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ASSESSMENT OF THE WORKER

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CASE HISTORY

A 25-year-old worker has been employed for 2 years in a small family bakery that employs three other bakers and two helpers.

1. During his apprenticeship course, the worker received information on possible allergies to cereals, enzymes, and other products in flour.
2. He started having sneezing at work 1 year before you see him, and his wife noticed some wheezy breathing at home in the evening in the past few months.
3. The local public health department had started a surveillance program in bakeries in the area. After some hesitation, the employer allowed an industrial hygienist from that department to visit the workplace and a nurse to meet with the workers.
4. An information session was offered and two short self-administered questionnaires (one for occupational asthma [OA], and one for occupational rhinitis [OR]) were completed by all attending workers.
5. Because the worker had positive responses on the self-administered questionnaires, he met with the occupational nurse, who inquired about the details of his symptoms with more detailed medical questionnaires, one for OA and one for OR. The results of these two questionnaires indicated that the worker had symptoms consistent with work-related rhinitis and asthma.
6. The worker was seen by the occupational physician of the local health department. The worker had been seen (without being referred) by an allergy specialist who had performed skin-prick tests (SPTs) to various cereals, which were positive. He was given inhaled salbutamol on demand.
7. The nurse and physician suggested that the worker make an appointment at a specialized center for further testing.
8. The worker, a recent immigrant with two children, feared losing his job because he had no other formal training but followed the advice and scheduled an appointment.
9. The worker mentioned that one coworker who was not at the meeting and had not completed the initial questionnaire had nasal symptoms and coughing. The industrial hygienist's evaluation showed that the flour dust levels in the bakery were quite high, but within the legal standards.

Introduction

Occupational asthma (OA) is an almost entirely preventable condition (1), and should be suspected in all adult patients with asthma. Developing such workplace and healthcare approaches, which primarily aim to prevent cases or identify possible cases early for further diagnostic assessment, is consequently of upmost importance.

How these approaches develop will depend on local and national expertise and will vary by resource available and medical practice in different countries. Some countries link claims for compensation, for example Finland (1), with investigations for OA, while others separate these requirements (2). Others have well-developed local protocols that consider in detail local allergen types (3) and diagnostic processes. It is likely that in other countries of lower economic development, systems may be less developed, although details are sparse (4).

Despite differences in approach by country, it is likely that globally the diagnosis of OA remains underreported, delayed when the diagnosis is made, and undercompensated (5, 6).

Health surveillance: The role of health surveillance for occupational asthma at work

The objective of health surveillance for OA in the workplace is to identify sensitized workers or those with the disease at an early and reversible stage, because clinical outcome is better when OA is diagnosed earlier (6, 7).

The optimal content of a surveillance program for OA is still a matter of debate despite the fact that such a program is mandated in many countries. In their review, Szram and Cullinan (8) state that almost all surveillance programs include a questionnaire that is generally self-completed. They concur that no questionnaires have been formally validated although it is likely that those which include standardized questions on asthma with an inquiry into any work relationship will have appropriately high sensitivity and specificity if they are completed accurately. They add that questionnaires should also include items relating to work-related rhinitis, which is not only a significant associated risk factor for asthma, but itself an indicator of failed exposure control.

The question of the accuracy with which questionnaires are completed has been raised, thus affecting the sensitivity of the test. Nicholson et al. (7) concluded that surveillance questionnaires may lead to an underestimation of the prevalence of asthmatic symptoms. Szram and Cullinan (8) state that there is good evidence that a high proportion of employees are unwilling to divulge their symptoms, because of uncertainties over confidentiality or the perceived consequences leading to job loss (9). They propose that several determinants are likely to influence the accuracy of responses: the employees' judgment on the relative importance of their health versus their employment, dependent on the severity of their symptoms and their individual attitudes; the circumstances and setting of their employment; and the attitudes of their employer. Fishwick and Forman (6) comment that despite the caveat of accuracy, questionnaires remain the key component of respiratory health surveillance schemes, as they are inexpensive and foster the culture of reporting new symptoms between surveillance visits.

Spirometry testing is a frequent tool in surveillance programs for OA, but it probably detects only few cases that would not otherwise be detected by a questionnaire (7). Szram and Cullinan (8) opine that it seems premature to reject all surveillance spirometry, but that it must be interpreted appropriately. Similarly, Fishwick and Forman (6) are in favor ofincluding high-quality workplace spirometry, in workplaces with at least a moderate risk of OA.

Immunological testing is helpful in some settings, particularly for workers exposed to high-molecular-weight (HMW) occupational allergens. Combined with assessment of nonspecific bronchial hyperresponsiveness (NSBH), the yield of immunological testing in terms of positive predictive value for OA (as confirmed by specific inhalation challenge [SIC]), is high (10, 11) as also shown in earlier studies (12).

Induced sputum (13) and exhaled nitric oxide (FeNO) (14) have been used in epidemiological surveys but their relevance and benefit, alone or combined with other tests, within a health surveillance program are unknown.

Health surveillance: What is the role of the occupational nurse in health surveillance for occupational asthma in the workplace?

The occupational nurse has a preventive and clinical role. The occupational nurse should be involved in the identification and assessment of health risks at work, and their prevention through health education and the surveillance program. The occupational nurse's actions must be based on rigorous methods and follow professional ethics and confidentiality standards.

