Running Head: OCCUPATIONAL ASTHMA

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Introduction

Occupational asthma (OA) is the most common occupational disease in industrialized countries and it is estimated that approximately 15% of all adult asthma is occupational in origin. Correct diagnosis and early management are key factors affecting disease prognosis and socioeconomic consequences. The individual patient is not the only one affected when measures are taken; the consequent changes in working conditions can also prevent the appearance of other cases at the patient's workplace or other sites. Thus, the benefits are important for the health of the workforce and also for the economy, both of individual companies and of society in general.

Definition

OA is a disease characterized by variable obstruction of airflow and/or airway hyperresponsiveness attributable to factors associated with the workplace rather than to stimuli found outside that environment. (Nicholson, 2002)

Classification

The following types of OA are distinguished according to the pathogenesis of the disease:

1. Immunologic OA or OA caused by hypersensitivity.

This requires a period of time for sensitization to the causative agent to develop, and therefore, there is a latent period between exposure and the appearance of symptoms. The following subtypes are distinguished according to the substances responsible for causing the

disease: – Immunologic OA caused by high molecular weight substances. This usually occurs via an immunologic mechanism involving immunoglobulin (Ig) E. – Immunologic OA caused by low molecular weight substances. In this case, there is generally no clear involvement of IgE. (Anees, 2004)

2. Nonimmunologic OA or irritant-induced OA.

This type of OA occurs as a result of irritation or toxicity. Two subtypes can be distinguished: – Reactive airways dysfunction syndrome (RADS). This is caused by single or multiple exposures to high doses of an irritant. Its onset, however, is linked to a single exposure. It is also known as OA without a latent period, since the symptoms appear within 24 hours of exposure. – OA caused by low doses of irritants. This occurs after repeated contact with low doses of the causative agent. It is a condition of particular current relevance but that is still under discussion.

3. Other variants of OA.

This category includes OA with special or distinctive characteristics: – Asthma-like disorders. These are due to exposure to plant-derived dust (grain, cotton, and other textile fibers) and also to dust from confined animals. – Potroom asthma. This occurs in workers involved in the production of aluminium.

Prevalence and Incidence

Notable discrepancies are found in the data on prevalence and incidence currently available in the medical literature. Differences in the design of epidemiologic studies, the definition of OA, the study population, and the country in which the study was performed account for some of the discrepancies and the consequent difficulty in making comparisons.

Some of the data can be found in a recent review article. It has been reported that 4% to 58% of all cases of asthma may be occupational in origin. A recent review of the literature estimated a mean value of 15%. Immunologic OA caused by high molecular weight substances is the most common form. (Anees, 2004)

The prevalence of the disease varies depending on the causative agent and it has been shown to occur in 4% to 12% of animal laboratory workers, 79% of bakers, and 1% to 7% of health care workers exposed to latex. The prevalence of OA caused by sensitization to low molecular weight substances is less clear, although some authors estimate it at around 40% of all cases of OA. The agents most frequently implicated in the disease in industrialized countries have generally been the isocyanates, which cause asthma in 2% to 10% of workers. (Nicholson, 2002)

In British Colombia, Canada, where the wood industry is very extensive, another agent, cedar wood, is more common and is responsible for causing asthma in 10% of workers. Other substances such as glutaraldehyde, cleaning products, and persulfates are emerging as disease-causing agents in workers involved in the health care, cleaning, and hairdressing industries. RADS is estimated to occur in 36% of cases referred to hospital for assessment of OA. In addition, 11% to 15% of all work-related asthma is reported to be caused by irritants. Monitoring through the use of registries allows the incidence of OA to be estimated. Such programs have been developed in many different countries. (Vandesplas, 2003)

Pathogenesis

Genetic predisposition.

Atopy is a risk factor for asthma induced by high molecular weight substances. For instance, OA in health care workers exposed to latex is more common in atopic than

nonatopic individuals. The same is true of workers exposed to laboratory animals or detergents. The phenotype of individuals with OA appears to be generated through the involvement of genes of the major histocompatibility complex on chromosome 6p coding for class II human leukocyte antigen (HLA) molecules However, the associations are not sufficient to generate preventative recommendations. Genes of the glutathione S-transferase and N-acetyltransferase superfamilies also appear to be involved in OA, especially that caused by isocyanates.

Causative agent.

