

Early incidence of occupational asthma is not accelerated by atopy in the bakery/pastry and hairdressing sectors

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SUMMARY

SETTING: Occupational asthma (OA) is most likely to develop in the very early years of exposure.

OBJECTIVE: To describe the early incidence of OA among bakers/pastry-makers (BP) and hairdressers and to explore the role of atopy.

DESIGN: Following a retrospective follow-up design, subjects were invited to undergo telephone interviews. Those who declared work-related respiratory or rhinitis symptoms and a sample group of others were offered a medical visit for OA investigations. Data from interviews and from medical visits were used to estimate the incidence of OA according to increasing durations of exposure.

RESULTS: A total of 866 subjects were interviewed (mean

age 25.3 years, 43.8% females), of whom 282 underwent a medical visit. Total estimated incidence rates of 'confirmed or probable' OA during the first 12 years of exposure were high in BP (2.63 per 100 person-years [py]) and in hairdressers (0.58/100 py), particularly in the first 4 years. Atopy is a strong risk factor for incidence among BP but, irrespective of the occupational sector, it does not influence the timing of OA symptoms.

CONCLUSION: OA symptoms occur soon after the start of exposure. Our results suggest that atopy does not precipitate the occurrence of symptoms in two different allergen exposure settings.

KEYWORDS: epidemiology; occupational asthma; atopy; incidence; diagnosis

OCCUPATIONAL ASTHMA (OA) is defined as asthma caused by exposure to an agent encountered in the work environment.¹ Disparities in OA prevalence exist across the different sectors of activity. In most West European countries, baking is one of the occupations with the highest risk of OA.^{2–8} The main causes of occupational asthma in this sector are cereal flours (wheat, rye and barley) and enzymes. Workers in other sectors also run a high risk of OA, such as painters (especially in the car manufacturing industry), hairdressers, chemical process workers and health care workers. In France, hairdressing ranks third among those occupations with the highest risk of OA, and is the highest among females.² Hairdressers are exposed to several reactive agents (perm lotion, hair dye or bleach) when performing techniques, with potentially irritant and sensitising effects on the airways and on the skin.

Most epidemiological studies on OA have been cross-sectional, a design that is subject to the 'healthy worker effect' and therefore underestimates the incidence of OA.⁹ Numerous authors have studied OA

incidence among bakers over the last 20 years, yielding incidence rates ranging from 0.334 to 4.44 cases per 1000 person-years (py).^{2–4,6–8,10–12} Among hairdressers, data are more scarce. According to figures derived mainly from surveillance systems or registers, OA incidence varies from 0.081 to 0.37 cases/1000 py.^{2–4,6,8,10} However, these figures are difficult to compare, due in part to methodological differences and lack of consensus about definitions, diagnosis criteria and occupational settings.

Few authors have explored the early natural history of OA. Studies evaluating the delay between the start of exposure and the onset of symptoms are recent, and seminal papers have been published on apprentices in high-risk activities such as bakery, dental hygiene or animal laboratory sectors.^{13–15} These studies described the risk factors of occupational sensitisation, including the characteristics of occupational exposure, the host and environmental factors. Among these, atopy is known to be a risk factor for OA, particularly in the baking sector and more generally in high molecular weight (HMW) allergen exposure

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Article submitted 13 November 2012. Final version accepted 8 February 2013.

environments.¹⁶ As a result, the hypothesis that atopy is a risk factor for an earlier incidence of OA, at least in sectors where HMW allergens are present, is plausible. With this in mind, we established the ABCD study (French acronym for Asthme en Boulangerie et Coiffeur Débutant, or early asthma in bakery and hairdressing), which seeks to explore the early incidence of OA during the first years of activity of young workers in high-risk occupations, focusing particular attention on the role of atopy.

MATERIALS

The details of our study design have been presented elsewhere,¹⁷ and ABCD is a retrospective follow-up study. Our source population comprised workers exposed to known occupational agents (bakers, pastry-makers and hairdressers) and non-exposed subjects, such as those in sales and food sectors (butchers, caterers, chefs, etc); the latter were used as the reference group. Our subjects graduated between 2001 and 2006 (the 'non-exposed' group in 2001) from nine vocational schools in the Lorraine region in North-East France.

First, subjects were invited to complete a medical questionnaire by telephone. The telephone interviews, conducted by nurses, allowed us to divide the subjects into three categories, according to whether they had declared 1) work-related* respiratory symptoms, 2) isolated work-related rhinitis symptoms that had appeared after the start of exposure, or 3) absence of work-related symptoms.¹⁷ The ABCD cohort was composed of all subjects who completed the telephone questionnaire.

Second, all subjects defined as 'putative' OA cases—the two first categories—and a random sample of 285 subjects who did not report symptoms, composed to represent the baseline study population for year of graduation, vocational school and occupational sector,¹⁷ were offered a medical visit at home. This included a clinical examination and interview, spirometry, blood sampling and peak expiratory flow (PEF) monitoring. The case-control study was nested within this cohort to explore factors related to diet and the work environment; the design and results are presented elsewhere.¹⁸

The research programme was authorised by the ethics committee of the CHU University Hospital in Nancy, France. Written informed consent was obtained from all subjects.

Diagnosis of occupational asthma after the medical visits and occupational asthma timing

Clinical history was explored using the Epidemiological study on the Genetics and Environment of

Asthma bronchial hyperresponsiveness and atopy questionnaire,¹⁹ while the time sequence of work-related symptoms was assessed using items derived from other dedicated questionnaires.^{20,21} Each subject who attended a medical visit was classified according to a decision tree for the definition of OA (Figure 1) into one of four categories: 1) confirmed OA, 2) probable OA, 3) possible OA, and 4) absence of OA. This classification was obtained (see Appendix† for details) on the basis of 1) the clinical definition of asthma proposed by the International Primary Care Respiratory Group,²² 2) recording of PEF curves over 3 weeks, 3) a spirometry with bronchodilator testing (short-acting β_2 agonists), and 4) work-related specific immunoglobulin E (IgE) assays, when available. A fifth category corresponded to subjects for whom OA diagnosis was indeterminate, when PEF monitoring was not useable and a reversibility test was not feasible due to contra-indications or lack of occupational exposure during the 15 days before the visit.²³ All the criteria were compared using a decision tree and the final classification was validated by an expert (CP). The date recorded for the incidence of 'confirmed' or 'probable' OA corresponds to the first occurrence of work-related respiratory symptoms.¹⁷

Calculation of the real cumulative exposure at work (corresponding to duration of exposure expressed in months among exposed subjects) entailed reconstruction of the occupational history of each subject from the start of the apprenticeship (duration of apprenticeship, diplomas obtained, hiring date, cumulative length of unemployment, date of sector dropout and date of administration of the phone questionnaire). As a result, the duration of exposure used in our study corresponds to the sum of the periods of exposure from engaging in apprenticeship (excluding classroom periods during apprenticeship or periods of inactivity) until the date of the telephone interview. This means that 1 year of cumulative duration of exposure encompasses more than 1 calendar year.

