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What are the questionnaire items most useful in identifying subjects with occupational asthma?

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ABSTRACT: The present study assessed the usefulness of key items obtained from a clinical ''open'' questionnaire prospectively administered to 212 subjects, referred to four tertiary-care hospitals for predicting the diagnosis of occupational asthma (OA). Of these subjects, 72 (34%) were diagnosed as OA (53% with OA due to high-molecular-weight agents) according to results of specific inhalation challenges, and 90 (42%) as non-OA.

Wheezing at work occurred in 88% of subjects with OA and was the most specific symptom (85%). Nasal and eye symptoms were commonly associated symptoms. Wheezing, nasal and ocular itching at work were positively, and loss of voice negatively associated with the presence of OA in the case of high-, but not low molecular-weight agents.

A prediction model based on responses to nasal itching, daily symptoms over the week at work, nasal secretions, absence of loss of voice, wheezing, and sputum, correctly predicted 156 out of 212 (74%) subjects according to the presence or absence of OA by final diagnosis.

In conclusion, key items, *i.e.* wheezing, nasal and ocular itching and loss of voice, are satisfactorily associated with the presence of occupational asthma in subjects exposed to high-molecular-weight agents. Therefore, these should be addressed with high priority by physicians. However, no questionnaire-derived item is helpful in subjects exposed to low-molecular-weight agents.

KEYWORDS: Asthma, bronchial diseases, occupational asthma, occupational diseases

Various diagnostic tools have been proposed for a stepwise approach in the investigation of occupational asthma (OA) [1, 2]. The first is the clinical history, which inquires about the nature of respiratory symptoms and their relationship to work and specific occupational exposures. Questions related to the presence of eye and nasal symptoms were also included because they often accompany respiratory symptoms, especially in the case of workplace high-molecular-weight proteinaceous agents [3]. In the latter instance, occupational rhinoconjunctivitis is often associated with OA [4, 5].

Although several items were proposed [2] and generally included in these clinical questionnaires, their usefulness in regards to their association with the presence or absence of OA has not been properly assessed. A study has evaluated the association of one frequently used item, *i.e.* improvement in symptoms at weekends and on vacations, with the presence or absence of OA [6]. It was found that improvement of symptoms at weekends and on vacations had sensitivities of 77 and 88% and specificities of 44 and 24%, respectively. In the present study, the general impression from questionnaire data obtained by the two physicians who were involved in the clinical investigation showed that an ''open'' questionnaire had a sensitivity of 87%, but a specificity of only 27% regarding the presence or absence of OA [6]. However, a detailed analysis of the association of several relevant questionnaire items, alone and in combination, with the presence or absence of OA has not been carried out to the best of the current authors' knowledge.

Therefore, the purpose of the present study was to assess the usefulness of a variety of questionnaire items in predicting the presence or absence of OA. For this, 212 subjects referred for possible OA in four tertiary-care hospitals in different countries were first questioned by clinicians in a systematic way using a detailed

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list of items. The subjects subsequently underwent nonspecific and specific inhalation challenges in order to identify whether they had OA, asthma, or neither condition.

SUBJECTS AND METHODS

The current study includes the first 212 subjects who were prospectively assessed in outpatient clinics of four hospital centres and who underwent objective testing with specific inhalation challenges in: a hospital laboratory (n=196); the workplace (n=10); or in both (n=6). Of these, 102 (48%) were seen in Yvoir, Belgium; 80 (38%) in Montreal, Canada (by three different chest physicians); 22 (10%) in Pavia, Italy; and 8 (4%) in Barcelona, Spain.