The high molecular weight substances that are able to generate sensitization are proteins that behave as complete antigens. In addition, there is evidence that some of those proteins have enzymatic activity that could aid antigen penetration. In contrast to the allergenic proteins, the low molecular weight substances that are able to cause OA are generally incomplete antigens (haptens) that must combine with other molecules to trigger an immune response. These agents are known to be highly reactive and capable of binding certain specific sites on proteins in the airway. In the case of RADS, it is reasonable to assume that the higher or lower irritant capacity of an agent would be involved in the pathogenesis of the disease.

Type of exposure.

The level of exposure appears to be the main determinant in the development of OA caused by agents that act through IgE-mediated mechanisms, such as the majority of high molecular weight substances but also certain low molecular weight substances such as platinum salts and acid anhydrides. The risk of developing OA is highest just after the first year of exposure to the causative agent and if symptoms of occupational rhinoconjunctivitis

appear prior to bronchial symptoms. Evidence also exists supporting an interaction between irritants and sensitizing agents. Smoking has been linked to an increase in sensitization to tetrachlorophthalic anhydride and platinum salts, and exposure to ozone may potentiate the development of bronchial hyperresponsiveness to hexachloroplatinate. (Newman-Taylor, 2003) In addition to the causative agent itself, the intensity of the exposure also appears to be an important determinant in the appearance of RADS.

IgE-dependent mechanisms.

Most high molecular weight substances that cause OA are animal- or vegetablederived proteins or glycoproteins that act via a mechanism involving IgE. These proteins behave as complete antigens that stimulate the production of IgE. Nevertheless, some low molecular weight substances (eg, acid anhydrides and platinum salts) can function as haptens and combine with carrier proteins to form a hapten-protein complex that will also stimulate IgE production. When these substances are inhaled they bind the specific IgE found on the surface of mast cells and basophils, triggering a sequence of cellular events that leads to the release of preformed or de novo synthesized mediators and the recruitment and activation of inflammatory reaction in the airways characteristic of asthma. (Anees, 2004)

IgE-independent mechanisms.

Most low molecular weight substances that cause OA act via a mechanism that, while probably immunologic, does not involve IgE. Specific IgG and IgG4 antibodies appear to be associated more with the level of exposure than with the disease itself. It is possible that cellular or delayed hypersensitivity is involved in these cases. CD4 lymphocytes play a supporting role in the production of IgE by B lymphocytes and may also induce inflammation by secreting interleukin (IL). IL-5 is a potent stimulator and activator of eosinophils and is

the main cytokine involved in the recruitment and activation of eosinophils during delayed asthmatic responses. Increased numbers of activated T lymphocytes (which express the receptor for IL-2), activated eosinophils, and mast cells have been observed in bronchial biopsies from patients with OA caused by low molecular weight substances. In addition, those substances can have nonimmunologic proinflammatory effects. (Nicholson, 2002) If they bind glutathione, they cause intracellular glutathione deficiency, which can reduce defense against oxidizing agents. In fact, it has been reported that exposure to isocyanates is associated with elevated intracellular concentrations of peroxide. Damage to cells of the bronchial mucosa caused by such a process could amplify or initiate a response to low molecular weight substances.

Irritation or toxicity.

The mechanisms underlying RADS deserve special mention. The massive initial epithelial lesion would probably be followed by direct activation of sensory nerves that would give rise to neurogenic inflammation. This would not only induce changes in vascular permeability but would also provoke an increase in mucosal secretion that would contribute to the chronic inflammation seen in biopsy material. During the process of recovery the inflammation would be resolved, leading to recovery of the epithelium, inhibition of neuronal activity, and improvement of vascular integrity. However, complete recovery would not always be achieved and sequelae of the inflammatory response would persist in the form of hyperreactivity and bronchial obstruction.

Diagnosis and Treatment of Immunologic Occupational Asthma

Diagnosis of immunologic OA requires a series of steps

Clinical History

A clinical history is essential for the diagnosis of OA. The patient should be questioned not only about the existence of bronchial symptoms but also about nasal symptoms and symptoms of the eyes, skin, and upper airways. Those symptoms often precede the appearance of asthma, particularly when high molecular weight antigens are involved. Prior to entering the symptomatic period of the disease there is normally a highly variable period of time that can last from a few weeks to a number of years. Therefore, detected, and if it can be, low sensitivity means that it is almost always of very little use. Only some low molecular weight substances, such as isocyanates, appear to display a good specificity. When a positive result is obtained, the possibility of an accurate diagnosis of OA should once again be considered in case of uncertainty or when a diagnosis of OA has previously been rejected.

