods and TDI)		
Wood dust challenge test	Bronchial hyperreactivity test positive	negative	Total
positive	2 (*)	5 (°)	7
negative	3 (')	3 (")	6
TDI challenge test			
positive	4 (§)	6	10
negative	2	6	8
Total	11	20	31

(*) 1 positive to Tanganyika; 1 positive both to Mansonia and TDI
(°) 2 positive to Tanganyika; 2 positive to Mansonia; 1 positive to Cherry
(') of which 1 was negative to Pine and Oak, but had positive skin test with the same type of woods
(") of which 1 was negative to Cherry, but had positive skin test with the same type of wood
(§) of which 1 was also positive to Mansonia

The RAST for Tanganyika wood was done, according to the classical method, with an aqueous extract and binding the antigen to a solid polystyrol phase. The test resulted strongly positive in 2 out of 3 subjects (Table VII), while it resulted negative in that subject who had a positive skin reaction also for Graminaceous pollen and was also positive to the bronchial provocation test with ultrasonic mist. Our RAST results differ from those of other authors.[8]

A first finding of a certain interest obtained in our study is that in wood workers, harmful agents in professional exposure comprise not only wood dust but also many other factors that have irritative and allergic properties for the respiratory airways: in fact, the exposure to paints and solvents was significant in 75% of our cases. More than 50% of the carpenters observed by us presented prevalently with bronchial symptoms; but after an accurate history study involving the conditions of onset and the evolution of the symptomology, it was found that in about 50% of those subjects with bronchitis the disease had begun many years earlier with typical asthma crises, while the onset of the bronchitis was subsequent. We believe that this is due to the long time interval that elapsed between the beginning of the symptomology and the beginning of appropriate diagnostic examinations (on the average of 4.6 years in the entire group): it is worthwhile to emphasize the importance of carrying out allergometric examinations as early as possible, especially in those cases of asthma that arise in work environments.[3]

The clinical and functional findings stress a high incidence of alterations of the rhinopharynx and paranasal sinuses. This is in agreement with data found in the literature concerning damage produced by wood dust on the upper respiratory airways, with possible rhinitis that can also be hemorrhagic. In fact, the average diameter of wood dust is greater than 5 μ and this justifies its localization in the upper respiratory airways.[11]

In our case studies the allergometric skin tests, considered as a whole, were positive in 33.3% of the asthmatic subjects (excluding all those with bronchitis from the total) and this percentage is lower than that of other case studies conducted on non-professional subjects with asthma (up to 50–60% skin test positive). This could imply a prevalently non allergic cause for asthma due to wood dust. On the other hand, studies on the chemical composition of woods conducted by us have shown that in nearly all the woods examined there was a presence of Polyphenols or Terpenoids, compounds that have properties that are notoriously irritative or allergic. This, together with the consideration that the extracts on the market with which the allergometric tests are carried out are of a protein nature and, therefore, do not contain those substances which also have potential haptenic properties, tends to strengthen the hypothesis that, like for Plicatic Acid,[10] at least a part of the cases is due to sensitization to haptenes and another considerable part is due instead to a pharmacological-irritative type of reaction. In-

Table VII

Serum Rast Values for Tanganyika Extract Obtained in 3 Subjects Who Responded to This Type of Wood Both with the Skin Test as Well as the Bronchial Challenge Test

Subject	Age	Work seniority	Skin reactivity to common allergens	Bronchial hyperreactivity	RAST value
V. C.	43	15	-	-	+++ (15.0%)
S. A.	45	11	-	-	+++ (12.5%)
F. P.	37	12	+	+	- (0.9%)
5 control subjects			+		-

stead, in those cases with a positive skin reaction to the protein extract, we believe that an allergic pathologic mechanism is the most probable.

As far as the bronchial challenge tests are concerned, we note that only one subject had a positive result to mist, Mansonian wood, and TDI; one was positive to mist and Tanganyikan wood; and three were positive to mist and TDI. Five subjects who were positive to mist had negative results with wood dust or TDI; on the other hand, 5 subjects who were positive to wood dust and 6 who were positive to TDI had negative results with mist. Regarding the type of response to the specific test, in 9 cases it was immediate, in 6 it was diphasic, and in 2 it was delayed.

The results of the specific bronchial exposure tests would seem to confirm a certain selectivity in the response, even in those subjects with aspecific bronchial hyperreactivity; nevertheless, they give us no indication as to the pathogenetic mechanism of the broncospastic attack, which can be either pharmacoirritative or allergic. In 2 out of 3 subjects who had given a positive response both to skin tests and bronchial exposure provocation tests with Tanganyikan wood, the specific IgE dosage by RAST, was strongly positive, bringing us to the conclusion that there are specific IgE's towards protein constituents of the wood. In those subjects with a positive result to the bronchial challenge test with wood dust, but negative to the skin test with an extract of the same type of wood, an irritative cause of the bronchospasm could be an explanation. But another explanation could also be a sensitization to some non protein substance contained in this wood (a haptene). The next step of our research program is to carry out tests both in vivo (skin reaction, patch tests, bronchial challenge tests) and in vitro (RAST) with the fractions isolated with TLC.

