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Diagnostic and therapeutic approach to occupational pneumonia

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ABSTRACT

We shall define occupational pneumonia as a disease of external origin, closely tied to the workplace setting and caused by biological microorganisms. The main pathogens are bacteria, fungi and viruses. There are a number of occupations specifically prone to the possibility of acquiring pneumonia when performing work duties.

In addition to the diagnostic methods and drug treatments current in infectious processes, a good clinical history, with avoidance and protection measures would be the most important tools for the management of occupational pneumonia.

Social and demographic changes in the last two decades have made zoonotic infections, and especially viruses, the main cause of new infections. Human health and animal health are closely linked, so collaboration between veterinarians and doctors, together with the necessary environmental respect and conservation, plus the appropriate public policies are essential to avoid these wide negative effects.

Keywords: Ocupaccional infections, comunity pneumonia, zoonotic infections, early diagnostic tests

INTRODUCTION

We shall define work-related or occupational pneumonia as a disease of external origin, which is closely tied to the workplace setting and caused by biological pathogens, including genetically modified pathogens and cell cultures, thereby leaving out the contracting of the disease in the community outside the workplace. With this definition, we therefore exclude from this review cases of occupational pneumonia caused by inorganic substances or allergic pneumonitis.

Community-acquired pneumonia (CAP) is not considered a work-related or occupational disease, so it is difficult to know how prone to develop it different occupations and working conditions may make workers. It is difficult to attribute pneumonia to an occupational or work-related source,when exposure to the pathogen is also present in the community. However, there are occupations that necessarily involve contact with certain pathogens to a higher or lesser degree, and thus give rise to the possibility of acquiring pneumonia while performing one's duties. These are listed as such in the Royal Decree on Occupational Diseases that we will be discussing later.

Improvements in hygiene and prevention have meant that some of these pneumonias, especially those of bacterial origin, have shown a marked decrease throughout the 20th century, to the point where they are now anecdotal. On the other hand, zoonotic infections, especially those due to emerging viruses, such as avian influenza (bird flu) or the coronavirus, are increasingly causing severe pneumonia after overt occupational exposure [1].

In this chapter we will be discussing some of the determining factors for the ways these pathogens spread, the occupations associated with pneumonia and the pathogens that cause it, as well as diagnostic and therapeutic approaches, followed by some final reflections on the future of these infections.

DISEASE SPREAD IN THE WORKPLACE AND ITS DETERMINING FACTORS

In the workplace, pneumonia-causing pathogens are usually transmitted mainly by the inhalation of infectious particles present in the environment, and only more rarely following

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bacteremia. As for the initial host, up to 75% of cases are of animal orign directly (zoonosis) or from the manipulation of animal-derived products, while on other occasions transmission originates in other human beings, as is the case of the flu or the coronavirus, as clearly shown in the health care setting [2].

The determining factors, as in other types of pneumonia, will depend both on the toxic effect of the inhaled pathogen and the intensity and duration of exposure, as well as how susceptible the infected host is.

It should also be noted that certain working conditions, involving contact with dust and sudden changes in temperature, behave as added risk factors rather than as causes of pneumonia [3].

OCCUPATIONS RELATED TO PNEUMONIA CASES ACQUIRED IN THE WORKPLACE

There are a number of occupations or risky activities related to the risk of acquiring pneumonia while performing work duties. These are listed as such in section 3 of Royal Decree RD 1299/2006, which provides a table of those occupational diseases approved by the Social Security system and establishes criteria for their notification and registration in Spain (Table1 [4]).

As a summary, we highlight the following occupations:

- Health care and laboratory personnel
- Veterinarians and staff who are in contact with animals
- Workers who work with and handle waste and human or animal excreta
- Farmworkers, nature conservation and exploration workers, hunters
- Construction workers and law enforcement agents

MAIN PATHOGENS CAUSING OCCUPATIONAL PNEUMONIA

Among the main disease-causing pathogens of occupational pneumonia, we include bacteria, fungi and viruses, as reflected in Table 2.

Bacteria: *Francisella tularensis, Leptospira interrogans, Burkholderia pseudomallei, Bacillus anthracis*, and some other more frequent bacteria such as *Coxiella burnetii, Chlamydophila psittacii, Legionella pneumophila, Mycoplasma pneumoniae*

Fungi: *Aspergillus*, *Histoplasma capsulatum, Coccidiodes immitis, Blastomyces*

Virus: Hantavirus, *Influenzae* (bird flu, swine flu) coronavirus (SARS, MERS, SARS-CoV-2)

In this brief review, we discuss some of these pathogens and the characteristics of each infection. There are pneumonic diseases caused by bacteria closely related to certain occupations, which were prominent in the past but are currently diagnosed only sporadically, such as tularemia, leptospirosis, anthrax or melioidosis. On the other hand, other diseases such as Q Fever, psittacosis or legionellosis are more common today and can be acquired both in the workplace and in the community.