Assessment of occupational asthma prevalence and incidence in the entire study population

Based on the degree of evidence about OA (Figure 1), three definitions were established: 1) confirmed OA (OAc) only, 2) confirmed or probable OA (OAcP) and 3) confirmed, probable or possible OA (OAcPP). The data on OA stemming from medical visits were extrapolated to the whole study population, including subjects who answered the telephone questionnaires without attending the visits. For this, the positive predictive values of each category of symptoms retrieved after the telephone interview—work-related

* Corresponding to symptoms that appeared after the start of the apprenticeship and that were present at work or after a working day.

†The Appendix is available in the online version of this article at <http://www.ingentaconnect.com/content/ijatld/ijtd/2013/00000017/00000007/art00020>

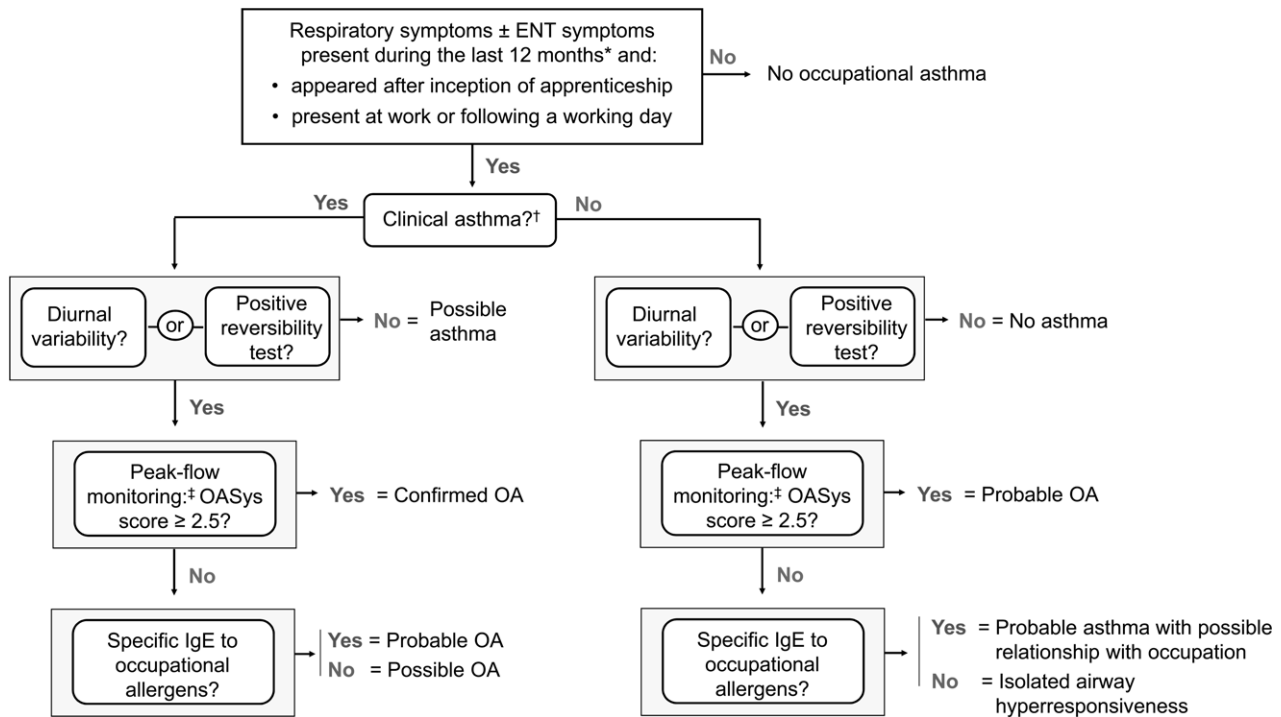


Figure 1 Decision tree for the definition of OA, from work-related respiratory symptoms to OA diagnosis. *If the person had left his/her activity or was found to take asthma medication, the 12-month period was defined before quitting and/or starting medication usage. †Symptoms complying with the clinical definition of asthma proposed by Levy et al.²² ‡PEFR was measured for 3 weeks four times a day: two in the workplace and two away from work (see Appendix). ENT = ear-nose-throat; OASys = Offender Assessment System (see Appendix); OA = occupational asthma; PEFR = peak expiratory flow rate.

respiratory symptoms suggestive of asthma, respiratory symptoms suggestive of asthma not related to work and work-related ear-nose-throat (ENT) symptoms—and the negative predictive value (absence of these symptoms) were assessed among those who also attended the medical visits ($n = 282$) for each occupational sector and for OAc, OAcP and OAcPP estimates, respectively. Results are presented below for OAcP cases. The other categories are shown in the Appendix, and the relevant differences between the three categories are given in the discussion.

Atopy

Specific IgE analysis was used to categorise subjects as atopic or non-atopic, based on the Phadiatop™ test (Phadia AB, Uppsala, Sweden). This test screens an IgE-dependent allergy with a median sensitivity of 96% (ranging from 70% to 100% across studies) and a median specificity of 95% (77–100%), according to a meta-analysis of a general adult population.²⁴ The Phadiatop test includes mite, pollen, mould and animal dander allergens, but the exact allergen composition is not issued by the company.²⁴

Statistical analysis

As we excluded all subjects who had declared having asthma before their apprenticeship, the prevalence of OA at a given point in time is also the cumulative incidence. The overall cumulative incidence

was assessed separately in the two occupational sectors of interest and among the reference group. We subdivided our study population ($N = 866$) into groups of increasing exposure duration by quartiles (Q1–Q4). Incidence rates were then computed over the successive quartiles and expressed as a number of cases per person-year (py). A global incidence rate by occupational sector was also calculated over all subjects, irrespective of their duration of exposure, to allow for comparisons with other studies. Incidence was estimated according to occupation among atopic subjects and non-atopic subjects who attended the visit.

The data were analysed using SAS 9.2 software (SAS Institute Inc, Cary, NC, USA). Proportions are expressed as percentages, and quantitative data are presented as means and standard deviations (SD). Characteristics such as sex, age, exposure duration and smoking habits were compared using the χ^2 or Fisher's exact test, Student's t -test or the Kruskal-Wallis test, as appropriate. Comparisons of incidence density were performed using the χ^2 test.