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THE PREVALENCE OF BAKERS ASTHMA IN THE FR OF GERMANY —RESULT OF A PILOT-STUDY

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ABSTRACT

Chronic obstructive airways disease (COAD) of bakers is a serious occupational problem. Since atopic disease is very common, many bakers are at risk to develop allergy against flow dust and baking additives. We studied 367 bakers from a closed region to establish prevalence rates of COAD and bronchial hyperreactivity. Intracutaneous skin tests with several occupational and ubiquitous allergens were performed in combination with measurement of specific IGE (RAST) and histamin liberation of blood basophils. Prevalence of wheezing at working place was found in 8% of hyperreactivity 22% and pathological increase of basal airway resistance in 11% of all bakers. Bakers with positive tests to allergens and rhinitis had an increased risk in developing COAD but sensitivity of allergen testing and even rhinitis is too low, to clearly predict development of the disease. Allergy to flow dusts are common and often without clinical relevance. Controlling and minimizing exposure is most effective for prevention. There is no reason to exclude bakers from working place when only skin tests or other tests for allergy are positive. Early detection of COAD is the most important measure to prevent severe disease.

No Paper provided.

ASBESTOS-INDUCED LESIONS AND ASBESTOS BODY BURDENS IN PATIENTS WITH LUNG CANCER

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ABSTRACT

Lesions of asbestosis and small airway disease were scored and asbestos bodies (AB) counted in the lungs from 106 consecutive patients operated for bronchial carcinoma. The occurrence of pleural plaques detected by CT scan and during surgery was also recorded. Among the 106 cases, 19 were found to have high AB burdens when compared to a control autopsy population, essentially because of more frequent occupational exposures. The greater frequency of high AB burdens among men with lung cancer (19.4%) versus controls (3.9%) suggest thus a possible role of asbestos in the etiology of malignant disease. Lesions of minimal or slight asbestosis (peribronchiolar fibrosis and AB in sections) were detected in only 7 of the 19 cases (37%) and pleural plaques in 8 of 19 (42%). Nevertheless scores of fibrosis and pigmentation of the respiratory bronchioles were significantly higher in the patients with high AB lung concentrations than in the others, and these scores correlated strongly with smoking history (in pack-years). The results of this study suggest a synergistic effect between asbestos fibers and tobacco smoke in the development of bronchial carcinoma, even when there are no associated signs of asbestosis (or pleural plaques).

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THE EFFECTS OF SILICA DUST EXPOSURE ON SMALL AIRWAYS

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INTRODUCTION

Recently Churg et al[2] have shown that dust-exposed workers may have markedly abnormal small airway pathologic findings. When this group was matched by age, sex and smoking habit to a dust-exposed worker group without pathologic abnormality they concluded that the first group had abnormalities of air flow greater than those induced by smoking alone. In fact we still do not know what role may smoking play on the pathogenesis of silica induced airway changes. Nery et al[7] have very recently shown that smoking and silica exposure may have an addictive effect on pulmonary epithelial permeability of ceramic workers.

The purpose of this investigation was to analyze the small airway function of non smoking silicotic ceramic workers with at least ten years of dust exposure.

MATERIAL AND METHODS

We studied 46 non smoking ceramic workers with the diagnosis of silicosis based on occupational history of silica dust exposure and on radiographic features. Their mean age were 48.3 ± 8.6 years (mean ± standard deviation) and the mean exposure time of the groups was 22.6 ± 5.4 (range from 10 to 40 years). Five patients had tuberculosis in the past and one was bronchitic.

Standard spirometric tests were performed using a 9.0 l Godart spirometer and measured forced vital capacity (FVCO, forced expiratory volume in one second (FEV_1) and forced expiratory flow at 25-75% (FEF 25-75%); it was calculated the ratio FEV_1/FVC. Forced spirometric curve was repeated 10 minutes after the inhalation of a beta two adrenergic drug (fenoterol—200 mcg) and FVC, FEV_1 and FEF 25-75% were calculated by the isovolume technique.[4]