In the province of Québec (Canada), public health departments are mandated by law to provide preventive occupational health services in targeted workplaces of all sizes, mostly in resources, manufacturing, and construction sectors. In Montréal, a standardized program was initiated in 2013 for the surveillance of OA and occupational rhinitis (OR) where there is a risk of sensitization (15). The occupational nurse plays a pivotal role in this context, as she/he is responsible for initiating and carrying out the program activities (16) (Figure 5.1). For the sake of efficiency, the program adopts a collective

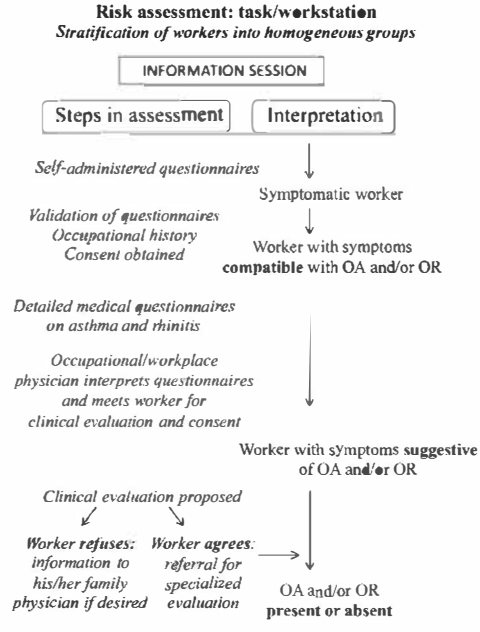

FIGURE 5.1 Severity of asthma symptoms by duration of exposure to allergenic substance.
Abbreviations: OA: occupational asthma; OR: occupational rhinitis.

approach (group information sessions for workers and employer's representatives), followed if needed by personal interactions with each worker. This strategy aims to ensure respect of each worker's autonomous decision in regards to issues that concern their health.

The occupational nurse's first task, in collaboration with industrial hygiene professionals, is to perform a risk assessment according to task and workstation, leading to stratification of workers into groups that receive a targeted information. The presentation starts with a clear explanation of the purpose of the surveillance program and items communicated are sensitizing agent(s), risky tasks/locations and exposure levels, and preventive measures (respiratory protection, ventilation, maintenance). Workers are informed about symptoms of OR and OA, their usual onset and progression, and the temporal relation with work exposure. Workers are also advised to be aware if any of these symptoms arise at work.

Self-administered questionnaires are given to workers and each question might be explained by the occupational nurse, if needed. (English questionnaires are available on pages 75 [OR] and 89 [OA] of the program document (15).) Workers are invited to meet or call the occupational nurse if they have difficulties reading and understanding the self-administered questionnaire.

It is of utmost importance to keep the content simple and at the appropriate educational level of the workers, because according to international surveys, a significant proportion of adults do not necessarily have the capacity to properly understand and use health information in written documents.

In the Montréal program, the occupational nurse meets only workers who make a request because of a self-administered questionnaire compatible with OA and/or OR. In other types of programs proposed by occupational health and safety administrations, it might be necessary to evaluate each worker individually, even after a group information session.

If the self-administered questionnaires are compatible with OR and/or OA, the occupational nurse meets the worker and gets an occupational history, with a focus on exposure to sensitizing agents. In order to obtain informed consent to proceed with further evaluation, the occupational nurse gives the worker relevant information about the advantages/disadvantages of the different options, using the standardized documentation of the program. The occupational nurse should validate that the worker understands the information, allow the worker to ask questions, and give them an appropriate period of time to decide whether or not they want further clinical investigation. In Québec, consent is legally required for any investigation required in the context of a surveillance program in occupational health. In other jurisdictions, such as the United States, the employer can require further evaluation if the worker wishes to maintain employment.

If the worker agrees to further evaluation, the occupational nurse completes more detailed medical questionnaires on OA and OR with them. The occupational nurse then forwards a request to the occupational health physician, who reviews with the worker the information already collected, interprets the two questionnaires (self-administered and detailed medical questionnaires), assesses the clinical condition, and revalidates the worker's consent to further evaluation, if needed. Workers with symptoms suggestive of OA or OR are referred for a specialized evaluation (Figure 5.1). If the diagnosis of OA/OR and causative agent are confirmed and a worker's compensation claim is accepted, the occupational nurse and the occupational health physician can assist in the relocation of the affected worker in their workplace, if that is the preferred option.

The situation at the workplace is revised every 1–2 years, with new workers invited to the full session, while the continuing workers complete the self-administered questionnaires.

The role of the occupational health physician

The role of the occupational health physician in relation to OA is to provide an expertise aimed at reducing the risk through prevention and implementation of health surveillance programs, with the help of a team of professionals that include nurses and industrial hygiene professionals. The specific tasks of the occupational health and safety department vary significantly depending on the organizational structure of the occupational health service at the workplace. In the internal model, which is increasingly rare, the surveillance is more readily integrated with the other elements of a primary preventive strategy (17). By comparison, the occupational health physician providing consultant work for many small-size industries might be asked to perform only the activities that comply with the regulatory requirements.