RESULTS

Study population

The student logs of the nine vocational schools provided information on 3275 apprentices—1775 bakers/pastry-makers, 1191 hairdressers and 409 sales/food

Table 1 Socio-demographic characteristics of the study participants: telephone interviews (*N* = 866)

Sector	<i>n</i>	Mean age years $\pm$ SD	Time at work* years $\pm$ SD	Smokers %	Women %	Sector dropout† %
Bakers/pastry-makers	455	24.6 $\pm$ 2.9	5.7 $\pm$ 2.6	51.7	8.1	35.2
Attended‡	148	24.6 $\pm$ 2.9	6.3 $\pm$ 2.4	50.7	9.5	18.2
Did not attend‡	307	24.6 $\pm$ 3.0	5.4 $\pm$ 2.7	52.1	7.5	43.3
Hairdressers	313	25.8 $\pm$ 3.1	7.1 $\pm$ 2.6	49.8	94.3	18.9
Attended‡	114	25.5 $\pm$ 2.6	7.0 $\pm$ 2.3	45.6	97.4	14.9
Did not attend‡	199	25.9 $\pm$ 3.1	7.2 $\pm$ 2.7	52.3	92.5	21.2
Sale or food workers	98	26.8 $\pm$ 1.5	7.4 $\pm$ 2.8	61.2	44.9	31.6
Attended‡	20	27.0 $\pm$ 1.4	6.5 $\pm$ 2.6	70.0	55.0	35.0
Did not attend‡	78	26.8 $\pm$ 1.5	7.6 $\pm$ 2.8	59.9	42.3	30.8
All	866	25.3 $\pm$ 2.9	6.4 $\pm$ 2.7	52.1	43.4	28.9
Attended‡	282	25.1 $\pm$ 2.8	6.6 $\pm$ 2.4	50.0	48.2	18.1
Did not attend‡	584	25.3 $\pm$ 3.0	6.3 $\pm$ 2.9	53.1	41.1	34.1

*In the sector from which the subjects graduated (taking into account the probationary period during apprenticeship).

†In the sector from which the subjects graduated.

‡Medical visit.

workers—who graduated between 2001 and 2006. Contact details for 2282 (70%) subjects were obtained through the parents. Of these, 866 (38%) completed the telephone interview and were included in our study. A summary flow chart is presented in the Appendix.

The main characteristics of the subjects are presented in Table 1. Additional information is available in the Appendix, allowing a comparison of participants and non-participants, including those who refused to participate in the telephone interview.

Medical visits and telephone interviews

Among the 866 subjects included in our study, 258 (30%) who reported work-related respiratory or rhinitis symptoms were offered a medical visit; 162 (63%) accepted. Among the putative OA cases, no difference was observed between subjects who completed the visit and those who declined regarding occupational sector ($P = 0.88$), work seniority (6.94 [2.47] vs. 6.37 [2.69], $P = 0.88$) and sector dropout (25.6% vs. 30.2%, $P = 0.50$); patterns in smoking prevalence were more contrasted (53.7% vs. 65.6%, $P = 0.10$). Among the 285 non-symptomatic subjects selected for a medical visit, 120 completed it (acceptance rate 42%).

The main characteristics of subjects who attended the visit ($n = 282$) and those who did not are also shown in Table 1. Sector dropout was greater among subjects who did not attend the visit compared with the attendees ($P < 0.001$); this difference was only observed among the bakers/pastry-makers when the sectors were analysed separately.

Occupational asthma classification

At the end of the investigations, participants were classified using the OA classification decision tree (Figure 1). Among the 282 subjects who were visited, 110 re-

ported work-related respiratory symptoms (with or without ENT symptoms) during the visit (55 BP, 50 hairdressers and 5 sales or food workers). They were split across 14 confirmed OA cases, 17 probable OA cases, 17 possible OA cases, 16 undetermined, 6 cases of airway responsiveness (the occupational origin being impossible to investigate among these subjects, as the OA diagnosis was not retained) and 40 non-OA cases (Figure 2); 54 reported only ENT symptoms.

Of the participants who declared work-related respiratory symptoms after the telephone interview, respectively 13%, 28% and 45% were classified according to our three definitions—OAc, OAcP and OAcPP—after the medical visit.

Early incidence of occupational asthma

Trends over time of the incidence of OA are presented in Figure 3. Among bakers/pastry-makers, incidence is high during the first quartile (Q1; upper bound 4.3 years) after the start of exposure. The average estimated incidence rate during this period is greater than in the other duration of exposure groups ($P = 0.002$, $P = 0.0004$ and $P = 0.0001$ for comparisons of Q1 with Q2, Q3 and Q4, corresponding to the upper bounds of 6.4, 8.6 and 16.3 years, respectively), where rates are similar. Figures are more stable over time among hairdressers, but tend to show a similar pattern, with higher rates after a short duration of exposure. No OA case was observed among the reference group (workers in the sales and food industries) during the same follow-up period.

Occupational asthma incidence and atopy

Although atopy is an established risk factor for OA among bakers/pastry-makers (rate ratio [RR] 7.54, 95% confidence interval [CI] 2.36–24.09), the association remains unclear (RR 3.40, 95%CI 0.70–16.61)

