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A M E R I C A N C O L L E G E O F
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Validation of an Exposure System to Particles for the Diagnosis of Occupational Asthma*

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Study Objective: We previously described a closed-circuit system for exposure to particles in humans. This system has three components: a particle generator, an exposure chamber connected to an orofacial mask, and monitors. We describe results of challenges in 56 subjects who underwent challenges with the apparatus using occupational sensitizers in particles.

Subjects: Fifty-six consecutive subjects referred for the investigation of occupational asthma to occupational sensitizers in particles were included. The agents were the following: flour and grains ($n=19$), cedar ($n=10$), psyllium ($n=9$), guar gum ($n=9$), drugs ($n=3$), persulfate ($n=2$), and miscellaneous ($n=4$).

Intervention: The duration of exposure was progressive and varied from one breath to a maximum of 180 min depending on the reaction. When no significant fall in FEV₁ occurred after exposure with the aerosolization device, the standard approach of tipping particles from one tray to

another was used.

Results: Twenty-nine subjects (52 percent) had a significant (≥ 20 percent) fall in FEV₁ after exposure. This includes 18 subjects with isolated immediate reactions, four with dual asthmatic reactions, and two with atypical reactions. In 20/24 instances (83 percent), the percentage of fall in FEV₁ did not exceed 30 percent, thus showing that dose-response curves can generally be obtained in a safe way. In all instances except one (26/27 cases), subsequent exposures using the traditional method did not result in significant falls in FEV₁.

Conclusion: This new procedure results in safe tests in terms of the percentage of changes in FEV₁ during the immediate reactions and very rare false-negative challenges. (Chest 1992; 102:402-07)

OD = optical density; PEFR = peak expiratory flow rate; TLV-STEL = accepted upper level for short-term exposure

Specific inhalation challenges using occupational sensitizers were proposed in the 1970s by Pepys and Hutchcroft¹ in the investigation of occupational asthma. These tests have since been considered as the gold standard in confirming the diagnosis. Indeed, neither the medical questionnaire addressed by experienced physicians² nor the immunologic assessment,^{3,4} have a sufficient validity to properly advise a worker or an employer on an individual basis. Although serial measurements of peak expiratory flow rates (PEFR) has been advocated,^{5,6} there are several pitfalls to this approach: collaboration and honesty from the worker, interpretation of graphs, and difficulty in disclosing nonspecific irritant reactions. Figures for sensitivity vary from 81 percent to 86 percent and, for specificity, from 74 to 89 percent.^{7,8}

Occupational sensitizers are in particle form in approximately one third of our challenges. In an effort to improve the safety of the test and to obtain information on the concentration and diameters of inhaled particles, we previously described a new aerosolization device.⁹

The aim of this work is to report on the validation

of the apparatus in a larger number of subjects.

MATERIAL AND METHODS

Apparatus

As previously described and shown in Figure 1, the apparatus consists of three parts: a particles generator, an aerosol delivery system connected to an orofacial mask, and monitors—a photometer and a cascade impactor.⁹ The dry powder (dessication made beforehand) is placed into a small plastic box (dimension = $10 \times 10 \times 6$ cm) that undergoes constant vibration. The vibrator feeds the powder into an endless screw that collects it at the bottom of the reservoir and brings it to a rotating plate. The magnitude of vibration of the reservoir, the speed of rotation and diameter of the screw, the speed of rotation of the plate, and the negative pressure in the vacuum can all be regulated in the aerosol delivery system. A vacuum is created by compressed air. The air leaving the generator, to which is added compressed air, is directed through a Venturi effect into the aerosol delivery system, a horizontal cylinder of plexiglass (109×13 cm). A hole in the wall of the cylinder allows the subject to breathe the aerosol through a face mask. A unidirectional thin membrane prevents particles from escaping through the face mask if the subject is not breathing through the apparatus. Expired air is directed to a tube that removes it from the laboratory through a closed ventilation system. Flow of air in the cylinder is adjusted to maintain a slight positive pressure ($+2$ cm H₂O). During aerosolization, powder concentration is measured and recorded on paper by a photometer located 4 cm from the subject's mouth. The diameter of the aerosolized particles was assessed once for each type of powder by a cascade impactor, 4 cm from the subject's mouth. The percentage of inhaled particles according to their size was then determined by weighing the filters of the cascade impactor. The aerosol was inhaled by the subject at tidal volume breathing through the mouth. The device was regulated to obtain concentra-

