



## Editorial

## Differential Factors in Fume Fever<sup>☆</sup>

### Fiebre por humos, qué debemos distinguir

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The effects of occupational exposure to toxic substances have been recognized for many years. One of the occupational diseases that affects the respiratory system is fume fever. It occurs, as the name suggests, after inhalation of harmful substances and is caused by a non-specific inflammatory response, rather than a hypersensitivity reaction. The principal entities of this type are metal fume fever (MFF) and polymer fume fever (PFF).<sup>1–3</sup> Although these are familiar processes, they are often overlooked in clinical practice,<sup>4</sup> hence the interest in making periodic updates of this entity.

MFF occurs as a result of occupational exposure to metal oxide fumes which are produced in certain situations where metals are heated above their melting point, during welding, for example.<sup>5</sup> Most cases occur after exposure to zinc oxide, but they have also been described in association with other metals (copper, iron, aluminum, mercury, cadmium, magnesium, manganese, antimony, and tin).<sup>1,2</sup>

PFF is caused by inhaling products derived from the thermal decomposition of certain fluoropolymers.<sup>6</sup> One of the common is polytetrafluoroethylene, used for its lubricating properties, thermal stability and electrical insulation. It is harmless except if heated above 300 °C, at which stage it will begin to release degradation products.<sup>2</sup>

The pathophysiology of these processes is not clear, although they seem to be caused by a direct toxic effect. Exposure to metal fumes causes neutrophilic alveolitis and the release of cytokines by the lung cells, including tumor necrosis factor- $\alpha$ , interleukin (IL)-1, IL-6, and IL-8.<sup>5,7,8</sup>

MFF can occur in any individual, and a particular sensitization to metal fumes is not a prerequisite. Exposed workers develop tachyphylaxis, that is to say, a rapid adaptation after repeated exposure with reduced symptoms which recur after several days of absence of exposure (“Monday morning fever”). A possible cause of this adaptation is the synthesis of metallothioneins, induced by exposure to metals. In contrast, workers affected by PFF do not develop tachyphylaxis. In this case, there is a strong relationship between the onset of symptoms and smoking.<sup>1,2,9</sup>

In clinical terms, both MFF and PFF manifest as a self-limiting febrile syndrome, similar to influenza. Onset is usually rapid, occurring between 3 and 12 h after exposure and resolution is spontaneous, usually within 24–48 h.<sup>1,2</sup>

In the case of the MFF, the exposed subject tends initially to experience a sweet or metallic taste in their mouth and, on occasion, changes in the taste of food or tobacco. Non-specific symptoms may subsequently appear (headache, asthenia, arthralgia, and myalgia). Moreover, there may be a sensation of pharyngeal dryness and irritation, hoarseness and cough. Fever, chills, chest tightness, and dyspnea develop later. Other common symptoms are abdominal pain and nausea, with or without vomiting. Physical examination findings depend on when the patient is evaluated, but, in general, tend to be minimal. In any case, it is very unlikely that complications related to MFF will occur.<sup>1,2</sup>

The clinical presentation of PFF is more varied,<sup>10</sup> but those affected do not experience the metallic taste in the mouth observed MFF. In addition, there is a greater dose-response relationship. Thus, if exposure is more intense, severe acute lung damage can occur, with chemical pneumonitis or non-cardiogenic acute pulmonary edema (APE).<sup>2</sup>

The diagnosis is based on clinical suspicion, and there is no diagnostic test for MFF or PFF. Clinical laboratory findings are non-specific.<sup>1,2</sup> Chest X-ray is usually normal, although the emergence of diffuse pulmonary infiltrates<sup>11</sup> and interstitial pattern<sup>2</sup> have been described. With regard to lung function, reductions in forced expiratory volume in 1 second (FEV<sub>1</sub>), forced vital capacity (FVC), FEV<sub>1</sub>/FVC ratio, diffusing capacity of the lung for carbon monoxide, and partial pressure of oxygen may be observed, although they are uncommon and rarely persist after the resolution of the clinical picture.<sup>12</sup>

With respect to differential diagnosis, the rapid resolution of symptoms in MFF is a key feature that differentiates this process from infectious syndromes. A differential diagnosis should also be performed with other entities, such as hypersensitivity pneumonitis, organic dust toxic syndrome, and chemical pneumonitis.<sup>13</sup>

There is no specific treatment for the MFF or PFF.<sup>1,2</sup> The best treatment is prevention, which includes various strategies, such as increasing general ventilation, installing combustion gas extractor hoods to reduce concentrations of fumes, and using personal protective equipment for the eyes and skin, as well as respirators delivering positive pressure air.<sup>2</sup>

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Temporary sick leave must continue until the remission of symptoms. Workers can resume welding operations after recovery and return to work, provided that adequate protective measures are taken, nor is it necessary to consider a change of job or a proposal for permanent disability. However, it should be borne in mind that severe episodes that are accompanied by extensive chemical pneumonitis, non-cardiogenic APE or reactive airway dysfunction syndrome can produce permanent functional sequelae that make it necessary to consider permanent disability.<sup>2</sup> In this respect, it should be noted that fever caused by metal fumes and other low molecular weight substances is recognized as an occupational disease.<sup>14</sup>

Finally, our ability to recognize a possible inhalation syndrome depends on two factors: knowledge of its etiology, and the compilation of an appropriate occupational history.<sup>15</sup> An early diagnosis can lead to more targeted management and rule out the possibility of a more severe inhalation syndrome.

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