In 1979, a reform of the Québec occupational health and safety system put under the same umbrella the different facets of prevention (including standards setting and enforcement/inspection) and the workers' compensation system, which is a public administration (Commission des normes, de l'équité, de la santé et sécurité du travail—CNESST) financed by the employers. The specificity is that the occupational health physician, who devises and puts into action the occupational health program in a workplace, must be associated with the public health department of the region and accepted by the employer and workers' representatives sitting on the local occupational health and safety committee. Furthermore, the occupational nurse and industrial hygiene professionals who operate the program are employees of the public health department. In Québec, there are no specific standards for health surveillance of workers. To foster efficiency and coherence, occupational health physicians in Montréal generally ask the regional team to coordinate the development of practice guidelines for frequently encountered risks such as asbestos, silica, noise, etc. The guide for sensitizer-induced OA was issued in 2013 (15) addressing also OR because it is often associated with OA (Chapter 22) (17, 18). The self-administered questionnaire used for OA was initially prepared by Labrecque et al. for a prospective diisocyanate surveillance project (19). It has been described and shown to have satisfactory discriminative qualities elsewhere (20). A detailed self-administered questionnaire for OR (not published) was prepared with the same rationale as for OA. Three of the authors of the present chapter (Bourdeau, Phénix, Seguin) were the lead initiators of the surveillance program and the Section "Health surveillance: what is the role of the occupational nurse in health surveillance for, occupational asthma in the workplace?" describes the main elements of the program carried out by the occupational nurse.

This surveillance program proposes a pragmatic approach, with different recommendations from expert groups available in 2013, this including among others the European Respiratory Society (21), the British Occupational Health Research Foundation (7), and the European Academy of Allergy and Clinical Immunology (18) while being compatible with the public health principles of empowerment and benevolence. Lately, the elements of the

program pertaining to OA became the basis of the provincial program prioritizing the risk associated with exposure to wood dust.

The main objective is to offer workers exposed to a known sensitizer the most relevant information and tools, so they can recognize the early symptoms of OA/OR (17) and ask for guidance if they choose to. From the start, workers make autonomous decisions as to what conduct is in their best interest, and the role of the occupational nurse and the occupational health physician is to foster their decision process by highlighting the advantages/disadvantages of the different options available. The worker has control of the sequential process and can refuse to proceed further if they foresee unfavorable socioeconomic consequences (21, 22) mainly on employment and insurance.

The program follows the suggestions of the World Health Organization, cited by Wilken et al. (23): it addresses a significant health problem (OA) that has a better prognosis if diagnosed early; OR has a significant impact on quality of life and productivity (24) and can be inferred as a proxy to early or coexisting OA (25); the process is acceptable to the worker, who is asked for their consent at all times; the different questionnaires have an interpretation grid that provide explicit criteria for proposing a presumptive diagnosis. Each question of the 11-item self-administered questionnaire as well as the whole questionnaire used in the Québec program show high sensitivity and negative predictive value (20), and therefore represents a satisfactory preliminary triage followed by the sequential use of a detailed questionnaire and occupational health physician's evaluation, all these means increasing the predictive value of the surveillance method (23); the cost/benefit ratio is favorable, because the occupational nurse already has the mandate to give information sessions on health risks and only symptomatic workers will require occupational nurse and occupational health physician attention/time. The utilization of more costly specialized resources is also limited to workers with a significant probability of being diagnosed with OA/OR.

Skin-prick tests (SPTs) have been integrated in epidemiological studies of asthma (26) and OA for many years (27) but they are not generally part of the surveillance program, for different reasons: availability of extracts with satisfactory allergenic quality, time required, quality control for SPT (Chapter 7), but, mostly, these tests need consent that addresses the possible consequences of a positive test on employment. They are reserved for workers whose symptoms are suggestive of OA/OR and want further evaluations. It is the same for spirometry, which, besides the logistical aspect, does not add any significant benefit over questionnaires (25).

In small workshops, employers are not always aware of the health risks in their workplace and of their obligations; the intervention of the public health department team increases their knowledge and hopefully helps change their attitudes, although this represents an ongoing challenge. If the employer has a satisfactory occupational health and safety organization, new employees are likely to receive appropriate health information. When the risk evaluation shows an unacceptable level of exposure, a link is made with the inspection agent who has the enforcement power for improving the situation.

In Québec, public health regulation specifies that OA is an occupational disease that should be notified, and each case is investigated by the public health department to ascertain whether other workers are also at risk and if exposure levels are acceptable. If appropriate, the program is applied to a specific workplace, even though it might not be in a prioritized sector of economic activity. OR is not an occupational disease that needs to be notified but this diagnosis is likely to increase the attention given to reducing exposure to possible causal agents present in the workplace (24).

A large proportion of Québec workers exposed to sensitizers do not have access to the surveillance program described here, because their workplace is not on the priority list. In these situations, it is the role of the family physician (primary healthcare provider, see below) to identify respiratory symptoms, see whether they might be work-related, and, if so, advise on proper referral. Suojalehto et al. make the point that an OA surveillance program increases awareness of OA symptoms and encourages workers to seek health care (25). In the Montréal program, a worker that refuses to go ahead with the evaluation is given a copy of their file, so she/he can bring it to a family physician.