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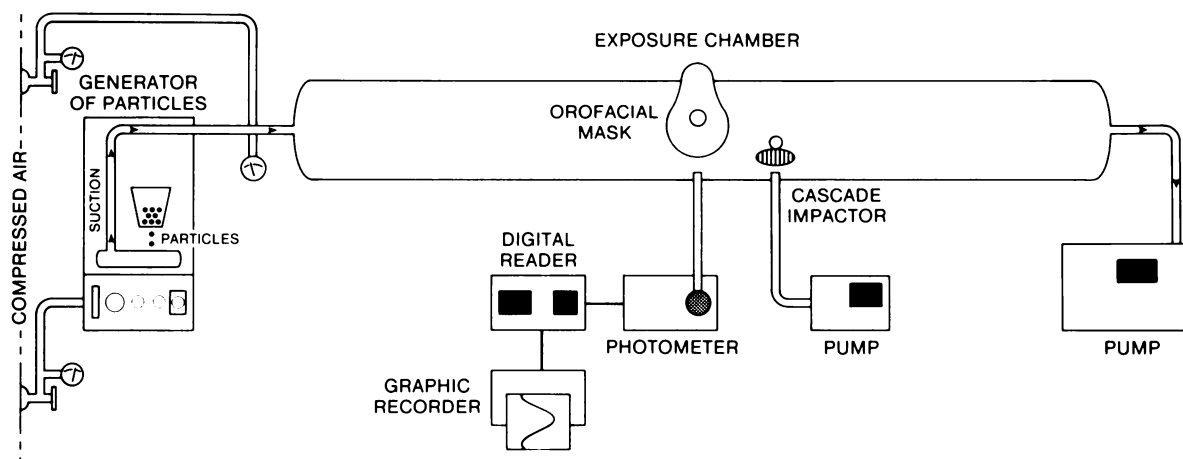


FIGURE 1. Aerosolization device made in three parts: (1) the generator of particles on the left end in which the particle is vibrated, taken to the rotating plate by an endless screw and sucked out; (2) the exposure chamber as such, a 100-cm long plexiglass cylinder with three holes in the center, one for the facemask, one for the photometer probe, and one for the cascade impactor probe; and (3) the recording instruments, ie, the photometer and the cascade impactor.

tions close to or below 10 mg/cu m, the accepted upper level for short-term exposure (TLV-STEL) to soft wood dusts. TLV-STEL had not been determined for the other powders used in this study, but the same TLV-STEL as for wood dusts was used as these also represented agents in powder form. The rationale for keeping concentrations low was in order to avoid nonspecific irritant reactions. The products were ground to reduce their particle size distribution and aliquots from the same initially prepared dust were used. Particles were desiccated and not reutilized. The photometer assesses the density of particles but not the mass. The constant factor to transform the density into mass therefore had to be obtained for each product by weighing the total in the cascade impactor during the procedure.

Subjects

Fifty-six subjects referred for the investigation of occupational asthma from 1986 to 1990 underwent specific inhalation challenges. Table 1 lists the relevant anthropometric, clinical, and functional information. All subjects had a history that was suggestive of occupational asthma and were in a clinical steady asthmatic state at the time of challenges.

Methods

Treatment with medications was withheld in the intervals recommended.¹⁰ Subjects receiving anti-inflammatory medication continued using these preparations during the challenge period but did not take their dose in the 8 h before the challenge. After a control day of exposure to another dust (lactose in the case of all agents except for wood dusts for which a control wood dust made of local species of fir trees, spruces, and Jack pines was used) for 30 min, subjects were exposed on the subsequent day(s) to the relevant occupational sensitizer. For substances for which an immediate bronchospastic reaction was suspected on the grounds that the mechanism was IgE dependent (flour, psyllium, guar gum, grain), increasing durations of exposure on the same day were set in the following way: one breath, 10 and 30 s, 1, 2, 5, 15, 30 min, etc, for a maximum total duration of 120 min except in one patient for whom it reached 180 min. For sensitizers whose mechanism is unknown and which are more likely to cause isolated late reactions, the increase in duration of exposure was progressive on a day-to-day basis (1, 5, and 30 min, 2 h). Twenty-seven subjects were exposed for 0 to 30 min, 13 were exposed from 31 to 60 min, 14 were exposed from 61 to 120 min, and two were exposed for more