The items of information that were planned and obtained prospectively from each participant are listed in Appendix 1. Each investigator had a form containing the list of all items for which they had to elicit a response at the time of the interview with the worker. These items were derived from a list suggested for the clinical assessment of OA [2] and included information on: 1) the type of job, work shift and agents that the workers identified as potential causes of symptoms; 2) the nature of symptoms during working periods, *i.e.* chest symptoms (cough, sputum, chest tightness, wheezing, shortness of breath at rest and/or on exertion, change in voice), general symptoms (fever, chills, muscle or joint pain), nasal symptoms (blocked nose, runny nose, sneezing, nasal or throat itching), eye symptoms (itching, runny eyes, redness of the eyes), and skin symptoms (rash, eczema). Information was also obtained on the timing of the onset of symptoms in relation to the beginning of the occupation and the interval between the last occupational exposure and the questionnaire. The relationship between work and respiratory, nasal, conjunctival or skin symptoms was also addressed by asking whether symptoms differed on days at work and away from work, whether there was a specific product causing onset of symptoms and whether there was an improvement in or disappearance of symptoms at weekends and on vacation. The temporal pattern of asthmatic symptoms was also addressed (time interval necessary to develop symptoms after starting work, persistence of symptoms after the work shift and presence of symptoms only on return from work). Interviews were conducted in French in Yvoir and Montreal (except in a few instances in which English was used), in Catalan in Barcelona and in Italian in Pavia.

Atopy was defined by the presence of a significant skin-prick test response ($\geqslant$3 mm wheal 10 min after the introduction of the antigen in the presence of a reaction to histamine phosphate 1 mg·mL^{-1}, and in the absence of a reaction to the diluent) to at least one of a battery of local inhalant allergens, which included 10–20 allergens depending on the centre. Spirometry [7] and bronchial responsiveness to methacholine [8] were assessed. The provocative concentration of methacholine causing a fall of 20% in forced expiratory volume in one second (PC_{20}) of $\leqslant$16 mg·mL^{-1} was considered suggestive of bronchial hyperresponsiveness [9]. Specific inhalation challenges were carried out using recommended methodologies [10–12]. A sustained fall in forced expiratory volume in one second of 20% was confirmation of a positive specific challenge.

Analysis of results

A diagnosis of OA was made in the presence of a positive specific inhalation challenge. A diagnosis of non-OA was kept if the specific inhalation challenge was negative, but the PC_{20} was $\leqslant$16 mg·mL^{-1}. If both the methacholine and the specific inhalation challenges were negative, the subject was categorised as having neither occupational nor non-OA. Univariate and multivariate regression analyses were used to examine the association between individual factors and a combination of factors derived from the questionnaire, and the presence or absence of OA and of probable asthma (defined as the presence of symptoms and bronchial hyperresponsiveness). Classification and regression trees [13] using the program Recursive Partitioning and Regression Trees in R [14] were used to examine which sequence of symptoms was the best predictor of the presence of OA. The order in the sequence of symptoms is given by the program in the process of building the classification tree. For this analysis, all factors were included in the model.

RESULTS

Table 1 shows baseline anthropometric and clinical characteristics of the 212 subjects. There was a preponderance of males, atopic and nonsmoking subjects in the whole group. Subjects had been exposed at work for a mean duration of nearly 12 yrs and took nearly 9 yrs at work before developing symptoms. On average, 8 months elapsed between the subjects' discontinuing work and filling out the questionnaire. This interval was significantly longer in Yvoir (15 ± 17.5 months). Most subjects had bronchial hyperresponsiveness. The diagnosis of OA was confirmed in 72 subjects and 90 subjects had what can be interpreted as non-OA (symptoms and bronchial hyperresponsiveness) [15]. Flour, latex and isocyanates were the most common causal agents, accounting for 60% of all cases. There were some disparities between types of agents in the various referral centres. Of the 32 cases for whom latex was the suspected agent, 23 (72%) were investigated at Yvoir and 22 (61%) of the 36 cases exposed to isocyanates were investigated in Montreal.

The interval between the interview and the last exposure at work was 7.8 ± 14 months in the group with OA, 11.4 ± 15.7 months in the group with non-OA and 5.9 ± 10 months in the group with neither asthma nor OA. Tables 2 and 3 show the frequency of symptoms in relation to work. Wheezing was the most common symptom in those with OA. Nasal, eye and skin symptoms were generally less common than respiratory symptoms. Respiratory symptoms (either cough, sputum, chest tightness, wheezing, shortness of breath at rest, shortness of breath on exercise, loss of voice alone or a combination depending on the subject) were more often worse at work on a daily basis than progressively over the week, and subjects were often able to identify a specific agent. A majority of subjects mentioned the complete disappearance of symptoms on vacations, while symptoms generally only improved at weekends. Subjects mentioned that the onset of symptoms generally occurred ~2 h after starting work and persisted after ending work. Only seven subjects (OA n=3, non-OA n=4) reported that their symptoms developed after the end of their work shift.