Bronchial Provocation in the Workplace

Bronchial provocation can confirm clinical suspicion of bronchial asthma caused by an agent that is present in the workplace or produced by work activities. The measurement relates the occupation to the disease but does not indicate which specific substance or agent is involved. However, if it is known that in that particular occupation a product is used that is commonly linked to OA, or if evidence of sensitization of the patient to a particular agent can be obtained through immunologic tests, diagnosis of OA caused by that agent is highly likely. The test must be performed during or after a period of time in which the patient is working and during or after another period in which the individual is not. Those periods must generally be at least 2 weeks long and interference in the test due to factors such as use of bronchodilators, presence of exacerbations, etc, should be prevented. In some cases, such as when it is suspected that irritant concentrations of particular substances are reached in the

workplace, it may be necessary to measure the concentrations of the agent under suspicion. (Vandesplas, 2003)

Specific Bronchial Provocation Test

Although specific bronchial provocation tests are considered the gold standard for diagnosis of OA, in most cases they cannot be considered for routine diagnosis. They may be indicated in the following situations: *a)* when there is a new agent that may be a possible cause of asthma; (Girard, 2004) *b)* to identify the causative agent from among various substances to which a worker is exposed; *c)* when severe asthmatic reactions may occur when the individual returns to work; and *d)* when diagnosis is still doubtful after other tests have been performed. Exposure to the agent can be performed in 2 ways, always in specialized clinics:

Via nebulization

When the agents are soluble and the immunologic mechanism is mediated by IgE. Antigen solutions are administered as aerosols at increasing concentrations. The concentration at which the technique is initiated is calculated using a formula based on the PC20 (mg/mL) for methacholine and the lowest concentration that generates a positive response in skin prick tests. Forced spirometry is performed 10 minutes after each nebulization. The test result is positive if there is a reduction in FEV1 of at least 20%. The results are expressed as the PC20 of the allergen, or as the PD20 of the allergen if a dosimeter is used. If the result is negative a higher concentration is administered. During the 24 hours following inhalation it is important to monitor FEV1 every hour to identify delayed responses. (Nicholson, 2002)

In a challenge chamber, when the agents are insoluble. The test involves exposure of the patient to a nonirritant concentration of the suspected causative agent. For this reason, means of measuring the concentration of those agents should be available if possible. The length of exposure varies according to the agent and the characteristics of the patient. The test results are positive if there is a greater than 20% reduction in FEV1, or a positive response or significant decrease in the PC20 compared with that performed prior to exposure.

If the test is negative, exposure is repeated for a longer period of time or with a higher concentration of the product on successive days. diagnosis should not be ruled out by a worker having performed the same job for years without presenting symptoms. Sudden-onset asthma in an adult with no history of respiratory or allergic disease may be cause for suspicion of OA. It is important to be able to link asymptomatic periods with absence of exposure and symptomatic periods with exposure. (Campo, 2004)

Sometimes the patient will spontaneously report the presence of symptoms minutes after exposure to the causative agent. In other cases, however, the symptoms are noted in the evening or only during the night. In those cases, it is less likely that patients will associate the symptoms with their daytime activities. In general, improvements are observed at the weekend or during holidays, but this is not always the case. In fact, this association is more common at the onset of clinical symptoms, since as the symptoms progress they often become more persistent and recurrent and this can prevent the patient from associating their asthma with work. Nevertheless, questions about the improvement of asthma symptoms during the weekend and especially during holidays display a greater diagnostic yield than those relating to the worsening of symptoms at work.

Sometimes, as occurs with red cedar and isocyanates, the symptoms continue for months or years after exposure is discontinued. Furthermore, in some industries the chemical and operational processes are complex and cause the release of substances that remain

completely unnoticed. For this reason, one of the keys to the diagnosis of OA is a year by year work history and awareness of the products found in the workplace that can cause asthma. It is useful to review the safety information provided with the products used by the worker and determine whether the causative agent thought to be involved has been previously linked to asthma of occupational origin. (Girard, 2004) A clinical history indicative of OA is not sufficient to establish the diagnosis, since the opinion of the physician only coincides with a true diagnosis of OA in slightly more than half of suspected cases.