Initial assessment of workers with possible occupational asthma by primary healthcare providers

Workers presenting to primary care physicians with recurrent respiratory symptoms need to be assessed for asthma and the possible relationship of their symptoms to work. A joint statement of the European and American Thoracic Societies concluded that the estimated population-attributable fraction (PAF) for the occupational contribution to incident asthma was 16% (95% CI = 10%-22%) (28) and another 21.5% of asthma in adults is aggravated by workplace exposures (29). Despite these estimates that work is an important contributor to the cause and exacerbation of asthma in adults, Mazurek and coworkers reported that only 9% of 50,000 working American adults with asthma were ever told by a physician that their asthma could be related to any job they ever had (30). An audit that included nearly 400 UK patients selected from a general practice population of 27,000 patients showed that occupation was recorded in only 14% of cases (31).

The American College of Chest Physicians (ACCP) consensus statement recommends the following four key questions for adult patients with new-onset asthma or with asthma that becomes more symptomatic (32):

1. Were there changes in work processes in the period preceding the onset of symptoms?
2. Was there an unusual work exposure within 24 hours before the onset of initial asthma symptoms?
3. Do asthma symptoms differ during times away from work such as weekends or holidays or other extended times away from work?
4. Are there symptoms of allergic rhinitis and/or conjunctivitis symptoms that are worse with work?

The medical history provided by the patient is not specific for the diagnosis of work-related asthma (WRA) but is sensitive, a quality also required for a tool to be kept in surveillance programs (33). If the symptoms involve loss of voice, then vocal cord dysfunction should be considered (34).

Recommended question 1 elicits whether there have been changes in the process such that a new chemical has been introduced or levels of exposure have changed. Question 2 asks about a previous acute exposure that immediately (within 24 hours) preceded the onset of symptoms to uncover the development of irritant-induced asthma and reactive airways dysfunction syndrome

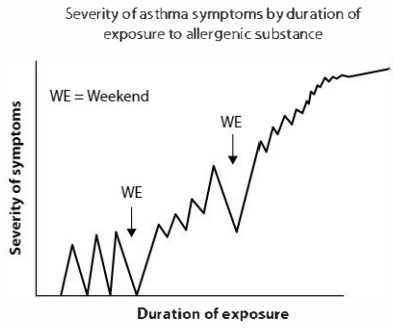

FIGURE 5.2 Typical temporal pattern of respiratory symptoms of OA with marked improvement away from work diminishing or even ceasing if the patient continues to be exposed to the substance causing the OA. (From Cartier A, Bourdeau N, Phénix P, Rosenman KD. Assessment of the worker. In: Malo JL, Chan-Yeung M, Bernstein DI, eds. *Asthma in the Workplace.* 4th ed. Boca Raton FL: CRC Press; 2013:77.)
Abbreviation: OA, occupational asthma.

Safety Data Sheet

1. Product Identification

PRODUCT NAME.....INSTANT-LOK (R)

2. HAZARDOUS INGREDIENTS

INGREDIENT NAME/CAS NUMBER/PERCENTAGE	EXPOSURE LIMITS
PARAFFIN WAX	OSHA.....2 mg/m3
CAS NUMBER.....8002-74-2	ACGIH....2 mg/m3
OSHA PERCENTAGE.....>1	STEL.....6 mg/m3
	CEILING..none

FIGURE 5.3 Example of an SDS of an adhesive, which provided only a partial listing of ingredients because the chemical company that wrote the SDS did not include colophony, a well-accepted cause of OA, as a hazardous ingredient. (From Cartier A, Bourdeau N, Phénix P, Rosenman KD. Assessment of the worker. In: Malo JL, Chan-Yeung M, Bernstein DI, eds. *Asthma in the Workplace.* 4th ed. Boca Raton, FL: CRC Press; 2013:78.)
Abbreviations: OA, occupational asthma; SDS, safety data sheet.

(RADS) (see Chapter 19). The typical response obtained from a patient with OA to question 3 is improvement of symptoms on weekends or vacations or even complete resolution after a prolonged time away from work for 1–2 weeks. This is particularly true early in the course of OA. Figure 5.2 illustrates the typical temporal pattern of symptoms related to work with continued exposure over weeks, months, and years after the onset of symptoms. As duration of exposure and symptoms increases, the patient is less likely to have symptoms resolve when away from work, to the point where there may be no improvement away from work. It is important to ask about temporal relationship of symptoms with work exposure at the time symptoms first began since temporal relationships may become less obvious or disappear with time (Figure 5.2).

Question 3 is the key question that assesses improvement away from the workplace. If a patient's asthma symptoms improve away from work, it is important to assess what the patient does and the potential exposures at work. The patient should be asked to describe precisely the tasks accomplished and what activities or exposures are associated with respiratory symptoms that either develop immediately and/or occur later even at home after work. Asking the patient to draw a floor plan of the workspace can be helpful to better understand potential exposures. The use of personal protective equipment and the patient's perception of the ventilation should be assessed. The frequency of spills and leaks, what the patient was doing at the time, whether the patient was responsible for cleaning up the spilled material, and whether they wore special protective equipment should be evaluated. Industrial hygiene reports of previous air sampling studies when available can be useful to document particular substances in the workplace and exposures levels. However, since the allowable air level standards for most workplace substances causing asthma were not implemented to prevent sensitization, measured levels that are below allowable Occupational Safety and Health Administration (OSHA) standards are no assurance that the suspected agent is not potentially causative.