Table 4 gives the list of factors that were found, by univariate analysis, to be significantly associated with the presence or

TABLE 1 Anthropometric and clinical characteristics of the subjects

Characteristics	
Subjects n	212
Male:female	125 (59):87 (41)
Age yrs	38.8±10.7
Atopy +ve:-ve:unknown	125 (59):84 (40):3 (1)
Smoking S:ES:NS	46 (22):67 (32):99 (47)
Duration of exposure at work yrs	11.9±10.0
Interval between onset of exposure and onset of symptoms yrs	8.6±9.2
Interval between onset of symptoms and questionnaire yrs	4.1±4.8
Interval between last exposure at work and questionnaire yrs	0.7±1.2
FEV_1 % pred	92.8±15.4
Values <80% pred	41 (19)
PC_{20} mg·mL^{-1}	
Values ⩽16 mg·mL^{-1}	157 (74)
Confirmed diagnosis of OA	72 (34)
No OA and PC_{20} ⩽16 mg·mL^{-1}	90 (42)
Molecular weight of the suspected agents high:low-molecular-weight agent	71 (33)/141 (66)
Molecular weight of the causal agents high:low-molecular-weight agent	40 (56)/32 (44)
Nature of causal agents	72
Flour and cereals	17 (24)
Latex	15 (21)
Isocyanates	11 (15)
Various chemicals	9 (12)
Wood dusts	7 (10)
Laboratory animals	4 (5)
Persulfate	3 (4)
Resins and glues	2 (3)
Various proteins	2 (3)
Metals	2 (3)

Data are presented as n (%) or mean±SD. +ve: positive; -ve: negative; S: smoker; ES: ex-smoker; NS: nonsmoker; FEV_1 % pred; forced expiratory volume in one second of per cent predicted; PC_{20}: provocative concentration causing a 20% fall in FEV_1; OA: occupational asthma.

absence of OA (the latter group including subjects with non-OA and those with neither OA nor non-OA). These include wheezing, nasal and ocular itching at work, which were positively associated with OA, and loss of voice, which was negatively associated. Separate analyses were performed for subjects with OA due to high- and low-molecular-weight agents. While no factors were significantly associated with the presence or absence of OA due to low-molecular-weight agents, it was found that, for the group of subjects exposed to high-molecular-weight agents, wheezing at work, nasal itching at work and improvement in symptoms at weekends and on vacations were significantly associated with the presence or absence of OA, with wheezing being the most specific. Loss of voice at work was negatively associated and had low sensitivity and specificity. Changes of symptoms at weekends and on vacations (the more common feature being the disappearance of symptoms in subjects with OA during vacations) were the most sensitive indices, but had lower specificity.

TABLE 2 Frequency of selected symptoms according to the presence of occupational asthma (OA), asthma (A) or neither

	OA	A	No A, no OA
Subjects n	72	90	50
Respiratory			
Cough	60 (83)	72 (81)	42 (84)
Chest tightness	29 (40)	47 (52)	20 (40)
Wheezing	64 (88)	64 (71)	31 (62)
Shortness of breath at rest	59 (82)	76 (84)	43 (86)
Shortness of breath			
On exercise	56 (78)	68 (76)	30 (60)
Loss of voice	12 (17)	31 (34)	11 (22)
Nasal			
Obstruction	43 (60)	58 (64)	22 (44)
Secretions	48 (67)	56 (62)	18 (36)
Sneezing	49 (68)	56 (62)	28 (56)
Itching	38 (53)	30 (33)	11 (22)
Ocular			
Itching	42 (58)	47 (52)	13 (26)
Watering	27 (38)	35 (39)	16 (32)
Redness	26 (36)	40 (44)	10 (20)
Skin			
Rash	22 (31)	19 (21)	11 (22)
Eczema	9 (13)	9 (10)	8 (16)
Chills or fever	3 (4)	10 (11)	5 (10)

Data are presented as n (%), unless otherwise stated.

