

## Review

## Farmer's Lung Disease. A Review<sup>☆</sup>



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## ARTICLE INFO

## Article history:

Received 11 June 2015

Accepted 9 December 2015

Available online 23 April 2016

## Keywords:

Diffuse interstitial lung disease

Hypersensitivity pneumonitis

Farmer's lung disease

## ABSTRACT

Farmer's lung disease (FLD) is a form of hypersensitivity pneumonitis (HP) caused by inhaling microorganisms from hay or grain stored in conditions of high humidity in the agricultural workplace. It is probably underdiagnosed, especially in northern Spain, where climatic conditions favor the development of this disease.

According to previous studies, the most common antigens are usually thermophilic actinomycetes and fungi. The epidemiology of the disease is not well known, and is based on studies conducted by Central European and Asian groups.

The clinical presentation may vary, differentiating the chronic (exposure to lower concentrations of the antigen over a longer period time) and the acute forms (after exposure to high concentrations of the antigen). In patients with respiratory symptoms and agricultural occupational exposure, radiological, lung function and/or anatomical pathology findings must be compatible with FLD, bronchoalveolar lavage must show lymphocytosis, and tests must find sensitivity to the antigen.

The main treatment is avoidance of the antigen, so it is essential to educate patients on preventive measures. To date, no controlled studies have assessed the role of immunosuppressive therapy in this disease. Corticosteroid treatment has only been shown to accelerate resolution of the acute forms, but there is no evidence that it is effective in preventing disease progression in the long-term or reducing mortality.

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### Revisión de la enfermedad del pulmón de granjero

## RESUMEN

La enfermedad del pulmón de granjero (EPG) es una forma de neumonitis por hipersensibilidad (NH) producida por la inhalación de microorganismos procedentes del heno o grano almacenado en condiciones de alta humedad en el ámbito laboral agrícola. Se trata de una enfermedad probablemente infradiagnosticada, sobre todo en el Norte de España, donde las condiciones climáticas son propicias para el desarrollo de la misma.

Según estudios previos los antígenos más frecuentes suelen ser hongos y actinomicetos termofílicos. La epidemiología de la enfermedad no es del todo bien conocida, y se basa en estudios realizados por grupos centroeuropeos y asiáticos.

La presentación clínica puede ser variada, diferenciándose las formas agudas (tras exposición a elevadas concentraciones del antígeno) y las crónicas (exposición a menores concentraciones del antígeno, pero más prolongada en el tiempo). En estos casos es esencial, en aquellos pacientes con clínica respiratoria durante la exposición laboral agrícola, demostrar una radiología y función pulmonar compatible, así como una sensibilización al antígeno, una linfocitosis en el lavado broncoalveolar en su caso y/o una anatomía patológica concordante.

## Palabras clave:

Enfermedad pulmonar intersticial difusa

Neumonitis por hipersensibilidad

Enfermedad del pulmón de granjero

<sup>☆</sup> Please cite this article as: Cano-Jiménez E, Acuña A, Botana MI, Hermida T, González MG, Leiro V, et al. Revisión de la enfermedad del pulmón de granjero. Arch Bronconeumol. 2016;52:321–328.

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El tratamiento principal es la evitación antigénica, por lo que la educación de los pacientes en las medidas preventivas es fundamental. Por el momento, no existen estudios controlados que permitan evaluar el papel de tratamientos inmunosupresores en esta enfermedad. El tratamiento con corticosteroides solo ha demostrado acelerar la resolución de las formas agudas, pero no hay estudios que demuestren su efectividad a largo plazo, con el fin de evitar la progresión de la enfermedad ni disminuir su mortalidad.

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## Introduction

Farmer's lung disease (FLD), first described by Campbell in 1932, is one of the most prevalent forms of hypersensitivity pneumonitis (HP).<sup>1</sup> It is caused by the inhalation of microorganisms from hay and the dust from grain or straw stored in very damp conditions. It is a significant cause of morbidity among farm workers in some countries.<sup>2,3</sup> Few studies have been published in Spain,<sup>4–6</sup> in contrast to the large series published in other regions with similar climatic conditions to northern Spain.