Patients should be asked to provide the names of the substances and the material safety data sheets (SDSs) of products they work with or are used by others around them. Exposures from nearby processes may be more important than the patient's own activity. SDSs are required to be made available to all workers but patients may not know how to access them or are afraid to request these from their employer. When patients can provide them, healthcare providers should be wary of their completeness (35). SDSs are prepared by the manufacturer or formulator of the product, who is not required to list all the ingredients in the product below 1%, Figure 5.3 shows the top half of the first page of an SDS of an adhesive used in a bottling plant to glue the labels. The SDS did not indicate that the adhesive contained 70% colophony, a well-known cause of OA. The developer of the SDS is required to provide a complete list of the ingredients even if they are trade secrets after the treating physician contacts address/phone number on the SDS. Chapters 12 to 19 discuss known asthma-causing agents. A comprehensive list of asthma-causing agents is regularly updated and can be consulted on the Association of Occupational and Environmental Clinics website (36) and elsewhere: https://reptox.cnesst.gouv.qc.ca/en/occupational-asthma/Pages/occupational-asthma.aspx

Since new substances causing asthma are described each year, the absence of exposure to a substance known to cause asthma in a patient with symptoms suggestive of WRA should not preclude further workup for OA. Guidelines for taking a complete occupational history have been prepared by the Centers for Disease Control and Prevention (CDC) Agency for Toxic Substances and Disease Registry (ATSDR) (https://www.atsdr.cdc.gov/csem/exphistory/docs/exposure_history.pdf).

The fourth recommended question asks about allergic rhinitis and conjunctivitis since these symptoms are common in subjects with OA (37).

The time between first exposure and development of symptoms may vary from weeks to years but is generally more common in the first 2 years after exposure (38). Symptoms that begin immediately or within days after initiation of work are not consistent

with OA unless the patient has had similar exposures in a previous job. Symptoms that begin so soon after initiation of work are more likely secondary to preexisting asthma or to upper airway irritation in the absence of asthma. Sensitization has been reported after an acute spill or leak but this is more commonly the history in a patient with RADS (see Chapter 19).

Other relevant items in the history include nonoccupational factors such as cigarette smoking and exposure to secondhand smoke, hobbies of the patient or members of the household, presence of pets, and a personal or family history of allergies. The presence or absence of these factors does not preclude the diagnosis of WRA, but the acquisition of a pet or the initiation of a hobby coincidental with a new job or work exposure may confound the evaluation of WRA. Chronic cigarette smoking may cause chronic obstructive pulmonary disease (COPD) that may be difficult to distinguish from asthma, especially in the asthma-COPD overlap (ACO). Cigarette smoking is not generally reported as being associated with OA except for very few agents (39). Atopy has been associated with an increased risk of sensitization to many HMW compounds and a few low-molecular-weight (LMW) agents (see Chapter 3). However, the risks associated with atopy or cigarette smoking are not sufficient to guide decisions regarding placement for new employees starting in work environments with known sensitizers.

The physical examination is of secondary importance to the history and pulmonary function studies (see section "Confirming the Diagnosis of OA"). A chest radiograph is generally sufficient to exclude nonasthmagenic causes of respiratory symptoms. A high-resolution computed tomography (CT) scan may be indicated when considering conditions such as hypersensitivity pneumonitis or bronchiolitis obliterans (see Chapter 24).

In some countries where there is a mandatory duty to report confirmed or suspected occupational diseases such as OA, the role of the primary care physician includes the reporting of patients to the public health agency. Notification helps to achieve more precise surveillance of the incidence of WRA and to identify trends and new causal agents. The notification may initiate an inquiry in the workplace with primary and secondary prevention objectives. The inquiry may help to identify sentinel cases (40) and other workers affected by the disease as well as to promote prevention initiatives.

Confirming the diagnosis of OA

A suggestive history, even in the presence of a known sensitizer, is not enough to confirm the diagnosis neither of asthma (41) nor of OA (42). The diagnosis needs to be confirmed objectively. The various tests used to confirm or exclude the diagnosis are outlined in the following paragraphs. Although specific inhalation challenges are considered the diagnostic reference standard, all steps involved in the investigation have their own value and contribute to establishing the diagnosis. Combining the various elements strengthens the likelihood of a proper diagnosis (11).

CASE HISTORY FOLLOW-UP

Following the administration of detailed medical questionnaires, the occupational nurse referred the worker to the occupational physician. The worker had been seen by an allergy specialist (without being referred) and SPTs to various cereals and enzymes had revealed immediate skin reactions to wheat and soy flour allergens. Following a second interview with the occupational physician and the positive results of the skin tests, the worker agreed to be referred to a specialized center for evaluation of OA.