Maximal expiratory flow volume curves were obtained with a "bag in box" system.[9] The bag dislocation was sensed by a Validyne differential pressure transducer ± 2 cmH_2O and volume was integrated electronically. Curves were registered on a X-Y Tektronics Storage oscilloscope and copied on a plastic card. They were obtained breathing air and then after three inspiratory vital capacities maneuvers of a mixture of 80% of helium and 20% of oxygen (HeO_2).[5] The best fit of three curves for air and HeO_2 were drawn and they were superimposed and matched at residual volume if the vital capacities were unequal. We calculated the flow at 50% and 25% of the curve breathing air ($\dot{V}$max 50% and $\dot{V}$max 25%) and at the volume were both curves had the same flow (Viso$\dot{V}$).[7]

Chest radiograms were classified according to ILO Classification, 1980.[3]

RESULTS

As there was a large variability in the radiological appearances concerning profusion, size and shape of the regular and irregular small opacities we grouped them according to the predominant lesion. We found 25 individuals with 1/1 profusion, 13 with 2/2 profusion and 8 with 3/3 profusion; 37 of them (80%) had a predominance of the p/p small opacities.

Spirometric parameters were considered as normal if the predicted values for FVC and FEV_1 were above 80%, above 60% for FEF 25-75% and above 70% for the ratio FEV_1 /FVC. Thirty five individuals (76.1%) were classified as having normal spirometry and 11 (23.9%) as having some degree of pulmonary impairment[9] predominantly obstructive and 2 restrictive).

The opposite was observed with the analyzis of flow-volume curve and isoflow volume; considering as an abnormal result the presence of at least one altered parameter ($\dot{V}$max 50%, $\dot{V}$max 25% or Viso$\dot{V}$) we observed that the abnormal results (71.7%) predominated over the normal ones (28.3%). These percentages differed significantly from the ones obtained with spirometry ($p < 0.05$).

The analysis of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$in the 33 individuals with normal spirometry show that 24 of them had already some degree of airflow abnormality (Figure 1).

$\dot{V}$max 25% could significantly detect more abnormalities than the other 2 parameters ($p < 0.05$) (Table I).[6]

After 200 mcg of inhaled fenoterol 61.4% of the group (27 out of 44) increased their FEF 25-75% by at least 15% (46.1 ± 36.6% increase); 24 out of 27 increased by 25% or more. Twenty individuals of the responsive group had normal spirometry (74.1%) and showed an increase in FEF 25-75% of 47.2 ± 38.4%, a very similar increase presented by the 7 responsive silicotics with abnormal spirometry, 40.1 ± 30.4% (Table II).

There was no association between the small opacities pro-

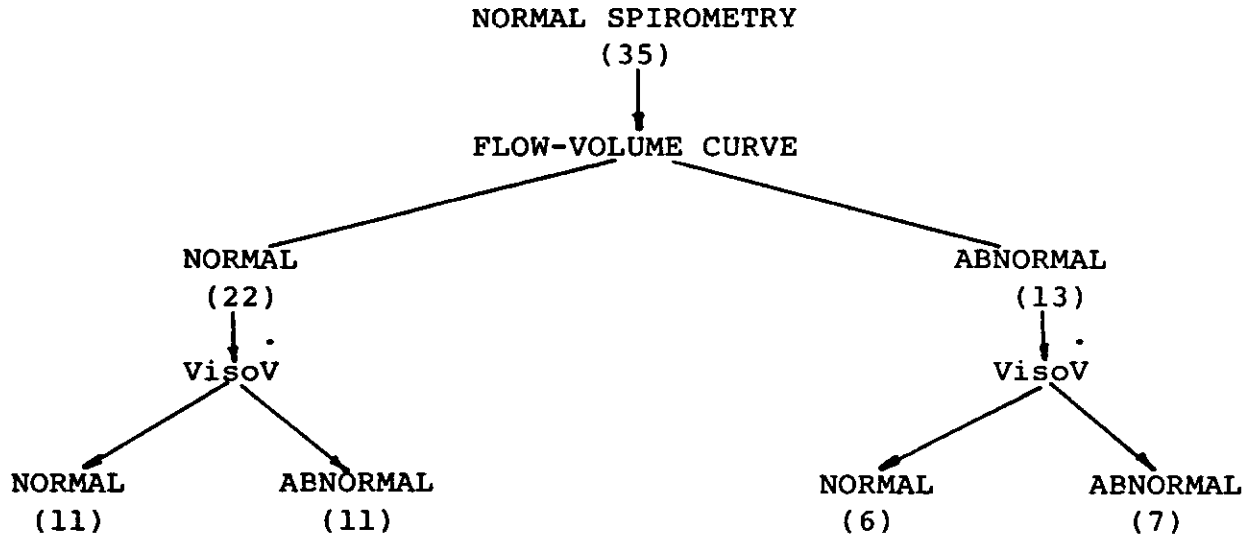

Figure 1. Diagram showing the distribution of the 35 individuals with normal spirometry after they performed a flow volume curve breathing air and helium for the analysis of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$.