## Epidemiology

The exact prevalence of FLD is difficult to determine, since the disease is influenced by many factors, including climate, geographical region, local customs, and differences in the nature and intensity of exposure to antigens.<sup>7</sup> Approximately 0.5%–3% of farmers may develop FLD, and the disease is associated with higher mortality rates. More recent studies performed among farmers in Asia described a prevalence of less than 6%,<sup>7,8</sup> but few epidemiological studies have been performed in our setting.<sup>9</sup>

## Etiology

The causative antigens in most cases of HP, including FLD, are bacteria, the most commonly described being thermophilic actinomycetes. This species includes *Saccharopolyspora rectivirgula* (previously known as *Micropolyspora faeni*, described as the main FLD antigen), *Thermoactinomyces vulgaris*, *Thermoactinomyces viridis*, and *Thermoactinomyces sacchari*, among others. These organisms reproduce in areas with high levels of humidity and at temperatures of between 40 and 60 °C. They are often isolated in contaminated farms (from moldy hay and other types of fodder), milking sheds and compost plants. These bacteria are among most common etiological agents in studies reported in Europe and North America,<sup>10,11</sup> but farmers are also exposed to other fungi and fungal fragments that can also cause FLD, such as *Alternaria*, *Aspergillus fumigatus* and *Botrytis*.<sup>11,12</sup> FLD, then, is common in farming areas,

particularly in the cold, wet seasons, when climatic conditions lead to increased levels of microorganisms in stored hay (Fig. 1).<sup>12</sup>

## Pathogenesis

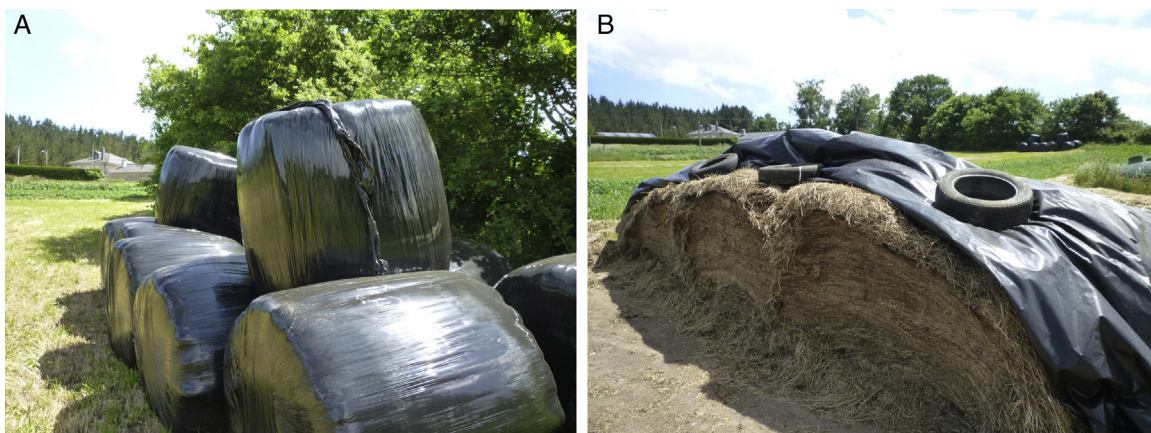
All HP diseases, including FLD, are caused by repeated exposure to antigenic particles in a susceptible, previously sensitized patient. The characteristics of antigens that determine their ability to induce an immunological response include their size, solubility, nature, resistance to enzymatic degradation, and inflammatory capacity. These antigens are implicated in the formation of antigen-antibody immune complexes, particularly of the IgG type, which intervene in complement activation. Antibody response alone is insufficient to cause disease: a cytotoxic CD8+ lymphocyte response is also required. Lymphocyte mediation is another mechanism involved in the process, particularly Th1 mediation, which is responsible for lymphocyte alveolitis and the formation of granulomas.<sup>1,13</sup> Some studies have shown that lymphocytes are also involved in the pathogenesis of FLD, and evidence of lymphocyte stimulation is considered as diagnostic proof of the disease.<sup>14</sup> Immediate hypersensitivity reactions, probably caused by IgG4 rather than IgE, may also play a role in the genesis of the immunological response.<sup>13,15</sup>

Little information is available on the particular host characteristics which determine susceptibility to developing FLD. It is more common in middle-aged men, although this probably reflects differences in exposure levels. It is also more common in non-smokers, probably because tobacco reduces the IgG response to inhaled antigens, affects cytokine production, and alters macrophage function.<sup>16,17</sup>

Known environmental risk factors include antigen load, duration of exposure, rhythm of exposure (frequency/intermittency), use or non-use of respiratory protection, and the type of working practices.<sup>11</sup>

## Clinical Forms

FLD is conventionally classified into 3 groups (acute, subacute, and chronic), depending mainly on clinical and radiological findings at the time of diagnosis.<sup>18</sup>



**Fig. 1.** (A, B) Different methods for storing hay, compacted (A) and covered (B). In this type of storage, certain climatic conditions can induce the growth of the microorganisms which cause farmer's lung disease.

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