than 120 min. Spirometry was assessed before exposure and after exposure, immediately, every 10 min for 1 h, every 30 min for 1 h, and hourly for 7 to 8 h. The 27 subjects who did not show a fall >10 percent in FEV₁ after being exposed to the aerosolization device were exposed either on the same day or on a subsequent day to the particles by asking him to tip the dust from one tray to another for periods ≥60 min, except in five subjects who started hyperventilating or refused to do the tipping for a period longer than 15, 18, 30, 37, and 45 min, respectively. The reason for not exposing subjects who reacted with the apparatus by the tipping method is that the tipping method results in much higher concentrations than with the apparatus. It would therefore be very unlikely that subjects had not reacted by the tipping while reacting with the

Table 1—Baseline Anthropometric, Clinical, and Functional Results

Factor	No.
No. of subjects	56
Sex, M/F	41/15
Age, yr, mean ± SD	40 ± 13
Atopy	33 (59%)
Medication	
None	15
Bronchodilators	23
Bronchodilators + anti-inflammatory drugs	18
Baseline FEV ₁	
Mean ± % pred	98 ± 18
No. with values <80% pred	10
Baseline PC 20, mg/ml	
0.03-<1	12
1-16	34
>16	10
Occupational sensitizers	
Flour	17
Cedar (Western red and Eastern white)	10
Psyllium	9
Guar gum	9
Drugs	3
Grain	2
Persulfate	2
Miscellaneous	4*

*Trimellitic anhydride, dye, azodicarbonamide, ash wood dust.

apparatus.

The mean $\pm$ SD concentration of particles at which subjects were exposed was 2.99 ± 1.68 optical density (OD) as read on the photometer. Considering the correcting factors that were obtained previously to determine the relationship between the mass of particles measured by the photometer and their actual weight and which vary from 1.6 to 4.5 mg/cu m depending on the particles,⁹ subjects were exposed to concentrations below or close to 10 mg/cu m, which is the recommended threshold limit value—short-term exposure (TLV-STEL). Keeping the concentration of particles low was relevant in order to avoid nonspecific irritant reactions in asthmatic subjects. The percentage of particles $\leq 10 \mu\text{m}$ (respirable dusts) varied from 30 to 87 percent depending on the dust as detailed in a preceding article.⁹

FEV₁ was assessed according to the standards of the American Thoracic Society.¹¹ Methacholine or histamine inhalation tests were done at the end of the control day. This was performed according to a standard methodology with a nebulizer (Wright) (output = 0.14 ml/min) for 2 min at tidal volume breathing.¹² The provocative concentration of methacholine or histamine causing a 20 percent change in FEV₁ was interpolated from the individual dose-response curves.

Analysis of Results

Significant changes in FEV₁ were set at ≥ 20 percent falls. Predicted values for FEV₁ were taken from Knudson and coworkers.¹³ Atopy was defined as at least one immediate skin reaction to 15 inhalant allergens. Significant bronchial hyperresponsiveness was defined at a PC 20 ≤ 16 mg/ml.¹⁴

Chi² analysis was used in the statistical analysis of results.