Results of the multivariate analysis incorporating factors that were significant at $p<0.1$ in the univariate analysis are given in

TABLE 3 Relationship of respiratory symptoms with work[#]

	OA	A	No A, no OA
Symptoms worse at work	65 (90)	83 (92)	45 (90)
Every day	36 (55)	51 (61)	21 (47)
Progressively over the week	11 (15)	12 (14)	10 (22)
On exposure to a specific agent	54 (75)	71 (80)	39 (78)
Disappearance at weekends	16 (23)	8 (10)	9 (19)
Improvement at weekends	43 (62)	65 (74)	29 (60)
Disappearance on vacation	30 (43)	26 (31)	17 (36)
Improvement on vacation	36 (52)	51 (61)	27 (57)
Interval between beginning of work and onset of symptoms h	2.2±2.5	2.7±2.6	2.0±2.5
Persistence of symptoms after ending work shift	50 (70)	70 (79)	32 (67)

Data are presented as n (%) or mean±SD. OA: occupational asthma; A: asthma. [#]: includes one or several relevant respiratory symptoms present at work (see table 2 for the full list).

TABLE 4 Results of the univariate analysis showing the association of selected symptoms with the presence or absence of occupational asthma (OA)[#]

Symptoms	OR (95% CI)	Sensitivity	Specificity	PPV	NPV	p-value
All subjects[¶]						
Wheezing at work	3.8 (1.7–8.6)	0.40	0.85	0.89	0.32	0.001
Loss of voice at work	0.47 (0.23–0.97)	0.22	0.62	0.17	0.70	0.05
Nasal itching at work	2.64 (1.47–4.77)	0.48	0.74	0.53	0.70	0.003
Ocular itching at work	1.82 (1.02–3.24)	0.41	0.72	0.58	0.56	0.07
Subjects exposed to high-molecular-weight agents[+]						
Wheezing at work	8.5 (2.5–29.2)	0.67	0.81	0.89	0.50	0.0006
Loss of voice at work	0.17 (0.05–0.64)	0.20	0.39	0.08	0.65	0.01
Improvement or disappearance of symptoms at weekends	3.7 (1.05–13.5)	0.76	0.54	0.41	0.8	0.06
Improvement or disappearance of symptoms during vacations	3.8 (1.3–11.3)	0.74	0.57	0.57	0.74	0.03
Nasal itching at work	4.0 (1.5–10.6)	0.68	0.65	0.68	0.65	0.01

OR: odds ratio; CI: confidence interval; PPV: positive predicted value; NPV: negative predicted value. [#]: the comparisons are between two groups, those with OA on the one hand and those (regrouped) with non-OA and neither OA nor non-OA on the other hand; [¶]: n=212; [+]: n=71.

table 5. For high-molecular-weight agents, wheezing, nasal and ocular itching were significantly positively associated with the presence of OA, and loss of voice was significantly negatively associated.

The classification tree showing the questionnaire items, in specific order, which best predicted the presence or absence of OA is illustrated in figure 1. The classification tree shows: 1) the total number of subjects at each bifurcation; 2) the key questionnaire item addressed at that point; and 3) the number of subjects with a yes (left-hand side) and no (right-hand side) answers. A terminal node or leave is reached when no other variable can be added to further improve the classification. The numbers of subjects with and without OA are given at each of these bifurcations. The prediction model based on responses to the items shown in figure 1 and in the order specified by the

TABLE 5 Results of the multivariate analysis showing symptoms at work associated with the presence or absence of occupational asthma

Symptoms at work	OR (95% CI)	p-value
All Subjects		
Wheezing	3.39 (1.43–8.0)	0.005
Loss of voice	0.39 (0.18–0.86)	0.02
Nasal itching	3.7 (1.8–7.8)	0.0006
Ocular itching	2.37 (1.06–5.30)	0.03
Subjects exposed to high-molecular-weight agents		
Wheezing	6.79 (1.53–30.0)	0.01
Loss of voice	0.14 (0.03–0.64)	0.01
Nasal itching	6.23 (1.49–26.1)	0.01

OR: odds ratio; CI: confidence interval.