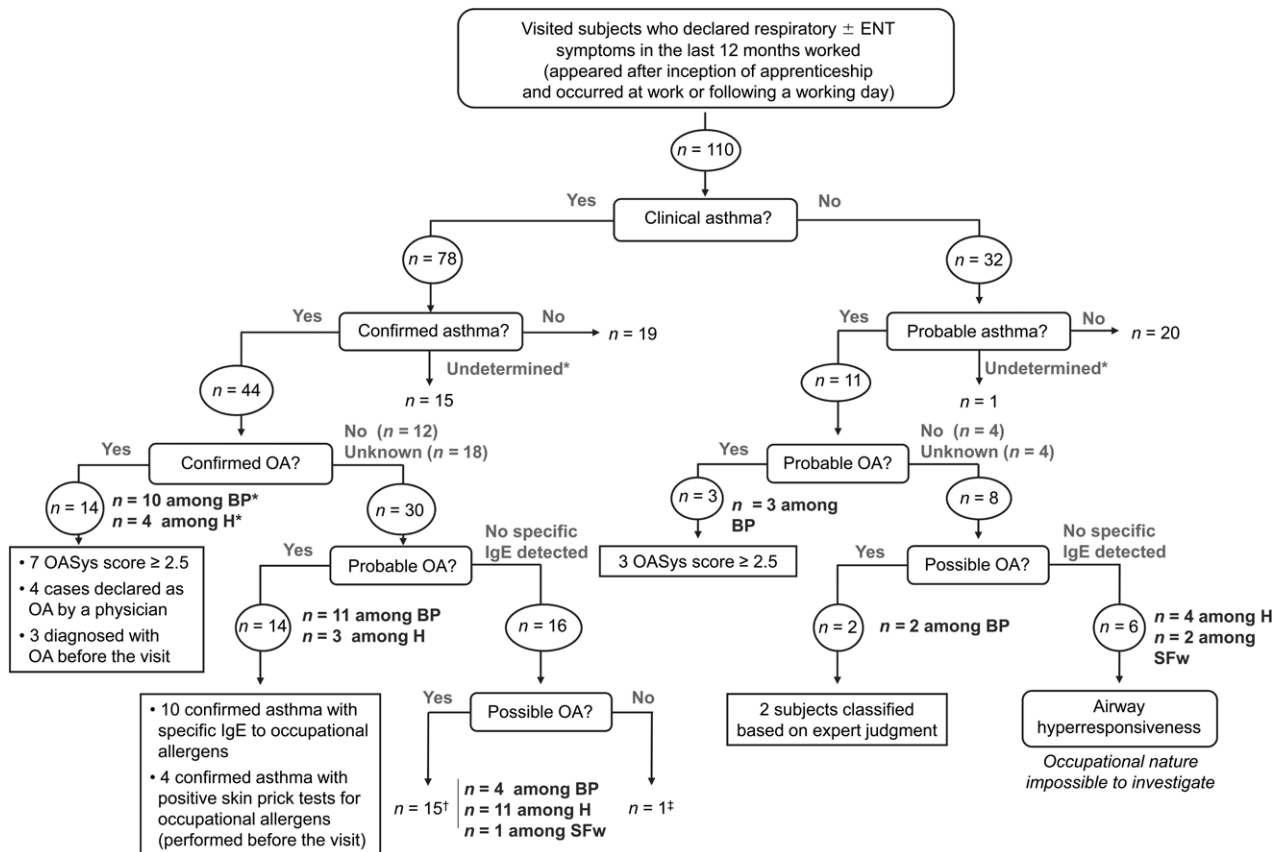


Figure 2 Distribution, after the medical visit, of subjects who had declared work-related respiratory symptoms. * Confirmation of asthma is not possible for subjects for whom the reversibility test is not performed (contraindicated) or non-contributory (subjects who no longer work in the sector), and for whom PEF monitoring cannot be interpreted. † 16 subjects in total: 1 subject (H) with non-work-related respiratory symptoms was classified as 'possible OA' after PEF monitoring. ‡ This subject (BP) performed complementary tests at hospital which ascribed asthma manifestations to household moulds (non-occupational asthma). ENT = ear-nose-throat; OA = occupational asthma; BP = bakers and pastry-makers; H = hairdressers; OASys = Offender Assessment System; SFw = sales or food workers.

among hairdressers. With regard to the prevalence of atopy, no difference was found between OA cases with short duration of exposure (Q1 86%) relative to OA cases with higher seniority (the three other quartiles, grouped for the sake of statistical power because of small numbers of cases, 82% [atopy prevalence was consistent across these three quartiles; data not shown]; Table 2). Relative risks associated with atopy are similar among early (Q1) and later (Q2, Q3 and Q4) OA-onset cases, both among bakers/pastry makers and among hairdressers (atopy RR 6.00, 95% CI 1.47–24.4 and 5.99, 95% CI 1.78–20.1, respectively, in the two occupational groups combined, Table 3). The relative risk for early—first quartile of exposure duration—vs. later occurrence is therefore 1.04 (95% CI 0.77–1.41).

Current active smoking was unrelated to OA (RR 0.91, 95% CI 0.47–1.75), even after adjusting for atopic status (RR 0.78, 95% CI 0.35–1.75).

Occupational asthma risk and sector

The risk of OA among bakers/pastry-makers is almost four times greater than among hairdressers (RR 3.64,

95% CI 2.04–6.49). No difference ($P = 0.93$) was observed across sectors for the latency period between start of exposure and asthma symptoms among OA cases (mean 3.34 years [SD 5.93] for bakers/pastry-makers vs. 2.83 years [SD 1.60] among hairdressers).

Total estimated incidence rates of OA during the first 12 years after inception of exposure (99th percentile of the exposure duration group) were 2.63 per 100 py for bakers/pastry-makers and 0.58/100 py for hairdressers.

DISCUSSION

In summary, while the incidence rate of OA is higher during the first quartile of exposure compared with longer durations among bakers/pastry-makers, atopy is not a risk factor for earlier incidence. Similar results were observed among hairdressers, but failed to reach significance because of the small numbers. Over the whole study period, early incidence rates were high in the two occupational sectors. Among the subjects who attended the medical visit, respectively 50% and 57% of all OA cases among bakers/pastry-makers and

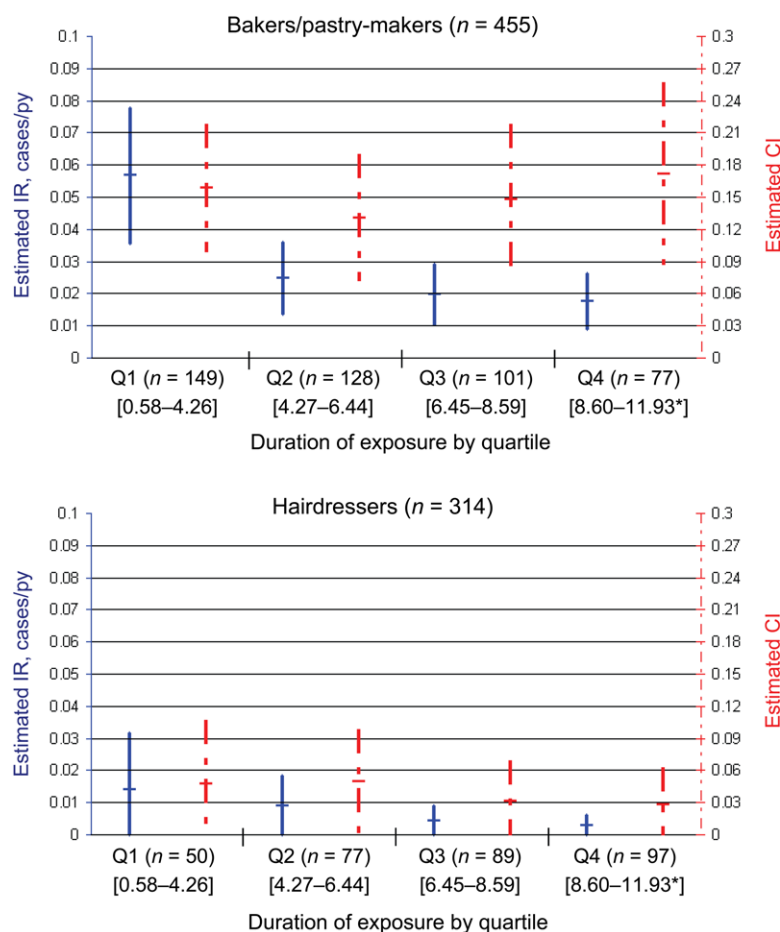


Figure 3 Evolution of the estimated cumulative incidence (dashed lines) and incidence rate (solid lines) of 'confirmed or probable' occupational asthma according to duration of exposure by occupational sector. *Value of the 99th percentile; few subjects had up to 16 years of seniority. IR = incidence rate; py = person-year; CI = cumulative incidence; Q = quarter. This image can be viewed online in colour at <http://www.ingentaconnect.com/content/ijutld/ijutld/2013/00000017/00000007/art00020>

hairdressers occurred during the first 3 years of exposure, within a 12-year (99th percentile) follow-up period.