Table 2—Duration of Exposure and Reactions during the Immediate Component in the 22 Subjects with Immediate and Dual Reactions*

No.	Agent	Last Exposure		First Previous Exposure		Second Previous Exposure		Third Previous Exposure		Fourth Previous Exposure	
		Duration	% Fall FEV ₁	Duration	% Fall FEV ₁	Duration	% Fall FEV ₁	Duration	% Fall FEV ₁	Duration	% Fall FEV ₁
1	Flour	70'	43	30'	8	10	5	...	...	...	...
2	Psyllium	4'	20	2'	17	1	16	40"	14	15"	7
3	Guar gum	2'	22	1'	17	45"	16	15"	6	...	...
4	Flour	15'	23	10'	15	5'	5	...	...	...	...
5	Psyllium	1	30	15"	11	1 breath	7	...	...	...	...
6	Guar gum	30"	25	15"	14	1 breath	7	...	...	...	...
7	Flour	15'	20	15'	15	15'	15	5'	10	2'	10
8	Flour†	...	...	...	...	...	...	...	...	...	...
9	Grain	30'	24	15'	9	10'	7	5'	7	...	...
10	Guar gum	2'	21	2'	17	40"	6	1 breath	...	...	...
11	Psyllium	30"	35	45"	15	15"	13	30"	6	...	...
12	Flour	2'	28	1'	15	1'	13	15"	13	...	...
13	Psyllium	60"	20	45"	19	30"	13	...	7	...	...
14	Persulfate	30"	52	15"	5	...	...	...	...	...	...
15	Flour	1 breath	21	...	...	...	...	...	...	...	...
16	Guar gum	15"	22	15"	8	...	...	...	...	...	...
17	Psyllium	15"	20	1 breath	7	...	...	...	...	...	...
18	Flour	8'	30	4'	5	...	...	...	...	...	...
19	Flour	1'	27	40"	12	15"	5	...	...	...	...
20	Flour	60'	20	60'	5	...	...	...	...	...	...
21	TMA‡	20"	51	10"	5	...	...	...	...	...	...
22	Flour	2'	26	1'	12	...	...	...	...	...	...
23	Psyllium	30'	25	30'	13	20'	8	...	...	...	...
24	Red cedar	5'	21	5'	16	...	...	...	...	...	...

*The duration and percent fall in FEV₁ are given for the last exposure and every previous exposure provided that the changes in FEV₁ had reached 5 percent.

†Subject 8 did not have a significant (< 20 percent) change in FEV₁ by this method and was challenged in the traditional way by asking to tip flour from one tray to another.

‡TMA = timellitic anhydride.

RESULTS

Eighteen subjects experienced an isolated immediate reaction; five, an isolated late reaction; four, a dual reaction; and two, an atypical bronchospastic reaction (squared-wave pattern, *ie*, no significant recovery after the immediate reaction until 8 h after ending exposure).¹⁵ In 27 subjects, no significant reaction was documented. Twenty-seven (93 percent) of 29 subjects with positive inhalation challenges had significant bronchial responsiveness as compared with 19 (73 percent) of 27 subjects with negative challenges ($\chi^2 = 4.9$; $p = 0.03$).

Twenty-four subjects experienced an immediate component in their reaction, *ie*, either an isolated immediate ($n = 18$) or a dual ($n = 4$) or an atypical asthmatic reaction with an immediate component ($n = 2$). Twenty (83 percent) of these 24 subjects had maximum falls in FEV₁ from 20 to 30 percent at the time of the immediate component of the reaction. Maximum falls in FEV₁ were respectively 35 percent, 43 percent, 51 percent, and 52 percent in the four remaining subjects, corresponding to changes in FEV₁ from 2.4 to 1.6 L, 3.2 to 1.6 L, 3.7 to 2.1 L, and 4.6 to 2.3 L. In most instances, the fall in FEV₁ was

progressive as shown in Table 2. Only three subjects had brisk reactions: patient 15 after a single exposure of one breath to flour, and patients 14 and 21 who experienced changes in FEV₁ >50 percent whereas the previous exposure had caused falls of only 5 percent. In the five subjects who experienced isolated late reactions, the maximum falls in FEV₁ were between 20 and 30 percent.

All subjects (n=27) who did not have significant reactions after exposure with the apparatus were challenged in the traditional way by asking them to tip the particles from one tray to another.¹ Only one of the 27 subjects (No. 8 in Table 2), exposed for 1 h with the closed-circuit method after which the maximum change in FEV₁ was 9 percent, had a significant fall in FEV₁ with the traditional approach by tipping flour for a total period of 8 min.