(SEE CASE HISTORY, ITEM NO. 7)

The worker described in the case history was subsequently seen at the OA clinic of the local university hospital. He had spirometry performed in the clinic, which was within normal values, but his methacholine challenge showed mild increased bronchial responsiveness with a PC20 of 2 mg/mL. Monitoring of PEF at and off work showed significant changes in PEF while at work with 20% fall in PEF on several occasions improving during weekends, particularly on Sundays. On Sundays, he had minimal variation in his PEF values. Sputum induction showed moderate eosinophilia (5% eosinophils for a total cell count of 2.5×10^6 cells/g) at the end of a working week. After 2 weeks off work, his PC20 improved to 9 mg/mL and he had 1% eosinophils in sputum for a total cell count of 1.9 cells/g. These data confirmed the diagnosis of OA, and the patient was taken off work as there were no jobs available where he would not be exposed to flour. The necessary information was also provided to the appropriate authorities for evaluation of the worker's right to compensation and reassignment services.

Confirming the diagnosis of asthma

The diagnosis of asthma is based on history and objective evidence of reversible airflow obstruction or increased nonspecific bronchial responsiveness (NSBR) (43).

Simple spirometry is often not performed early in the medical evaluation of workers suspected of OA. Although documentation of reversible airflow limitation confirms the diagnosis of asthma, most workers investigated for OA have normal spirometry when seen in the clinic. Furthermore, pre- and postshift monitoring of forced expiratory volume in 1 second (FEV_1) has not proven sensitive or specific enough to be a useful tool in the evaluation of OA (7).

Even if increased NSBR is the hallmark of asthma, its presence does not alone establish a diagnosis of OA. The absence of increased NSBR assessed shortly (minutes, hours) after a work shift in a worker with symptoms virtually excludes OA (44). Even in workers with confirmed OA, NSBR may normalize after several days (a weekend may be enough [45] or weeks to months away from work). Subsequent return to work or even exposure via a specific inhalation test may be adequate to cause increased NSBR (46, 47).

Use of investigations to confirm or exclude occupational asthma

Workers with OA must fulfill the diagnostic requirements for asthma, and further assessment is needed to confirm an occupational cause.

Symptoms and lung function

Most patients with OA complain of typical WRA symptoms, but some may not. For example, there may be evidence of work-related

changes in lung function (such as PEF, FEV_1, airway responsiveness, or an accelerated annual decline in FEV_1 [48]) in the absence of symptoms that might suggest further investigation is necessary. The intent is to identify symptoms, or other features as above, that suggest the need for further investigation. In the case of sensitizer-induced OA, symptoms should also have a latency, that is a period of sensitization between the beginning of exposure and the onset of symptoms. Rhinitis is a common accompanying feature. It should always be inquired of, as the likelihood of developing OA is higher in the first few years after starting exposure to HMW agents such as laboratory animals.

Questionnaires are highly sensitive (although not specific) tools to collect this information. Measuring lung function with spirometry should always be carried out. All measures should be quality controlled and conform to relevant guidelines (49). Whenever possible, further confirmatory tests are required to make a diagnosis of OA, guided by a multidisciplinary approach.

IgE-mediated immunity: Skin testing and specific IgE assessment

SPTs and specific IgE testing to occupational agents are useful diagnostic tools to confirm sensitization to an occupational allergen, particularly HMW agent. A meta-analysis of specific IgE assessment identified a 74% sensitivity and 71% specificity for HMW agents and of 28% and 89%, respectively, for LMW agents (10). The lack of availability and immunological validity for a wide range of allergens also limits their use (Chapter 7).

Tests to assess airway inflammation: Sputum eosinophils and FeNO

These tests are markers of airway inflammation and are useful in the investigation of OA (Chapter 7). Measured alone, a high (≥2%) sputum eosinophil count or an elevated FeNO (≥ 25 ppb) each has a low sensitivity for OA (50). However, when used in combination and together with the assessment of NSBR, their sensitivity is significantly improved (50). One study suggests that this may predict accelerated lung function decline in continually exposed workers (51).

Functional tests

Peak expiratory flow (PEF) measurement Serial measures of PEF are regarded as the next important investigation (Chapter 8). A meta-analysis has identified pooled sensitivity and specificity of serial PEF measurements of 75% and 79%, respectively, for a diagnosis of OA (52), with more complete data improving these indicators. Workers will need to be taught the importance of making these recordings and encouraged, ideally through the period of data collection.

NSBR testing Achieved by provoking the airway with a variety of inhaled agents that can cause transient airway narrowing (principally methacholine), is useful for confirming a diagnosis of asthma. The presence of NSBR well may support a diagnosis of asthma, and thus OA, but its absence does not exclude OA if the worker has been away from work or has become asymptomatic (53). Assessment of NSBR may further be improved by measures of FeNO and sputum eosinophilia.

Specific inhalation challenges (SIC) (Chapter 8) Are still considered the reference standard to confirm the diagnosis of OA (54–56), although not widely available given the expertise required. Originally done in the laboratory and aiming to mimic work exposure, these are also done in the workplace (57). They are indicated when there is discrepancy between results of PEF monitoring and PC20 or sputum induction or when history is highly suggestive of OA despite negative monitoring. Specific challenges in the workplace are particularly useful when the worker is exposed to several sensitizers or when the offending agent is unknown.