Atopic status was not a determinant of early onset of OA in any of the two exposed groups, whatever OA definition was used. Irrespective of the occupational sector, our results suggest that atopy does not influence the timing of OA symptoms, which are not precipitated among atopic compared to non-atopic

Table 2 Prevalence of atopy according to duration of exposure among bakers/pastry-makers and hairdressers who attended the medical visits

Prevalence of atopy among cases	Duration of exposure	
	Quartile 1	Quartiles 2, 3, 4*
Among bakers and pastry makers	0.91	0.85
Among hairdressers	0.67	0.75
Total	0.86	0.82

* Because of small numbers, quartiles 2, 3 and 4 were grouped together to contrast with subjects with shorter duration of exposure (quartile 1).

subjects. While atopy is well known as a predisposing factor for OA in bakers/pastry-makers, this correlation is unclear among hairdressers (71% atopic subjects among OA cases vs. 40% among non-OA cases: RR 3.47, 95%CI 0.70–17.05). Published results are controversial in this sector. Albin et al. found that atopy had no effect,²⁵ nor was it associated with persulphate-related asthma in the subjects studied by Moscato et al.²⁶ or Munoz et al.²⁷ Akpınar-Elci et al., however, found an increased risk among atopic hairdressers.²⁸ However, because atopic status was assessed at the end of our study, sometimes several years after the onset of symptoms, there is some imprecision in the measurement of these associations.

Our data confirm that the average rate of occurrence of OA is high during the first years of activity and exposure, as already demonstrated elsewhere.^{29, 30} Beyond four years of exposure, the average estimated incidence rates of OA remain stable, resulting in gradually increasing cumulative incidence among bakers/pastry-makers (for the OAcP and OAcPP case

Table 3 Prevalence of occupational asthma according to duration of exposure and atopic status among bakers/pastry-makers and hairdressers who attended the medical visits

	Prevalence of OA and associated risk			
	Quartile 1 exposure		Quartiles 2, 3, 4 exposure*	
	Atopic % (n/N)	Non-atopic % (n/N)	Atopic % (n/N)	Non-atopic % (n/N)
Among bakers and pastry-makers	45.5 (10/22) RR = 8.18 (95%CI 1.15–58.03)	5.6 (1/18)	25.6 (11/43) RR = 6.65 (95%CI 1.55–28.40)	3.9 (2/52)
Among hairdressers	33.3 (2/6) RR = 3.33 (95%CI 0.37–29.40]	10.0 (1/10)	9.7 (3/31) RR = 4.16 (95%CI 0.45–38.15]	2.3 (1/43)
Total	42.9 (12/28) RR = 6.00 (95%CI 1.47–24.39)	7.1 (2/28)	18.9 (14/74) RR = 5.99 (95%CI 1.78–20.08)	3.2 (3/95)

*Because of small numbers, quartiles 2, 3 and 4 were grouped together to be contrasted with subjects with shorter exposure duration (quartile 1).

OA = occupational asthma; RR = rate ratio; CI = confidence interval.

estimates), an observation that corresponds to that described by Jacobs et al.³¹ On the other hand, cumulative incidence is stable among hairdressers after 6.5 years. These time patterns express a combination of processes, such as the force of early OA incidence, the severity of symptoms and the measures that can be taken by asthma patients to manage their condition, including leaving their jobs or, if possible, modifying their activity or workplace.

With regard to the incidence of OA, our results are higher than previously published incidence rates, with a rate almost six times greater among bakers/pastry-makers and nearly sixteen times greater among hairdressers (0.44% py and 0.037% py, respectively^{2–4,6–8,10–12}). Several factors may explain this difference, including methodology, data sources, case definition and work practices. We think this observation is also likely to highlight the underreporting of OA cases in many published papers, due to inappropriate methodology.

We chose bakers/pastry-makers on one hand, and hairdressers on the other, because the physical and chemical nature of the agents involved in asthma development, and possibly the underlying mechanisms, differ substantially. Previous results from our team have shown that the early incidence of bronchial hyperresponsiveness was greater among bakers/pastry-makers engaged in apprenticeship than among hairdressing students.³² Our results do not support the view that these differences across occupational sectors translate into the duration of the latency period.

Based on data from subjects who underwent the medical visits, 50% of all OA cases among bakers/pastry-makers occurred during the first 3 years of exposure (71% among hairdressers), given the fact that we decided to set the date of asthma onset to when the first respiratory symptoms were declared by the study participants. From a prevention point of view, this confirms that early screening of OA in these at-risk occupations would be most appropriate at the

end of the apprenticeship (median duration of exposure during apprenticeship = 2.8 years). It has been shown that the medical outcome is best when OA is diagnosed soon after the onset of symptoms and workers are removed from further exposure or undergo appropriate treatment.³³

Some limitations of this study warrant further discussion. Although spirometry is a recommended method for measuring airflow limitation and reversibility for the diagnosis of asthma, it lacks sensitivity. Repeated testing over time was not practical with our study design, so we recorded PEF as an alternative method and looked for diurnal variation in PEF > 20%. Use of the specific inhalation challenge, the gold standard for confirming a diagnosis of OA, was not possible in the context of our study, leading to a probable overestimation of the true incidence of OA. The date recorded for the diagnosis of OA was that of the occurrence of the work-related respiratory symptoms, to avoid overestimation of the latency period. This may also have resulted in an overestimation of the OA incidence in the first exposure duration groups and, conversely, an underestimation in the last ones.

Accurate monitoring of the PEF rate depends on patient compliance and honesty. Diurnal variation could not be interpreted for 49% of the subjects considered as 'putative' OA cases (results sheet not completed, data incorrect or PEF not returned) and the OASys (see Appendix) score was evaluable for only 22% of the subjects (more PEF records are required than for the interpretation of diurnal variation, and it is not computable for workers who have left the training sector). Moreover, the period without work exposure was usually short, limited to 2 days per week, a fact that could reduce the diagnostic yield of the OASys score. Finally, PEF monitoring does not entirely exclude the possibility of work-aggravated asthma.

Different definitions were used to ascertain OA with different levels of proof. For bakers/pastry-makers, the definition of 'confirmed' or 'probable'

OA seemed to us to be the most suitable. Nevertheless, the true incidence of OA is likely to be greater, as assessing the association of asthma with work is prone to uncertainties (e.g., OASys score not calculable or IgE assays not comprehensive). For hairdressers, the same diagnostic criteria tend to more heavily underestimate the incidence of OA. The reason is that it is hard to demonstrate sensitisation to bleaching agents, and particularly to persulphate salts, the main causes of respiratory symptoms and of hairdressers' OA. Tests were either unavailable (for IgE assays) or unfeasible in the context of our study (French regulations prohibit skin prick tests in a non-medical environment). As a consequence, contrasts between the two sectors might be exaggerated in the OAcP estimate.