DISCUSSION

It is reported that Charles Blackley was the first author who performed specific inhalation challenges using pollens.¹⁶ Specific inhalation challenges were used in the 20th century using common allergens by various authors.¹⁷⁻²⁰ Herxheimer²¹ described late bronchial reactions after exposure to common allergens. In the 1970s, Pepys and Hutchcroft¹ introduced this procedure using occupational sensitizers by asking subjects to reproduce their working environment in small, well-ventilated cubicles. This procedure has represented an immense adjunct in the investigation of subjects with symptoms suggestive of occupational asthma and in our understanding of the physiopathology of asthma. These tests are still regarded as the gold standard in the confirmation of work-related asthma.

There are, however, several pitfalls to this approach, as discussed in a previous report⁹: (1) the level of concentrations of the agents can be erratic and high at times; this can result in unduly severe immediate reactions²² and make the differentiation of "irritant" from "sensitizing" reactions difficult, especially in subjects with marked bronchial hyperresponsiveness; the pattern of recovery from the bronchoconstriction of immediate reactions caused by pharmacologic agents²³ or unconditioned air²⁴ cannot be distinguished from the one described for common or occupational sensitizers for which the mechanism can be IgE or non-IgE mediated;¹ (2) it is difficult to draw a dose-response curve since the concentration of particles cannot be set; and (3) there are risks of sensitization of the personnel responsible for the tests. We have described previously an apparatus allowing exposure to particles at stable, low concentrations and shown that dose-response curves can be generated.⁹

We now extend the validation of the method of aerosolization by showing that, in the majority of cases

(23/26 [88 percent]) dose-response curves can be generated resulting in maximum changes in FEV₁ that lie between 20 and 30 percent. This is also the threshold that is aimed at using nonspecific inhalation challenges to pharmacologic agents for which the provocative concentration or dose causing a fall of 20 percent in FEV₁ is required for a test to be positive.^{12,25} Moreover, we have shown that in general, this maximum change in FEV₁ can be achieved in a progressive way, by increasing the duration of exposure. Even if we have not attempted to do so, it is reasonable to assume that progressive increase in the concentrations of particles would reach a similar goal. We have also shown that there are very few instances of false-negative tests using this new methodology. All subjects with negative challenges using the new method were challenged using the conventional method of tipping particles from one tray to another, which has been shown to result in large amounts of particles.⁹ Only one subject who had negative challenges with the new apparatus had a positive challenge with the traditional approach. Even if this subject had a positive skin reaction to flour antigens and bronchial hyperresponsiveness, it cannot be excluded that this reaction was of an "irritant" mechanism. We did not challenge subjects by the tipping method if they had a positive reaction with the new apparatus. It is indeed known that the concentrations of particles are much higher (nearly ten times more) by the tipping method,⁹ which makes it very likely that they would have reacted using the tipping method. It is also very unlikely that we had false-positive reactions using the apparatus as we kept concentrations low, therefore avoiding "irritant" bronchospastic reactions.

For agents in particles that are water soluble like flour, dilutions of these agents can be used for specific inhalation challenges.²⁶ However, it is not sure that all the antigens in flour are water-soluble. Moreover, even if the antigen is water-soluble and can be used for skin testing, it is not necessarily because someone has a positive skin testing that he has developed occupational asthma to this agent. Skin reactivity most often reflects sensitization but not necessarily that the target organ (bronchi) is affected. In a survey of pharmaceutical workers exposed to psyllium, we have shown that 19 percent of them had skin reactivity.³ However, only 4 percent of subjects had occupational asthma. Some authors have advocated the use of skin testing and bronchial responsiveness to pharmacologic agents to predict the magnitude of the immediate reactions.²⁷ The validity of the prediction reaches 80 percent for common^{28,29} and occupational³⁰ sensitizers whose mechanism of action is IgE mediated. This means that if someone has immediate skin reactivity to an allergen and increased nonspecific bronchial responsiveness, there is an 80 percent chance that he or she is going

to experience an immediate bronchoconstrictor response on challenge with this product. Moreover, some agents used in challenging our subjects are not water-soluble at higher concentrations (psyllium, guar gum). For Western red or Eastern white cedar, the active agent, plicatic acid, is not commercially available. Therefore, this apparatus is useful when it is necessary to challenge subjects with particles.