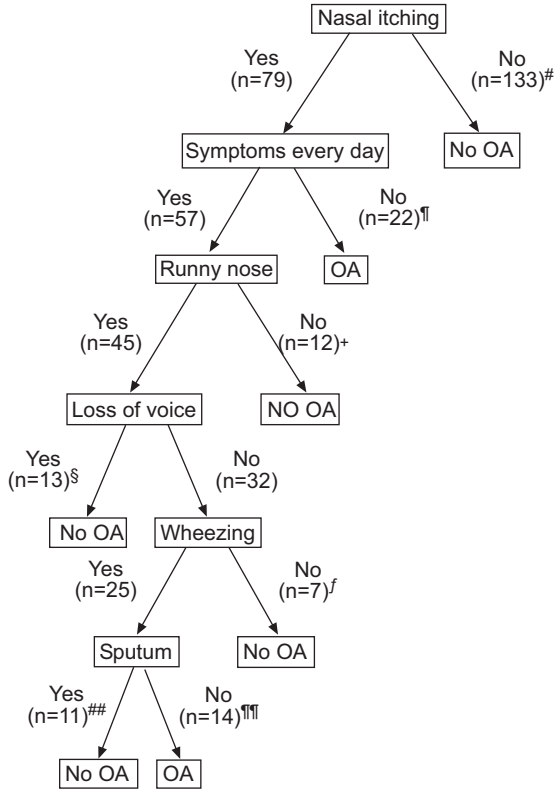

FIGURE 1. Schematic diagram illustrating the results of the decision tree analysis for 212 subjects in total. Using the pathway, it is shown that a total of six questionnaire items proved useful in the classification of the presence or absence of occupational asthma (OA) with the final yield given in table 6. [#]: 99 or 74% correct; [¶]: 16 or 73% correct; [+]: 10 or 83% correct; [§]: 10 or 77% correct; [ƒ]: 5 or 71% correct; [##]: 6 or 55% correct; [¶¶]: 10 or 71% correct.

TABLE 6 Results of the regression tree analysis by comparing presence and absence of occupational asthma (OA) predicted from the model

Final diagnosis	OA	No OA	Total
OA	26#	46	72
No OA	10	130#	140
Total	36	176	212#

#: number of situations in which the model correctly predicted the actual situation (156 out of 212 cases; 74%).

regression tree program are: nasal itching; daily symptoms over the week at work; runny nose; loss of voice; wheezing; and sputum, which correctly predicted 156 out of 212 (74%) subjects according to the presence or absence of OA by final diagnosis (table 6).

By partitioning the subjects into three groups: OA; non-OA; and no OA and no non-OA, a prediction model based on responses to the following items, in the specified order, correctly predicted the presence of these three outcomes in 125 (59%) out of 212 subjects (table 7): 1) nasal itching; 2) loss of voice; 3) wheezing; 4) number of respiratory symptoms; 5) ocular redness; 6) ocular watering; 7) daily symptoms over the week at work; and 8) number of nasal symptoms. Only six (8%) out of 72 subjects with OA were falsely categorised as having neither OA nor asthma, but 17 (34%) out of 50 with neither OA nor asthma were considered as having OA.

The data was also partitioned into two sets, one comprising the patients from the three European participating centres (n=132) and the other comprising the rest of subjects from Montreal (n=80). The model was cross-validated by developing the criteria in one set (training set) and applying it to the other (test set), and vice-versa. All the predictions were then pooled to obtain a realistic validation of the classification-tree procedure. The objective of the cross-validation process was to provide an answer to the argument that a given subject is used to build its own classifier. In this instance, the classifier is set in an independent sample in the hope that its behaviour will be representative of its application to any other sample. The model developed in Montreal correctly classified 64% of the subjects in the three European centres, while the other did so only for 36%. Following both procedures, the model was correct in 88 (42%) out of 210 subjects (table 8; Appendices 2 and 3).