The asthma status of subjects for whom diurnal variability was not available and the reversibility test was not performed (or was not contributory if the subject was no longer exposed) remains uncertain. When these 'undetermined' cases ($n = 16$) were excluded, the total cumulative incidences of OA were reduced by 3.8–5.3% among bakers/pastry-makers depending on the context, and by 7.0–9.3% among hairdressers, mostly women, including pregnant women, among whom the reversibility test with salbutamol was not performed.

Another limitation of this study is that 256 workers refused to complete the initial telephone questionnaire. Data on 74 of these non-participants, for whom minimal information could be obtained despite the refusal to participate, did not show any differences compared to those who did participate as regards the prevalence of asthma-like symptoms (see Appendix). Also, 96 subjects (37%) classified as 'putative' OA cases after the telephone interview refused to attend the medical visit, resulting in imprecisions in the assessment of OA incidence. Because these subjects did not exhibit differences in OA-relevant characteristics, we think that extrapolation of the OA frequencies observed among those who underwent the medical visit is appropriate. Comparisons between bakers/pastry-makers who attended and those who did not showed a greater sector dropout among non-attendees; this might be because they felt less concerned by the study topic. However, this difference was unrelated to medical conditions.

The above limitations tend to underestimate the incidence of OA in our study, possibly with a greater impact on hairdressers than on bakers/pastry-makers. To estimate the cumulative incidence of OA, the predictive values of symptoms declared after the telephone interviews were calculated on the basis of all the subjects who also completed the medical visit, by occupational sector. Due to the limited size of our study sample, we computed these predictive values over all exposure durations, which might result in reduced contrasts in incidence estimates between quartiles of duration of exposure.

CONCLUSIONS

Atopy was not a risk factor for the earlier onset of OA among bakers/pastry-makers and hairdressers. Occupational asthma symptoms occur soon after the inception of exposure, with higher incidence rates among the former, an observation that highlights a need for early screening of OA by the end of apprenticeship in these at-risk occupations.

Acknowledgements

The authors are grateful to the young workers who volunteered for this study and to their families for the preliminary recruitment step. They thank the directors and the administrative personnel of the nine vocational training centres of Lorraine: Bar-Le-Duc, Forbach, Gérardmer, Epinal, Laxou, Metz, Nancy, Epinal and Thionville. This project received funds from the Agence française de sécurité Sanitaire de l'environnement et du travail (contract EST-08-03), the Programme national hospitalier de recherche clinique (Hospital clinical research programme; 2008), the Lorraine Region, the Grand Nancy Urban Community and the Meurthe et Moselle Département. T Rémen and D-S Acouetey were recipients of doctoral grants from the Lorraine Region.

Conflict of interest: none declared.

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APPENDIX

METHODS

Diagnosis of occupational asthma after the medical visits

Several criteria were used in the decisional tree to assess whether a subject had asthma and whether it was occupational asthma (OA).

Asthma diagnosis

This step enables a differential diagnosis with non-asthmatic respiratory conditions (such as chronic bronchitis). A positive response to any of the questions below suggests an increased likelihood of asthma and is considered 'clinical asthma'.¹

- 1 Have you had wheezing or whistling in your chest at any time in the last 12 months?
- 2 Have you been woken up at night by an attack of coughing at any time in the last 12 months?
- 3 Have you been woken up at night by an attack of shortness of breath at any time in the last 12 months?
- 4 Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?

Additional information was used to confirm asthma. Subjects who reported work-related respiratory or rhinitis symptoms were asked to perform complementary tests.

Monitoring of the peak expiratory flow rate (PEFR)

Subjects were given a peak-flow meter (Asma-1[®], Vitalograph, Ennis, Ireland), a results sheet, instructions on how to use the device and a prepaid parcel for its return. They were asked to measure their PEFR for 3 weeks² four times a day: two at the workplace (the first 2–3 hours after starting work and the second at the end of the work shift), and two out of work hours (one before going to work and the other before going to bed).^{3,4} For each measurement, the subjects needed to record the best of three attempts on the result sheet (which was also kept by the automatic data log). PEFR variability is calculated between values at work and those out of work, for each day, during the 3 weeks of follow-up. Diurnal variability was defined as a variation in PEF of >20% (with twice daily readings, >10%).⁵

Bronchial obstruction reversibility test

All subjects who presented work-related respiratory symptoms or rhinitis were asked to perform a bronchial obstruction reversibility test (in the absence of contraindications). After validation of the respiratory function test by an expert panel (PM, HB and PC), reversibility was assessed, characterised as a rapid improvement in FEV₁ and at least 12% and 200 ml of baseline value,⁶ measured 15 min after the inhalation of 400 µg of salbutamol.

Taking asthma treatment

Taking treatment was not enough to confirm asthma, due in part to lack of consensus about definitions and diagnostic criteria between physicians. That is why this step does not appear in the decisional tree. However, subjects taking beta-2 mimetics or corticosteroids might mislead the interpretation of the peak-flow monitoring or the reversibility test. For subjects under such treatment for whom PEF monitoring was normal and the reversibility test negative, an expert (PC) was responsible for confirming or not the suspected asthma, on the basis of the patient's record (medical questionnaire, case report form and test results).

If the confirmation of asthma was not available, mainly due to diurnal variations that were not assessable and contraindications for performing the reversibility test, OA status remained indeterminate.

Reliability of the association of symptoms with work

Once the diagnosis of asthma was confirmed, two methods with different standards of proof were used to link asthma to work. The OASys (Offender Assessment System) score was thought to have the best level of proof. Data obtained from the PEF monitoring were captured in OASys-2 software (<http://www.occupationalasthma.com>). OASys-2 uses a discriminant analysis to score the record between 1 and 4 using a cut-off of 2.5. Scores above this have 94% specificity for occupational asthma and 75% sensitivity in reference to independent methods of diagnosis.⁷ Thus, a low score cannot be used to disregard occupational asthma. Specific occupational IgE assays were also used, but with a lower level of proof. Due to different exposures, IgE assays depend on the occupation sector. For bakers and pastry makers, occupational sensitisation was considered if 1) Phadia Pax 3 (mixes of *Aspergillus fumigatus*, *Alternaria alternata*, rye pollen, wheat pollen) test was positive, if 2) Phadia Pax 4 (mixes of wheat, soya bean, *alpha-amylase*, *Sitophilus granarius*) test was positive (sensitivity and specificity for these tests were not available), or if 3) specific IgE for Latex (Phadia, k82) was >0.35 kU/l (Se = 92.8%, Sp = 94.1%).⁸ As no test for occupational sensitisation to persulphate was available for hairdressers, occupational sensitisation was considered in this sector if 1) a specific IgE test for quaternary ammonium was positive (percentage of 125I-anti-IgE absorbed onto the solid phase >2.3%⁹) or if 2) specific IgE for latex (Phadia, k82) was >0.35 kU/l. For sales and food-related jobs, only specific IgE assays for latex (Phadia, k82) were used. Assays were performed on Immunocap 100TM (Phadia, Sweden). At least one positive test characterised occupational sensitisation. When associated with a diagnosis of asthma with a time relationship with work, this suggests a strong case for OA.