Asthma is now the most frequent occupational respiratory ailment in several countries as reported by physicians³¹ or for sake of medicolegal purposes.^{32,33} In a national US survey of more than 6,000 individuals, 8 percent identified asthma as a personal medical condition; 15 percent of all those with asthma attributed it to workplace exposures.³⁴

Considering the frequency of this condition and the important sociomedical implications of the diagnosis, it is mandatory to use objective tools to confirm the diagnosis. As discussed in the introduction, neither the medical questionnaire nor immunologic testing nor the assessment of bronchial responsiveness is sufficient to confirm the diagnosis. Monitoring of PEFR is a more accurate tool, although it is open to criticism due to the need for honesty and collaboration from the subject. It is therefore expected that specific inhalation challenges, either in the laboratory as described in this report or at work under direct supervision, will be more often used in the confirmation of the diagnosis.

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REFERENCES

- 1 Pepys J, Hutchcroft BJ. Bronchial provocation tests in etiologic diagnosis and analysis of asthma. *Am Rev Respir Dis* 1975; 112:829-59
- 2 Malo JL, Ghezzo H, L'Archevêque J, Lagier F, Perrin B, Cartier A. Is the clinical history a satisfactory means of diagnosing occupational asthma? *Am Rev Respir Dis* 1991; 143:528-32
- 3 Bardy JD, Malo JL, Séguin P, Ghezzo H, Desjardins J, Dolovich J, et al. Occupational asthma and IgE sensitization in a pharmaceutical company processing psyllium. *Am Rev Respir Dis* 1987; 135:1033-38
- 4 Cartier A, Grammer L, Malo JL, Lagier F, Ghezzo H, Harris K, et al. Specific serum antibodies against isocyanates: association with occupational asthma. *J Allergy Clin Immunol* 1989; 84:507-14
- 5 Burge PS, O'Brien IM, Harries MG. Peak flow rate records in the diagnosis of occupational asthma due to isocyanates. *Thorax* 1979; 34:317-23
- 6 Burge PS, O'Brien IM, Harries MG. Peak flow rate records in the diagnosis of occupational asthma due to colophony. *Thorax* 1979; 34:308-16
- 7 Côté J, Kennedy S, Chan-Yeung M. Sensitivity and specificity of PC 20 and peak expiratory flow rate in cedar asthma. *J Allergy Clin Immunol* 1990; 85:592-98
- 8 Perrin B, Lagier F, L'Archevêque J, Cartier A, Boulet LP, Côté J, et al. Validity of investigating occupational asthma with serial monitoring of peak expiratory flow rates and bronchial responsiveness as compared to specific inhalation challenges [abstract]. *J Allergy Clin Immunol* 1991; 87:200
- 9 Cloutier Y, Lagier F, Lemieux R, Blais MC, St-Arnaud C, Cartier A, et al. New methodology for specific inhalation challenges with occupational agents in powder form. *Eur Respir J* 1989; 2:769-77
- 10 Cartier A, Bernstein IL, Burge PS, Cohn JR, Fabbri LM, Hargreave FE, et al. Guidelines for bronchoprovocation on the investigation of occupational asthma: report of the subcommittee on bronchoprovocation for occupational asthma. *J Allergy Clin Immunol* 1989; 84:823-29
- 11 American Thoracic Society. Standardization of spirometry—1987 update. *Am Rev Respir Dis* 1987; 136:1285-1307
- 12 Cockcroft DW, Killian DN, Mellon JJA, Hargreave FE. Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy* 1977; 7:235-43
- 13 Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis* 1983; 127:725-34
- 14 Malo JL, Pineau L, Cartier A, Martin RR. Reference values of the provocative concentrations of methacholine that cause 6% and 20% changes in forced expiratory volume in one second in a normal population. *Am Rev Respir Dis* 1983; 128:8-11