SICs are safe when performed under the close supervision of an expert physician and by trained personnel and are thus limited to specialized centers. A statement (55) and handbook (58) on methodology have been proposed. Further details on the method of specific challenges are given in Chapter 8. A positive test is generally defined by a fall of ≥ 15%–20% from baseline, although another means of interpretation has been suggested in the case of late reactions (59), and confirms the diagnosis of OA, whereas a negative test in the workplace, or in the laboratory, does not absolutely rule out the diagnosis of OA in a worker who has not been exposed to work for several months as they may have become "desensitized." This is particularly true if there is a change in methacholine PC20 following a negative response to SICs. Such a worker should return to work for serial monitoring of PEF and bronchial responsiveness for at least a few weeks before excluding the diagnosis. False-negative challenges in the laboratory may also be due to exposure to the wrong agent or inadvertent administration of a forbidden drug (e.g. inhaled β-2 agonist) before the test. Indeed, Rioux et al. showed that as high as 20% of challenges done in the laboratory may be false negative, particularly when workers are exposed to LMW agents (57). However, if the subject experiences their usual symptoms during the challenge procedure without any spirometric changes, these tests are conclusive in excluding the diagnosis of OA.

Workplace challenges collect serial physiology during normal work activities, comparing airway responses between periods of exposure and nonexposure (or not at work). They may be useful if SIC is not available, and in the context of mixed or complicated exposures that are difficult to re-create in the laboratory setting (57). Again, analysis can use the 95% CI of all measures taken on nonexposed days (59), with a significant fall in FEV_1 on an active day defined as one that falls below the lower bound of the confidence limit from control days.

Figure 5.4 illustrates the algorithm for the investigation of OA summarizing the various steps required to exclude or confirm the diagnosis depending on the level of certainty required.

What other diagnosis should be considered when investigating a worker for work-related asthma?

Workers presenting with symptoms suggestive of WRA may require consideration of alternate or coexisting diagnoses, given the relatively low diagnostic specificity of common respiratory symptoms:

i. *Occupational hypersensitivity pneumonitis* (HP) (Chapter 24) should always be considered in workers with work-related respiratory symptoms. It is plausible that HP could present in a similar manner to WRA, given that respiratory complaints are commonly seen in HP, often along with systemic features such as fever and weight loss. Previous workplace outbreaks of occupational lung disease have described both conditions occurring that were attributed to the same cause (60). More focused airway inflammation, such as seen in (ii) *eosinophilic bronchitis* (Chapter 21),

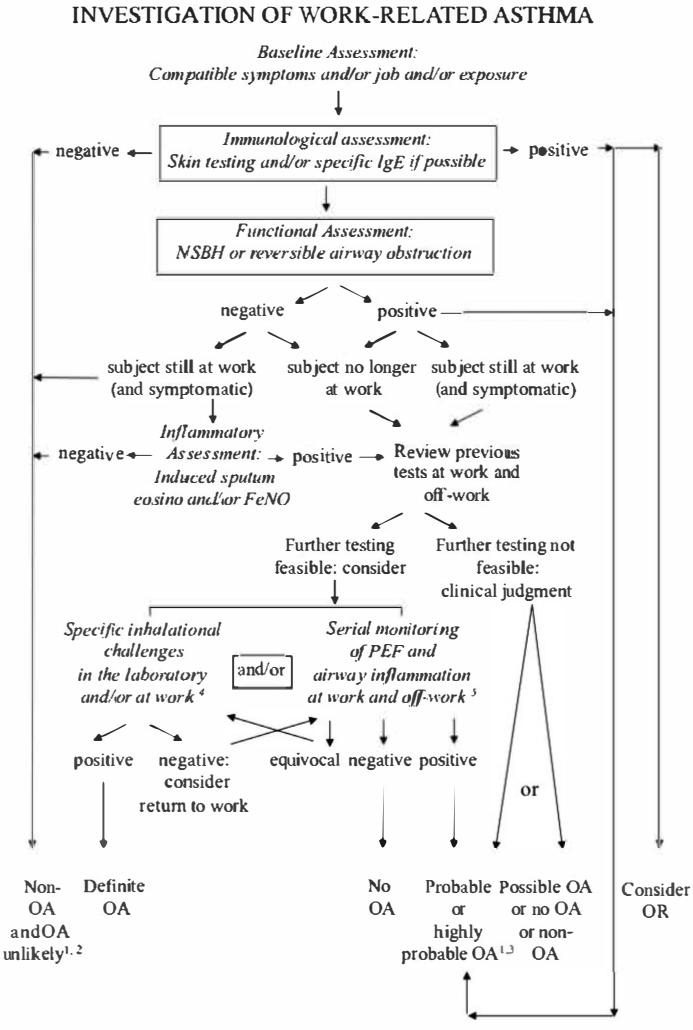

FIGURE 5.4 Proposed stepwise algorithm for diagnosing occupational asthma. (Adapted from Cullinan, P, Vandenplas ●, Bernstein ●. Assessment and management of occupational asthma. *J Allergy Clin Immunol Pract.* 2020;8(10):3264–3275. By permission.)
Abbreviations: eosino: eosinophils; FeNO: exhaled nitric oxide level; NSBH: nonspecific bronchial hyperresponsiveness; OA: occupational asthma; OR: occupational rhinitis; PEF: peak expiratory flow.