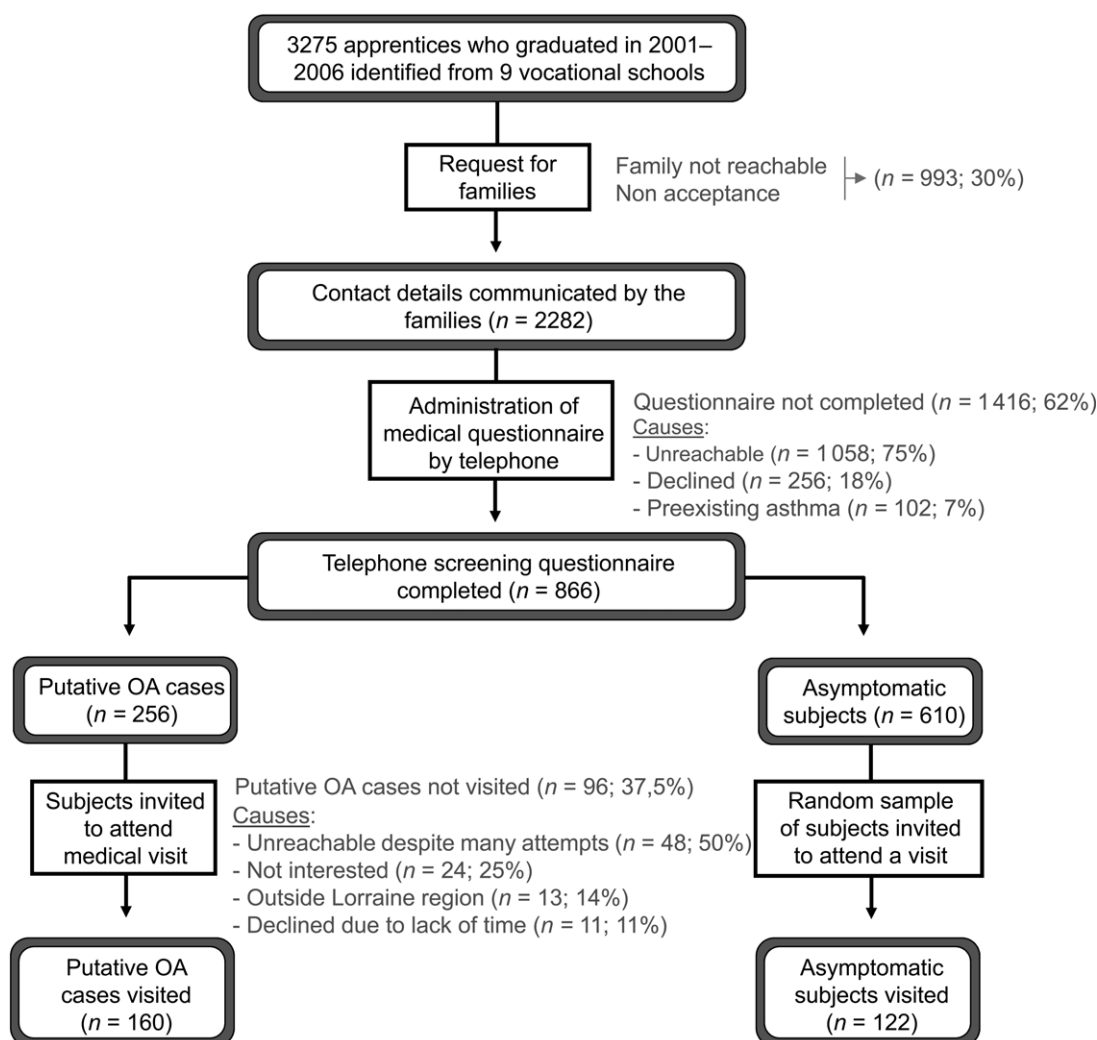


Figure A.1 Summary flowchart. OA = occupational asthma.

Evidence of sensitisation to occupational agents was also considered conclusive when subjects brought the results of skin prick tests to the medical visit. Because the tests performed for the IgE assays were not exhaustive (only the most common allergens were looked for), they can be false-negative. Some workers had left the sector many years previously; furthermore, as non-IgE-dependent mechanisms are invoked among hairdressers, lack of sensitisation cannot be used to disregard OA.

RESULTS

A summary flowchart is presented in Figure A.1. On the basis of the whole population source ($n = 3275$), comparisons were made between respondents (who answered the telephone interview) and non-respondents about the work sector ($P = 0.14$, slightly more hairdressers among respondents), sex ($P = 0.10$, slightly more females, due to the above) and year of graduation ($P = 0.04$): respondents graduated earlier than non-respondents (38%, 26% and

36% vs. 34%, 29% and 37% for diplomas obtained in 2001–2002, 2003–2004 and 2005–2006, respectively). Participation in the telephone interview by occupational sector does not change ($P = 0.86$). The 256 subjects who refused to complete the initial telephone questionnaire did not differ from those who

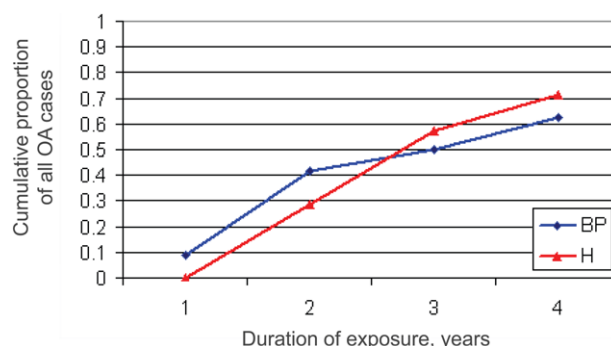


Figure A.2 Cumulative proportion of OA cases among bakers or pastry makers (BP) and among hairdressers (H) during the 4 first years of exposure. OA = occupational asthma.