- 15 Perrin B, Cartier A, Ghezzo H, Grammer L, Harris K, Chan H, et al. Reassessment of the temporal patterns of bronchial obstruction after exposure to occupational sensitizing agents. *J Allergy Clin Immunol* 1991; 87:630-39
- 16 Taylor G, Walker J. Charles Harrison Blackley, 1820-1900. *Clin Allergy* 1973; 3:103-08
- 17 Stevens FA. A comparison of pulmonary and dermal sensitivity to inhaled substances. *J Allergy* 1933-4; 5:285-87
- 18 Juhlén-Dannfelt C. On the significance of exposure and provocation test in allergic diagnostics. *Acta Med Scand* 1950; 239 (suppl):320-27
- 19 Dominjon-Monnier F, Carton J, Guibert L, Burtin P, Brille D, Dourlisky R. Épreuves ventilatoires aux extraits de moisissures atmosphériques. *Rev Franç Mal Resp* 1962; 2:191-202
- 20 Coldahl H. The importance of inhalation test in the etiological diagnosis of allergic diseases of the bronchi and the evaluation of the effects of specific hyposensitization treatment. *Acta Allergol* 1967; 22:7-12
- 21 Herxheimer H. The late bronchial reaction in induced asthma. *Int Arch Allergy Appl Immunol* 1952; 3:323-28
- 22 Cartier A, Malo JL, Dolovich J. Occupational asthma in nurses handling psyllium. *Clin Allergy* 1987; 17:1-6
- 23 Malo JL, Gauthier R, Lemire I, Cartier A, Ghezzo H, Martin RR. Kinetics of the recovery of airway response caused by inhaled histamine. *Am Rev Respir Dis* 1985; 132:848-52
- 24 Malo JL, Cartier A, L'Archevêque J, Ghezzo H, Martin RR. Kinetics of the recovery from bronchial obstruction due to hyperventilation of cold air in asthmatic subjects. *Eur Respir J* 1988; 1:384-88
- 25 Chai H, Farr RS, Froehlich LA, Mathison DA, McLean JA, Rosenthal RR, et al. Standardization of bronchial inhalation challenge procedures. *J Allergy Clin Immunol* 1975; 56:323-27
- 26 Block G, Tse KS, Kijek K, Chan H, Chan-Yeung M. Baker's asthma. *Clin Allergy* 1983; 13:359-70
- 27 Tiffeneau R. Hypersensibilité cholinergo-histaminique pulmonaire de l'asthmatique: relation avec l'hypersensibilité allergénique pulmonaire. *Allergy* 1958; 5:187-221
- 28 Cockcroft DW, Ruffin RE, Frith PA, Cartier A, Juniper EF, Dolovich J, et al. Determinants of allergen-induced asthma: dose of allergen, circulating IgE antibody concentration, and bronchial responsiveness to inhaled histamine. *Am Rev Respir Dis* 1979; 120:1053-58
- 29 Cockcroft DW, Murdock KY, Kirby J, Hargreave F. Prediction of airway responsiveness to allergen from skin sensitivity to allergen and airway responsiveness to histamine. *Am Rev Respir*

Dis 1987; 135:264-67

- 30 Malo JL, Cartier A, L'Archevêque J, Ghezzi H, Lagier F, Trudeau C, et al. Prevalence of occupational asthma and immunologic sensitization to psyllium among health personnel in chronic care hospitals. *Am Rev Respir Dis* 1990; 142:1359-66
- 31 Meredith SK, Taylor VM, McDonald JC. Occupational respiratory disease in the United Kingdom 1989: a report to the British Thoracic Society and the Society of Occupational Medicine by the SWORD project group. *Br J Ind Med* 1991; 48:292-98
- 32 Lagier F, Cartier A, Malo JL. Medico-legal statistics on occupational asthma in Quebec between 1986 and 1988. *Rev Mal Respir* 1990; 7:337-41
- 33 Gervais P, Rosenberg N. Occupational respiratory allergy: epidemiological and medicolegal aspects. In: Reed CE, ed. *Proceedings of the 12th International Congress of Allergology and Clinical Immunology*. St Louis: Mosby Co Ltd, 1986:480-85
- 34 Blanc P. Occupational asthma in a national disability survey. *Chest* 1987; 92:613-17

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