Physical Examination, Chest Radiography, Standard Workup, and Lung Function Testing

Physical examination, chest radiography, standard workup, and lung function testing do not differ in OA from those performed in any other asthmatic patient. However, they should be used because, firstly, they allow a diagnosis of asthma to be made, and secondly, they allow OA to be differentiated from other workrelated conditions with which the disease can be confused. It must be taken into account that often when patients attend the clinic they are completely asymptomatic and only report a sensation of dyspnea or tightness in the chest, sometimes without wheezing or other symptoms. (Anees, 2004) A test to reveal nonspecific bronchial hyperreactivity, such as the methacholine or histamine test, is necessary when the bronchodilator test is negative due to the absence of bronchial obstruction at that time. This test, along with clinical assessment by the physician, is a useful approach to diagnosis of bronchial asthma in patients whose history, physical examination, or lung function are indicative of atopy. In addition, if the methacholine or histamine test is negative, the existence of OA can be ruled out in practice, so long as the test is performed when the patient is working, since airway hyperresponsiveness can normalize following a variable period without exposure to the causative substance.

Immunologic Tests

The results of immunologic tests can indicate exposure and sensitization but by themselves are unable to confirm a diagnosis of OA. A positive test does not always imply the existence of clinical signs. To prevent erroneous interpretations, the sensitivity and specificity of each of the antigens used must be known when any such tests are performed, since various substances can give rise to false positive or negative reactions. Either in vivo (prick test) or in vitro (analysis of specific IgE antibodies) techniques can be used. (Vandesplas, 2003) Sometimes allergen extracts have to be prepared in the laboratory due to a lack of commercial availability. In general, high molecular weight substances display a high sensitivity and in some cases the absence of a reaction allows the possibility that the substance with which the test was performed is responsible for the symptoms of the patient to be ruled out. (Pickering, 2002) Most low molecular weight substances are irritants and, therefore, prick tests are not appropriate.

Likewise, if there is no clear IgE mediated immunologic mechanism, this antibody cannot be When non-water-soluble dust is used, it can be passed from one tray to another mixed with lactose to produce a cloud of dust. The use of lactose alone allows a placebo test to be performed. Drug-inhalation devices that employ capsules containing a specific amount of dust have also been used. When gases or fumes are tested, the methods used to generate a given concentration can be classified as static or dynamic (continuous flow). In the static systems, a known quantity of gas is mixed with another of air to produce a given concentration. (Anees, 2004) In dynamic systems, the airflow and the addition of gas is controlled to produce a specific dilution. These systems offer a continuous flow and allow rapid and predictable changes in the concentration to be made, favoring good mixture and minimizing loss through adsorption to the walls of the chamber. As an alternative or to avoid the use of a challenge chamber, some hospitals have developed equipment for closed-circuit

exposure, which in theory offers greater control over exposure and makes it safer for health care personnel. (Campo, 2004)

Treatment and Prognosis

In most cases of immunologic OA it appears to be obligatory to recommend discontinuation of exposure to the processes or substances responsible. Wherever possible, the solution lies in a change of work situation. If that is not possible and the worker continues to be exposed, the safety procedures of the company should be assessed and exposure should be avoided as far as possible through protection of the airways. (Nicholson, 2002) In such cases, the effectiveness of the intervention must be demonstrated on a regular basis through respiratory function tests. Limitation of contact through the use of protective masks in animal care facilities and the pharmaceutical industry has been associated with a certain improvement in clinical condition and respiratory function.

A beneficial effect has also been observed with the use of inhaled bronchodilators and anti-inflammatory drugs in this type of patient. Discontinuation of exposure to the causative agent is associated with an improvement in symptoms and lung function that does not normally exceed 50% in affected individuals. Lung function is only normalized and nonspecific bronchial hyperreactivity stopped in around 25% of individuals. (Girard, 2004) In general, the prognosis of a given patient in whom contact with the causative agent is removed depends on the severity of the condition when diagnosis was established. On the other hand, if exposure to the causative agent continues, it almost always leads to clinical and functional deterioration of the patient. (Vandesplas, 2003) Following diagnosis of OA, available information indicates that from a socioeconomic perspective there is a substantial deterioration if the patient stops work, since the system of support appears to be insufficient

in Western countries. In fact, a third of workers do not discontinue exposure to the causative agent following diagnosis to avoid adverse financial consequences.