1. High negative predictive value (NPV) and positive predictive value (PPV) are applicable only for selected populations of subjects with a high pretest probability of ●A (i.e. investigated in tertiary centers).
2. NPV >95% for the combination of absence of immunological reactivity and NSBH.
3. In subjects with NSBH (when immunological tests have been validated by comparison with specific inhalation challenge) increasing the cut-off value for a positive sIgE test ≥2.22 kU_A/L for wheat flour, ≥9.64 kU_A/L for rye flour, and ≥4.41 kU_A/L for latex provides a PPV for a positive specific inhalation challenge result > 95%.
4. Especially useful when: SIC can be performed efficiently and safely; the subject is no longer exposed at work; the highest level of diagnostic confidence is required; there is need to identify a particular agent; PEF records are inconclusive.
5. Especially useful when: the subject is exposed to multiple asthmagens at work; no agent known as causing OA has been identified at work; facility for SIC is not easily available; the conditions of exposure at work cannot be reproduced in the laboratory.

considered as a potential precursor of asthma, may also need consideration; (iii) *Chronic obstructive pulmonary disease* should also be considered in a worker being investigated for OA, although it is relatively easily distinguished from asthma (Chapter 25). COPD itself may be related or unrelated to workplace exposures, but irrespective of causation can still cause work-related symptoms. Workers may display features of both asthma and COPD (asthma-COPD overlap). Other less common respiratory conditions that affect the airway (and/or the parenchyma) should always be considered in the differential diagnosis. These include (iv) *obliterative bronchiolitis* (Chapter 25) (61), seen most notably following diacetyl exposure, or rarely (v) *organizing pneumonia* with an occupational attribution (61). Episodes of shortness of breath associated with systemic features should also raise the possibility of (vi) a *fume fever*; such as caused by metal (Chapter 16) or polymer fume (62). Similarly, such episodes might, in the correct occupational context, suggest that bioaerosols, or specifically endotoxin exposure, might be responsible for an (vii) *inhalation fever* (Chapters 23 and 24) that may mimic OA. Long known to influence breathing and important to exclude, (viii) *disorders of the vocal cords* (Chapter 19) should also be considered in a worker with OA. Inducible laryngeal obstruction, an inappropriate, transient, reversible narrowing of the larynx in response to external triggers (63), may also potentially be seen in occupational contexts.

Research needs

It would be relevant to:

- assess the validity of surveillance programs in high-risk workplaces in relation to the nature of occupational agent and type of exposure;
- improve surveillance questionnaires for identifying the most relevant questions in terms of sensitivity/specificity;
- examine whether objective tests can be preferred to questionnaires; and
- obtain information on the level of knowledge and awareness of workers about the nature and risks of products.

Conclusion

While it may be difficult to distinguish work-exacerbated asthma from OA (Chapter 20), a combination of diagnostic tools will help the clinician to come to a proper diagnosis. Suspicion of the diagnosis can result from surveillance programs led by occupational nurses and physicians, and primary care providers. Referral to a specialized center is often necessary. Objective confirmation of asthma and WRA is essential as history is neither sensitive nor specific enough. SIC is still considered the reference standard although a combination of tests carried out in a stepwise approach may achieve a high diagnostic yield.

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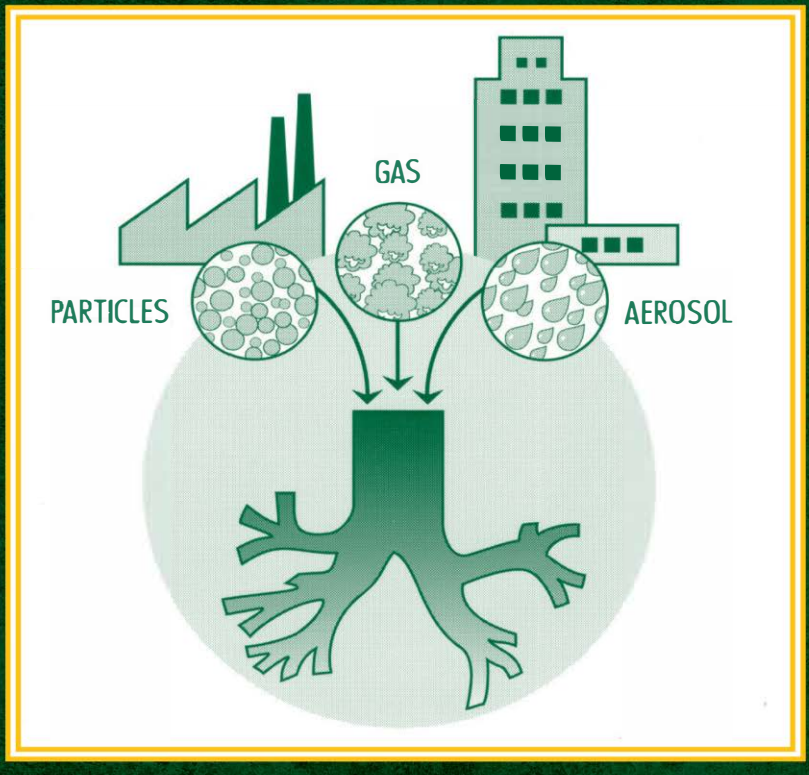

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