TABLE 7 Results of the regression tree analysis by comparing the presence or absence of occupational asthma (OA), asthma (A) or neither OA or A

Final diagnosis	OA	A	No OA, no A	Total
OA	51#	15	6	72
A	27	56#	7	90
No OA, no A	17	15	18#	50
Total	95	86	31	212#

#: number of situations in which the model correctly predicted the actual situation (125 out of 212 cases; 59%).

TABLE 8 Results of the regression tree analysis by predicting results from the three European Centres and subjects from Montreal and vice-versa

Final diagnosis	OA	A	No OA, no A	Total
OA	34#	33	5	72
A	35	46#	9	90
No OA, no A	9	33	8#	50
Total	78	112	22	212#

OA: occupational asthma; A: asthma. #: number of situations in which the model correctly predicted the actual situation (88 out of 212 cases; 42%).

DISCUSSION

The aim of the present study was to identify items used in a clinical ''open'' questionnaire in the assessment of subjects referred for possible OA. Topics such as wheezing at work, nasoconjunctival symptoms and loss of voice were found to be significant predictors of the presence or absence of OA.

The diagnosis of OA is an important challenge to physicians. Several functional, immunological and inflammatory marker tools have been proposed alone or in conjunction in a stepwise approach specific inhalation challenges represent the most specific test [1, 2]. The first diagnostic approach is the questionnaire addressed by a physician. A list of items to be included in such questionnaires has been proposed [2], but the usefulness of specific proposed items has not been assessed in details as this was proposed in the current study. To the current authors' knowledge, only one item has been prospectively examined in a previous study. MALO *et al.* [6] found that improvement of symptoms at weekends and on vacations had sensitivities of 77 and 88% and specificities of 44 and 24%, respectively. This compares, respectively, closely to sensitivity and specificity values of 75 and 55% in the current study. All subjects underwent specific inhalation challenges to confirm or eliminate OA. Although this test can be falsely negative at times, it is generally considered the gold standard in the diagnosis of OA.

The intention of the present study was not to validate a questionnaire to be used in the investigation of OA, but rather to assess the relative importance of items generally addressed by clinicians in an ''open'' interview, as this represents the usual situation of a clinical context. To do so, a series of items were used that have been proposed by others [2], and that were systematically and prospectively addressed by clinicians at the time of their interview of referred subjects. Although some items seem particularly useful, it would probably not be practical to suggest developing with these a standardised questionnaire, such as those used for epidemiological studies. Indeed, contrary to the situation in an epidemiological study, where questions have to be addressed in a standardised

manner to ensure validity of results, an ''open'' questionnaire is the preferred clinical mean.

A clear distinction was found in the identification of questionnaire items for high- and low-molecular-weight agents. High-molecular-weight agents often cause nasal and eye symptoms [3, 5]. In the current study, besides wheezing, nasal and ocular itching, runny nose was significantly associated with the presence of OA due to high-molecular-weight agents. Loss of voice was more prevalent in subjects without OA, suggesting that upper airway dysfunction could be responsible for work-related respiratory symptoms in some subjects. The current authors do not have an explanation for the fact that there were fewer instances of loss of voice in the group with OA. It cannot be attributed to inhaled steroids, as 56% of the subjects with OA were on inhaled steroids at the time of the visit as compared with 57% in the group of subjects with non-OA and 20% in the group with neither condition. In the case of low-molecular weight agents, no questionnaire item was found to be significantly predictive of the presence or absence of OA. The reasons for this are only speculative. First, low-molecular weight agents cause nasoconjunctival symptoms less often than high-molecular weight agents [3]. Nasoconjunctival symptoms commonly accompanied asthma due to high-molecular-weight agents and are predictive of the presence or absence of OA. Secondly, low-molecular-weight agents are chemicals that may more easily cause nonspecific irritation of the airways with symptoms in subjects with non-OA, making distinction between OA and work-aggravated asthma more difficult. Thirdly, low-molecular-weight agents causing OA often induce late asthmatic reactions [12] that, contrary to immediate reactions, are more difficult to relate temporarily to work.