Diagnosis and Treatment of Nonimmunologic Occupational Asthma

Reactive Airways Dysfunction Syndrome

Even though cases had already been described, the term RADS was not used until 1985, when Brooks et al described a series of 10 patients. The diagnostic criteria for RADS established by those authors continue to be used. Absence of prior respiratory symptoms. Exposure to a gas, smoke, or vapor present at high concentrations and with irritant qualities. Onset of symptoms within the first 24 hours of exposure and persistence for at least 3 months. Symptoms similar to asthma with cough, wheezing, and dyspnea. Objective evidence of bronchial asthma. Other types of lung disease ruled out RADS occurs through direct toxic mechanisms. Destruction of the respiratory epithelium and inflammation have been demonstrated to take place during the acute phase and with collagen regeneration and proliferation in subsequent phases. Once exposure has occurred, only treatment appears able to influence the course and prognosis of the disease. Reports of experience with a small number of cases have indicated that early treatment with high doses of corticosteroids can improve prognosis.

However, many patients with RADS continue to present symptoms of bronchial irritation and hyperreactivity years after exposure. Consequently, once stabilized following the acute phase, patients should be treated as asthmatics. On the other hand, since they do not display any greater susceptibility than other asthmatic patients to reexposure to nonirritant doses of the causative agent, they can return to work so long as preventative measures remove the possibility of contact with products at irritant concentrations. **(**Marabini, 2003**)**

Occupational Asthma Caused by Low Doses of Irritants

The appearance of cases with symptoms of asthma following repeated exposure to moderate or low concentrations of irritants is currently of particular interest. In Tarlo (2003), upon introducing the term "irritant-induced asthma," already included workers who developed asthma following single or multiple exposure to the irritant, even if exposure was at low concentrations. Chan-Yeung et al also described cases of asthma with those characteristics. The terms "low-dose RADS" and "delayed RADS" were later proposed. However, it was not clearly demonstrated in those case series that multiple moderate-intensity exposure could cause asthma, and furthermore, other studies have demonstrated that repeated moderate inhalation of an irritant is not associated with persistence of airway hyperresponsiveness, whereas such persistence is observed with exposure to higher concentrations, even in the case of single exposure. As admitted by Tarlo, there is currently a genuine debate regarding the existence of asthma produced by low or moderate doses of irritants. Further studies will be necessary to clearly establish and characterize the condition. (Tarlo, 2003)

Asthma caused by exposure to grain dust.

Asthma caused by exposure to dust from cereal grain occurs mainly in workers involved with grain silos, mills, or bakeries but is also seen in agricultural workers. The specific cause is unknown but could be a component of the cereal, of parasitic fungi such as smut or rust, of saprophytes such as *Aspergillus* species, of organisms such as weevils or mites, or of gramnegative bacteria. The reported prevalence varies markedly in different studies. The asthma is often mild and the individual's work is not affected. In close to 50% of cases the symptoms improve or disappear spontaneously, suggesting a process of desensitization in some cases. (Anees, 2004)

Differential Diagnosis

Work-Aggravated Asthma

The term work-aggravated asthma refers to the situation in which there is evidence of worsening of preexisting asthma as a consequence of environmental exposure in the workplace. Although it manifests as an increase in the frequency and/or severity of asthma symptoms and/or an increase in the medication required to control the disease during working days, diagnosis should be performed on the basis of changes in bronchial diameter, the degree of bronchial hyperresponsiveness, or the extent of inflammation of the airway in relation to workplace exposure. However, demonstrating such changes in a patient with asthma prior to workplace exposure is not always easy. As a consequence, some authors have suggested that work-aggravated asthma be distinguished from symptoms of asthma aggravated by work. The second entity appears to be much more common than the first, although few publications have looked at its pathogenesis, treatment, and course.

Eosinophilic Bronchitis

Eosinophilic bronchitis causes chronic cough, expectoration, dyspnea, and on rare occasions, wheezing. Its main characteristic is the presence of a large number of eosinophils in sputum and the absence of variable airflow obstruction and/or bronchial hyperresponsiveness. It should be noted that cases of eosinophilic bronchitis have been described associated with exposure to certain workplace-related substances. In such cases, and in the absence of recognizable bronchial hyperresponsiveness, diagnosis is provided when significant reproducible changes in the number of eosinophils in sputum are seen to be associated with workplace exposure. Some authors have classified eosinophilic bronchitis as

a variant of OA; however, the condition clearly does not fulfill the criteria that define bronchial asthma.