Table I

Distribution of Normal and Abnormal Values of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$ in 46 Individuals Exposed to Dust Silica

	ABNORMAL VALUE	NORMAL VALUE	TOTAL
$\dot{V}$max 50%	12	34	46
$\dot{V}$max 25%	22	24	46
Viso$\dot{V}$	21	25	46

fusion and the response to bronchodilator (Table III) or flow volume-isoflow abnormalities (Table IV).[10]

DISCUSSION

We have shown that flow-volume curves breathing air and a mixture of HeO_2 are able to detect a large number of individuals with airflow obstruction that otherwise would be classified as normals. Isoflow volume was abnormal in 50% of the individuals with normal spirometry while $\dot{V}$max 25% alone would detect 33.3% of them. The combined use of $\dot{V}$max 50%, $\dot{V}$max 25% and Viso$\dot{V}$ were altered in 24 individuals with normal spirometry, a 66% early detection. Despite the fact that Viso$\dot{V}$ has been described for a long time as a tool for early diagnosis of small airway disfunction it has not largely been used in occupational medicine.[7,11]

There seem to be no influence of the length of exposure since the group exposed from 10 to 20 years and the one exposed over 20 years presented very similar Viso$\dot{V}$ values, 11.7% and 12.7%, with 40% of abnormal individuals in each group.

The second point we want to stress is the increased bronchial motor tonus these individuals presented; approximated 60% of the ones with normal spirometry (the same percent for the whole group) responded to inhaled fenoterol with an increase in their FEF 25-75%. There was a slight negative correlation between the initial value and the FEF 25-75%

Table II

Association of Bronchodilator Response (Concerning a 15% Increase in FEF 25–75%) to the Normality or Not of the Spirometric Values

BRONCHODILATOR RESPONSE	SPIROMETRY		
	NORMAL	ABNORMAL	TOTAL
POSITIVE	20 (60.6)	7 (63.6)	27
NEGATIVE	13 (39.4)	4 (36.4)	17
	33	11	44

Table III

Association of FEF 25–75% Increase (Positive Response) to Bronchodilating Drug and Small Opacities Profusion in the Chest X-ray of 44 Non-smoking Silicotics (Non Significant)

	X-RAY PROFUSION			
	1/1	2/2	3/3	TOTAL
POSITIVE	13	9	5	27
NEGATIVE	11	4	2	17
TOTAL	24	13	7	44

Table IV

Association of Altered $\dot{V}$max 50%, $\dot{V}$max 25% or Viso$\dot{V}$ to Small Opacities Profusion in the Chest X-ray of 46 Non-smoking Silicotics (Non Significant)

$\dot{V}$/V and Viso$\dot{V}$	X-RAY PROFUSION			
	1/1	2/2	3/3	TOTAL
NORMAL	18	7	8	33
ABNORMAL	7	6	0	13
TOTAL	25	13	8	46

response (r: -30, $p < 0.05$). As these individuals were not smokers and had no symptoms of asthma we conclude that silica dust is the causal agent of this abnormal response.

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EXPOSURE TYPE RELATED PULMONARY SYMPTOMS IN DENTAL LABORATORY TECHNICIANS—RESULTS OF A QUESTIONNAIRE SUPPORTED SURVEY

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ABSTRACT

Dental laboratory technicians (DT) are exposed to various dusts including quartz and alloys containing Co, Cr and Mo, both arising predominantly in model casting technique (MCT) presumably to be responsible for pneumoconiosis in DT. In order to assess the influence of occupational dust exposure on pulmonary symptoms questionnaires were mailed to 3,415 West German dental laboratories employing 24,588 DT. 5,238 questionnaires were returned; 4,328 qualified for assessment. 51.7% DT had experience in MCT, 69.7% in processing precious alloys (PAT), 85.9% in dental resins (DRT); ceramic techniques were less often used. Simultaneous practice of several techniques was common. ***Methods:*** In order to evaluate the effect of different exposure types on pulmonary symptoms by multivariate analysis we computed exposure time differences in MCT, PAT and DRT, controlling smoking habits, sex, age and even the total time of work in dental laboratories. ***Results:*** Male smoking DT who complained the following symptoms were significantly (WILCOXON) longer exposed in MCT than the nonsymptomatic: Dry cough ($p<0.01$), cough with phlegm ($p<0.05$) and breathlessness on exercise ($p<0.01$), conversely cough with phlegm was related to significantly shorter time in DRT for all subgroups. ***Conclusion:*** In concordance to casuistic reports and own clinical studies on 104 DT these epidemiological data strongly indicate a causal relationship between exposure in MCT (probable due to Co-Cr-Mo alloys and quartz) and pulmonary disease of DT. Cigarette smoking seems to exert an important synergistic influence.

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