The decision-tree analysis showed an overall validity of 59% for the model that predicted OA, asthma and neither condition. This was less than the 74% obtained by categorising the subjects into those with and without OA. However, the figure obtained in the present study for the prediction of asthma (62%) was slightly lower than the figure for the prediction of OA (71%). The cross-validation analysis of the classification and regression analysis procedure testifies to the inherent difficulties of employing a culturally sensitive tool, such as a questionnaire, across heterogeneous populations (subjects were recruited in one North American and three European countries), exposed to various agents and living in countries where the expression of perceived symptoms and health as well as medicolegal systems differ. Besides geographical and cultural factors, the possibility that other determinants could explain these results cannot be excluded. This includes the following. 1) The longer interval between the end of exposure at work and the administration of the questionnaire at Yvoir, which could have generated a possible recall bias. 2) The nature of the agent; for the purpose of keeping a sufficient number of subjects in the analysis, the exposure was grouped under high- and low-molecular-weight agents, but this does not take into account the possibility that specific agents within each group (viz. flour, latex, isocyanates, persulfates, *etc.*) could induce different symptoms. Also, there were not enough subjects to cross-validate the analysis in each site independently. The majority of symptoms listed in table 2 were clearly not predictive, which is of great interest in the context of keeping only key features for questionnaires administered in the clinical investigation of OA.

The diagnosis of OA was based on the result of the specific inhalation challenge. Whereas this is generally considered as the gold standard [10–12], the possibility of false negative results cannot be excluded, especially in subjects who underwent testing several months after ending exposure. However, LEMIÈRE *et al.* [16] have shown that this test generally remains positive in subjects with OA who no longer demonstrate increased nonspecific responsiveness to methacholine even years after stopping exposure [16].

In conclusion, occupational asthma still poses important diagnostic challenges. Although several tools are available, they are not sufficiently nor properly used. Whereas some tests (*e.g.* peak expiratory flow assessment) have undergone a proper validation process, more has to be done using the simple and inexpensive tool, the clinical questionnaire. The current results show that improvement in symptoms at weekends and on vacations is sensitive, but the presence of wheezing at work is more specific. Inclusion of these questions might, therefore, result in either more sensitive or more specific results depending on the purpose of the study. More sensitive questions would be preferable in a surveillance programme, however, once subjects are referred to specialised centres, the use of more specific questions is relevant. This being said, sensitivity and specificity of questionnaire items still remains low and need to be improved, therefore, justifying the use of other diagnostic tools.

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APPENDIX 1. INFORMATION COLLECTED FROM THE QUESTIONNAIRE

1. Occupational data
Job title
Duration of work under the same job title
Products made by the company
Workshift
Products causing symptoms
2. Nature of symptoms
2.1. Respiratory
Cough
Sputum
Chest tightness
Wheezing
Shortness of breath at rest
Shortness of breath on exercise
Loss of voice
2.2. Systemic
Fever
Chills
Muscle or joint aches
2.3. Rhinitis
Nasal obstruction
Runny nose
Sneezing

Nasal/pharyngeal itching

2.4. Conjunctivitis

Ocular itching

Watery eyes

Redness of the eyes

2.5. Skin symptoms

Rash/urticaria

Eczema

3. Timing of symptoms in relation to work

Interval between onset of exposure at work and onset of symptoms

Interval between onset of symptoms and current questionnaire

Interval between last occupational exposure and current questionnaire

4. Relationship of work and respiratory symptoms

4.1. Status of respiratory symptoms on working days as compared with days away from work

Better, worse, the same

If better or worse:

1. Every day;

2. Progressively over the week;

3. As a function of working conditions; if yes,

On physical exertion

On exposure to mist, hot or cold temperature

On exposure to dust, fumes, gas

4.2. Possibility to identify a process or a product that is responsible for respiratory symptoms

Yes, no

If yes, identify the process or product

If yes, is this exposure regular or intermittent?

4.3. Status of respiratory symptoms on weekends

They disappear

They improve

No change

4.4. Status of respiratory symptoms on vacations (more than one week)

They disappear

They improve

No change

If they disappear or improve, after how many days?