Bronchiolitis

The term bronchiolitis applies to various diseases involving inflammation of the bronchioles. The symptoms will depend on the underlying disease, although the majority of patients present cough, dyspnea, tightness of the chest, and occasionally, expectoration and/or wheezing. As an occupational disease, constrictive bronchiolitis has been associated with the inhalation of various agents found in the workplace, such as nitrogen dioxide, sulfur dioxide, ammonia, or hydrochloric acid, and more recently it has been described in workers in a popcorn factory, probably due to exposure to diacetyl, an organic chemical used in the preparation of that product. Inhalation of asbestos, iron oxide, aluminium oxide, talc, mica, silica, silicates, and carbon can cause bronchiolitis secondary to inhalation of mineral dust. (Girard, 2004) The condition is characterized by inflammation of the respiratory bronchioles and occasionally of the alveoli, leading to airflow obstruction. These changes can occur in the absence of concomitant pneumoconiosis. Finally, lymphocytic bronchiolitis has recently been described in workers in the nylon industry.

Hypersensitivity Pneumonitis

Hypersensitivity pneumonitis is a lung disease that occurs as a result of inhalation of antigens to which the patient has been previously sensitized. Many of those antigens may be present in the workplace and cause occupational disease. It is important to distinguish this condition from OA, taking into account that both the causative agents and the clinical symptoms may on occasions be the same. Thus, it is known that an appreciable percentage of patients with hypersensitivity pneumonitis present wheezing, airway hyperresponsiveness,

and a normal chest radiograph. Nevertheless, the diagnosis of hypersensitivity pneumonitis, unlike asthma, is suspected and/or confirmed in the presence of systemic symptoms, reduced diffusing capacity with or without functional restriction, diffuse radiographic abnormalities, lymphocytosis in bronchoalveolar lavage, granulomatous pathologic reactions, and/or positive alveolar response to specific challenge test. (Pickering, 2002)

Vocal Cord Dysfunction

Vocal cord dysfunction is characterized by paradoxical vocal cord adduction during inhalation. This anomalous adduction causes airflow obstruction that can be manifested as stridor, wheezing, tightness of the chest, dyspnea, and/or cough. Differential diagnosis with asthma is difficult and it is possible that many patients with vocal cord dysfunction are misdiagnosed and treated as if they were suffering from asthma. The disease is suspected if flattening of the inspiratory flow profile is seen in forced spirometry. Diagnosis is confirmed by fiberoptic bronchoscopy on observation of anomalous adduction of the vocal cords during inhalation. Although the condition has been associated with various psychiatric disorders, it has recently been proposed that certain types of workplace exposure, especially to irritants, can cause vocal cord dysfunction. (Vandesplas, 2003) Distinguishing this condition is important, since the treatment is radically different from that prescribed for asthma. Patients with vocal cord dysfunction can benefit from educational treatment aimed at training the muscles that cause the laryngeal dysfunction. Inhaled or systemic corticosteroids and bronchodilators have not been proven to be of benefit.

Multiple Chemical Sensitivities Syndrome

Multiple chemical sensitivities syndrome is a condition acquired following a documented toxic exposure and is usually characterized by recurrent symptoms that affect

multiple organ systems. Those symptoms appear in response to exposure to unrelated chemical compounds at doses lower than those known to be toxic in the general population. The following criteria are used to establish diagnosis: *a)* the symptoms are reproduced with repeated chemical exposure; *b)* the disease is chronic; *c)* a low level of exposure causes the syndrome; *d)* the symptoms improve or disappear when the triggers are removed; *e)* the symptoms occur in response to multiple chemically unrelated substances; *f)* the symptoms affect multiple organ systems; and *g)* not all of the symptoms can be explained by a multiorgan disease. The symptoms reported by the patients are highly variable, although the most frequent are neurologic, digestive, and respiratory. In relation to the respiratory system, patients usually report cough, dyspnea, tightness of the chest, and presternal pain during inhalation.

Clinical examination is usually normal, as are the various complementary tests, including tests of lung function and bronchial hyperresponsiveness. The agents most commonly implicated in this syndrome are petrochemical-derived products, pesticides, synthetic fragrances, cleaning products, paints, and detergents. It is important to note that the symptoms can occur in response to a wide variety of agents, commonly leading to a substantial reduction in patient quality of life. **(**Marabini, 2003**)** Since there is no specific treatment for this syndrome, many authors favor encouraging patients to carry on with their lives as normally as possible, including the work activities that have caused the disease, and to learn to live with the symptoms, since to date it has not been demonstrated that this leads to deterioration of any organ in particular.