Table A Evolution of cumulative incidence and of average incidence rates (in number of cases per 100 person-years) for 'confirmed' OA (OAc) and 'confirmed, probable or possible' OA (OAcpp) according to duration of exposure and occupational sector

Sector	Case definition	Q1*	Q2*	Q3*	Q4*
		cumulative incidence (95% CI)	cumulative incidence (95% CI)	cumulative incidence (95% CI)	cumulative incidence (95% CI)
Bakery or pastry-making	OAc	0.06 (0.02–0.11)	0.04 (0.00–0.07)	0.06 (0.01–0.11)	0.05 (0.00–0.10)
	OAcpp	0.19 (0.12–0.26)	0.14 (0.07–0.20)	0.19 (0.11–0.27)	0.23 (0.13–0.33)
Hairdressing	OAc	0.03 (0.00–0.09)	0.04 (0.00–0.10)	0.02 (0.00–0.05)	0.01 (0.00–0.04)
	OAcpp	0.15 (0.05–0.26)	0.13 (0.05–0.21)	0.07 (0.01–0.13)	0.12 (0.05–0.19)
Sale or food sector	OAc	0	0	0	0
	OAcpp	0.06 (0–0.17)	0	0	0
		Incidence rate (95% CI)	Incidence rate (95% CI)	Incidence rate (95% CI)	Incidence rate (95% CI)
Bakery or pastry-making	OAc	0.023 (0.008–0.038)	0.007 (0.000–0.013)	0.008 (0.001–0.014)	0.005 (0.000–0.010)
	OAcpp	0.068 (0.045–0.091)	0.027 (0.015–0.038)	0.025 (0.015–0.036)	0.023 (0.013–0.033)
Hairdressing	OAc	0.010 (0.000–0.025)	0.008 (0.000–0.017)	0.002 (0.000–0.007)	0.001 (0.000–0.004)
	OAcpp	0.045 (0.015–0.075)	0.025 (0.010–0.039)	0.010 (0.002–0.017)	0.012 (0.005–0.019)
Sales or food industry	OAc	0	0	0	0
	OAcpp	0.020 (0.000–0.060)	0	0	0

* Q1 (Quartile 1) median duration of exposure = 3.2 years; Q2 = 5.3 years; Q3 = 7.5 years; Q4 = 9.6 years.

responded for the same characteristics. Among the subjects who declined the interview, 74 accepted to provide basic data. Based on this information, no difference was seen between participants and non-participants in terms of history of wheezing and whistling at work ($P = 0.90$) or of asthma medical diagnosis ($P = 0.64$) after starting the apprenticeship. The dropout rate from the activity sector they had been trained for was greater among non-participants than among participants (43% vs. 32%, $P = 0.06$), with 3% of subjects ($n = 2$) declaring they had left their occupation sector due to health reasons (occupational allergy).

Seniority

Seniority was obtained by the aggregation of working periods during apprenticeship (i.e., training periods) and after apprenticeship. Among the 866 subjects included in this study, the median duration of apprenticeship was 3.8 years (min = 0.5, max = 8). The corresponding work seniority during apprenticeship varied from 0.5 to 5.7 years (median = 2.8), as all training is not equivalent in terms of working time. Regarding seniority out of the apprenticeship period, the median value was 3.8 years (min = 0, max = 12.8). Some subjects ($n = 11$) began to work before 2001, then followed an apprenticeship to complete their training, information that explains the high seniority observed in some subjects. Finally, the median seniority (including practice periods during apprenticeship) was 6.4 years (min 0.6, max 16.3 years).

Occupational asthma

A high proportion of OA cases that occurred over the whole observation period did so during the first years of exposure (including apprenticeship) among bakers

and pastry makers or hairdressers who underwent the visit, where timing of asthma incidence is the most reliable (Figure A.2).

Concerning early incidence of OA, the corresponding data for the two other OA definition categories are presented in Table A.

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R É S U M É

CONTEXTE : L'asthme professionnel (AP) se développe généralement lors des premières années d'exposition.

OBJECTIF : Décrire l'incidence précoce de l'AP chez les boulangers-pâtisseries (BP) ou chez les coiffeurs, et explorer le rôle de l'atopie.

MÉTHODE : Dans le cadre d'une étude longitudinale rétrospective, les sujets furent invités à répondre à un entretien téléphonique. Ceux déclarant des symptômes respiratoires ou une rhinite en lien avec le travail, et un échantillon de ceux ne présentant pas ces symptômes, furent sollicités pour bénéficier d'une visite médicale visant à rechercher un AP. Les données issues des entretiens et des visites médicales furent utilisées pour estimer l'incidence de l'AP en fonction de durées d'exposition croissantes.

RÉSULTATS : Au total, 866 participants furent inter-

viewés (âge moyen 25,3 ans ; 43,8% de femmes), parmi lesquels 282 réalisèrent la visite médicale. L'incidence globale estimée de l'AP confirmé ou probable au cours des 12 premières années d'exposition est élevée chez les BP (2,63 pour 100 personnes-années [p-a]) et chez les coiffeurs (0,85 pour 100 p-a), en particulier lors des 4 premières années. L'atopie est un facteur de risque important de l'incidence de l'AP, mais quel que soit le secteur d'activité, n'influence pas le délai de survenue des symptômes d'AP.

CONCLUSION : Les symptômes d'asthme professionnel apparaissent rapidement après le début de l'exposition. Nos résultats suggèrent que l'atopie ne précipite pas la survenue de symptômes dans deux contextes différents d'exposition à des agents sensibilisants.

R E S U M E N

MARCO DE REFERENCIA: El asma profesional aparece con mayor frecuencia durante los primeros años de la exposición.

OBJECTIVO: Describir la incidencia de asma profesional en los panaderos y pasteleros y en los peluqueros e investigar la función que cumple la atopía en estos casos.

MÉTODOS: En un diseño de seguimiento retrospectivo se invitó a las personas a responder a una entrevista telefónica. Se propuso una consulta médica a las personas que declararon síntomas respiratorios o de rinitis relacionados con el trabajo y a una muestra de todas las demás personas, con el objeto de realizar una investigación del asma profesional. Con los datos recogidos durante las entrevistas y las consultas médicas se calculó la incidencia de asma profesional, en función de duraciones progresivas de la exposición.

RESULTADOS: Se entrevistaron 866 personas (promedio

de la edad 25,3 años; 43,8% de mujeres), de las cuales 282 acudieron a una consulta médica. La tasa de incidencia global calculada de asma profesional confirmada o probable durante los primeros 12 años de exposición fue alta en los panaderos y los pasteleros (2,63 por 100 años-persona [a-p]) y en los peluqueros (0,58 por 100 a-p), sobre todo durante los primeros 4 años. La presencia de atopía constituye un importante factor de riesgo de aparición de asma profesional en los panaderos y pasteleros, pero independientemente del sector de ocupación, la atopía no influye sobre el momento de aparición de los síntomas de asma profesional.

CONCLUSIÓN: Los síntomas del asma profesional ocurren poco tiempo después del comienzo de la exposición. Estos resultados indican que la atopía no precipita la aparición de los síntomas en dos entornos diferentes de exposición a alérgenos.