4.5. Timing of respiratory symptoms in relation to work

Interval between onset of work and onset of symptoms

Persistence or reappearance of symptoms on return to home

Onset of symptoms only on returning home

Change of timing of symptoms over time

5. Relationship of work and nasal, conjunctival or skin symptoms

5.1. Status of symptoms on working days as compared with days away from work

Better, worse, the same

If better or worse:

1. Every day;

2. Progressively over the week;

3. As a function of working conditions; if yes,

On physical exertion

On exposure to mist, hot or cold temperature

On exposure to dust, fumes, gas

6. Other information

6.1. Smoking habits: smoker, non-smoker, ex-smoker; number of pack-years

6.2. Presence of chronic bronchitis

6.3. Asthma before starting work that causes symptoms

6.4. Respiratory drugs at the time of investigation

APPENDIX 2. CLASSIFICATION TREE OF PRESENCE AND ABSENCE OF OCCUPATIONAL ASTHMA (OA) OR ASTHMA (A) FOR SUBJECTS FROM MONTREAL

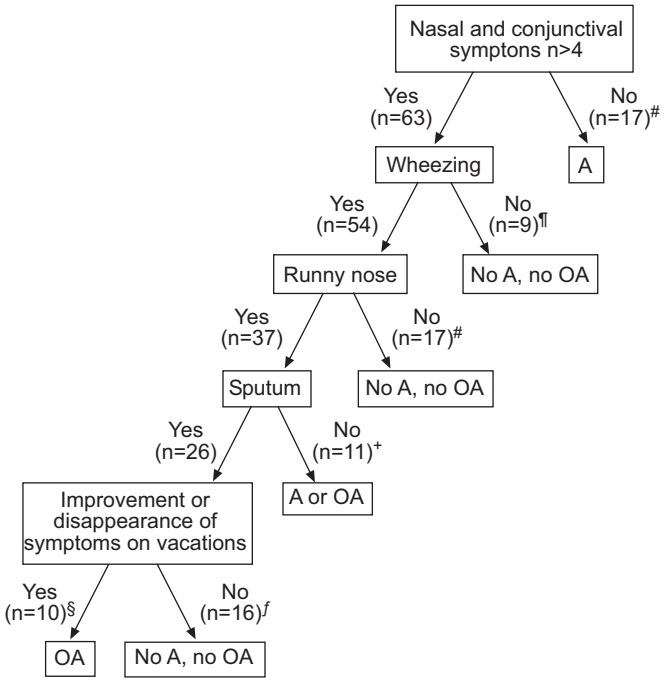

FIGURE 2. Classification tree for subjects of Montreal. A: asthma; OA: occupational asthma. #: 9 or 53% correct; ¶: 7 or 78% correct; +: 10 or 91% correct; §: 5 or 50% correct; f: 10 or 63% correct.

APPENDIX 3. CLASSIFICATION TREE OF PRESENCE AND ABSENCE OF OCCUPATIONAL ASTHMA (OA) OR ASTHMA (A) FOR SUBJECTS FROM EUROPE

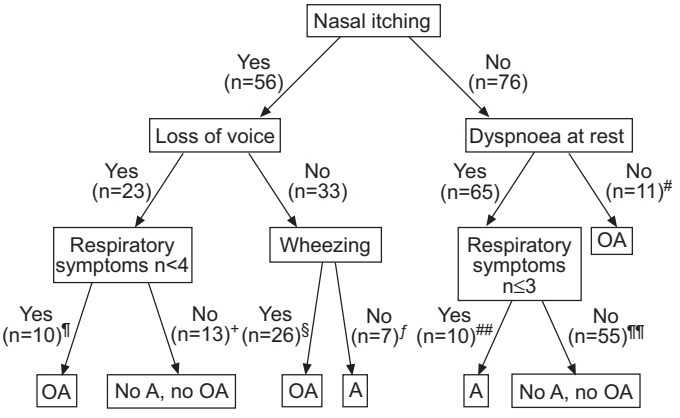

FIGURE 3. Classification tree for subjects of Europe. OA: occupational asthma; A: asthma. #: 6 or 55% correct; ¶: 5 or 90% correct; +: 10 or 77% correct; §: 21 or 81% correct; f: 3 or 43% correct; ##: 6 or 60% correct; ¶¶: 32 or 58% correct.

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