Impairment and Disability: Medicolegal Considerations

The concept of workplace prevention is relatively recent compared with that of compensation for injury caused to workers. European countries, led by Switzerland,

Germany, and Austria, began to provide compensation for industrial injury at the end of the 19th century and later other countries followed suit. According to this system, employees agree not to take legal action for workplace injuries against the company that contracts them in return for financial compensation, medical treatment, and rehabilitation paid for by private or state insurance schemes. Diseases caused by inorganic material, particularly silicosis, were the first and have been the most frequent motives for compensation. However, OA is currently surpassing it as a motive for compensation in many industrialized countries. The regulations affecting compensation policies vary according to the country or region. The difficulties associated with definition and diagnosis of the disease, the involvement of factors such as atopy or smoking in causing asthma or the difficulty in detecting the cause, the possibility of prior asthma, the variability of the disease, and its persistence following discontinuation of work represent some factors that complicate the development of regulations. (Anees, 2004)

Consequently, some countries prepared lists or tables of types of asthma, occupations, and causes in order to establish when compensation should be provided for OA. These were soon found to be too restrictive and they were not updated often enough in response to new scientific tests that would have obliged changes to be made. Even today, although many countries accept claims for any occupational disease, obtaining appropriate compensation is still problematic. In Spain, although the diagnosis of OA is not subject to rigid criteria, when associated disability is proposed, certain premises and recommendations are usually considered. (Pickering, 2002) Confirmation of occupational disease, defined as disease contracted as a result of work activities performed as an employee and that fall within established regulations, whenever the disease involves substances or elements that are indicated for each occupational disease within the aforementioned regulations.

Notably, a positive bronchial challenge test is not required as a criterion. Consideration of a series of causative agents. OA appears in the section covering occupational diseases caused by chemical agents (up to 43 agents are included) and in those diseases caused by inhalation of agents not included in other categories.

Once diagnosis of OA has been made, the best option is to relocate the patient in the workplace to a role in which they are no longer exposed to the causative agent if the OA is caused by hypersensitivity, or return the worker to their original role once stabilized, so long as the patient is not unable to perform the job and the safety conditions are appropriate, if the asthma was caused by irritants. In this last case it would also be acceptable to relocate the worker to a post in which they were exposed to lower levels of irritants. If those options are not possible, disability should be assessed. At this point, it is important to realize that there is one set of terminology that is medical and another that is legal. The latter is specific to each country and is essentially the concept on which compensation is based. (Campo, 2004)

In relation to medical terminology, the World Health Organization has established 3 terms:

1. Impairment refers to functional deficit or loss, which in asthma would be assessed quantitatively by spirometry and the measurement of nonspecific bronchial hyperreactivity.

2. Disability refers to the difficulty or inability to perform a job (occupational disability) or day to day activities (general disability). This is a difficult concept to quantify since it involves assessment both by the doctor and the worker.

3. Handicap refers to the negative repercussions of impairment and disability in the life of the individual. Assessment of handicap does not generally form part of the evaluation for possible industrial compensation.

From a legal standpoint, while suffering from OA the worker may be in the following situations:

1. Temporary occupational disability, when the worker is temporarily disabled for the purposes of work. This is normally an observation period whilst further studies are performed or whilst the individual awaits a new work position. The maximum length of this period is 12 months, extendable for up to 6 more in receipt of benefits. Periods of temporary occupational disability for the same disease are added together until the maximum period is reached, even when periods of work are interspersed, so long as those periods are less than 6 months.

2. Permanent total disability for the individual's usual occupation, when the individual can undertake a different one. This occurs when the individual cannot be transferred to another position in the company without continuing to be exposed to the causative agent. The level of compensation would correspond to 55% of the calculation basis.

3. Qualified total permanent disability, when the circumstances of the beneficiary suggest that they will have difficulty in obtaining a different type of work. This can be accessed from the age of 55 years and the amount can reach 75% of the calculation basis.

4. Absolute permanent disability, when the worker is unable to undertake any occupation. The amount of the compensation would be 100% of the calculation basis. In the case of OA, this would occur if the disease caused symptoms that prevented the individual from undertaking any task.

In such cases, the worker would have to be evaluated once he or she were stable, receiving appropriate treatment, and at least 2 years after diagnosis and without exposure to the causative agent, after which time it is assumed that functional improvement would have plateaued. Various guidelines are available for assessment of asthma-related disability.

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