Table 1 Professions related to occupational pneumonic processes

CODE	PROFESSIONS
3B0101	Farmers
3B0102	Ranchers
3B0103	Butchers
3B0104	Furriers
3B0105	Tanners
3B0106	Veterinarians
3B0107	Leather garment designers
3B0108	Handling, loading, unloading, transport and use of animal offal
3B0109	Shepherds
3B0110	Health personnel
3B0111	Laboratory personnel
3B0112	Slaughterhouse staff
3B0113	Personnel that care, collect, breed and transport animals
3B0114	Rural workers
3B0115	Butchers
3B0116	Veterinarians
3B0117	Poultry farmers
3B0118	Pet shops
3B0119	Work with risks of injury in a potentially dangerous environment
3B0120	Handling of human or animal excreta
3B0121	Farmers
3B0122	Game warden
3B0123	Forestry work
3B0124	Farm workers
3B0125	Paddy field reapers
3B0126	Swineherds
3B0127	Sewer works (rats)
3B0128	Cowboys
3B0129	Professions in contact with equine livestock
3B0130	Nature Conservation personnel
3B0131	Law enforcement personnel
3B0132	Jobs involving handling or exposure of animal excreta: ranchers

*Occupational diseases approved by Social Security System in Spain [4].

Table 2 Microorganisms associated with occupational pneumonia.

Disease (pathogen)	Reservoir	Risk populations
Bacteria		
Respiratory tularemia (*Francisella tularensis*)	Wild rabbits and rodents	Laborers, Military Personnel, Laboratory Workers, Hunters/Trappers, Agricultural Workers
Leptospirosis (*Leptospira interrogans*)	Water, soil, rodent urine	Farmers and veterinarians
Melioidosis (*Burkholderia pseudomallei*)	Soil, stagnant water, rice fields	Military personnel, agricultural workers
Inhalation anthrax (*Bacillus anthracis*)	Animal products (wool, fur)	Agricultural workers, tanners, slaughterhouse workers, textile workers, laboratory workers
Ornithosis (*Chlamydophyla psittaci*)	Birds	Pet shop workers, poultry production workers, veterinary care workers, laboratory workers
Q Fever (*Coxiella burnetii*)	Domesticated animals (cattle, sheep, goats)	Laboratory workers, textile workers, slaughterhouse workers, dairy cattle workers, veterinary care workers
Legionnaire's disease (*Legionella* spp.)	Contaminated water sources (for example, cooling towers, evaporative condensers)	Healthcare workers, laboratory workers, industrial laboratory workers, water well diggers
Atypical pneumonia (*Mycoplasma pneumoniae*)	Humans	Military personnel, healthcare workers, institutional workers
Fungi/Mycobacteria		
Histoplasmosis (*Histoplasma capsulatum*)	Earth; bird or bat droppings (endemic to eastern North America)	Agricultural workers, laboratory workers, manual workers
Coccidioidomycosis (*Coccidioides immitis*)	Soil (endemic to western North America)	Military personnel, agricultural workers, manual workers, textile workers, laboratory workers
Blastomycosis (*Blastomyces dermatitidis*)	Soil (endemic to eastern North America)	Laboratory workers, agricultural workers, manual workers, forestry workers
Paracoccidioidomycosis (*Paracoccidioides brasiliensis*)	Soil (endemic to Venezuela, Colombia, Brazil)	Farm workers
Sporotrichosis (*Sporothrix schenkii*)	Plant debris, tree bark and garden plants	Gardeners, florists, miners
Tuberculosis (*Mycobacterium tuberculosis, M. bovis, M. africanum*)	Humans and cattle	Laboratory and health care workers, slaughterhouse workers, veterinary care workers
Virus		
Hantavirus	Rodents	Farm workers, herders, rodent control workers
Measles	Humans	Healthcare and laboratory workers
Rubella	Humans	Healthcare and laboratory workers
Varicella zoster	Humans	Healthcare and laboratory workers, military personnel
Respiratory syncytial virus	Humans	Healthcare and laboratory workers
Adenovirus	Humans	Healthcare and laboratory workers, military personnel
Parainfluenza virus	Humans	Healthcare and laboratory workers
Influenza	Humans	Healthcare and laboratory workers
Coronavirus	Humans	Healthcare and laboratory workers

BACTERIA

Tularemia [5]. This is a disease caused by *F. tularensis*, an obligate intracellular Gram-coccobacillus. The reservoir is usually rodents (hares, rabbits...) and it can be acquired by inhalation, which causes pneumonia, or by insect bites, which produces an ulceroglandular form that is the most frequent. It is not transmitted between people. When it affects the lung, it causes lobar infiltrates, lymphadenopathy and, on occasion, effusion. Diagnosis is through blood tests, by culture (rich in cysteine), which gives a late result, and by PCR tests. Treatment is with antibiotics (aminoglycosides, doxycycline, or fluoroquinolones).

Leptospirosis [6]. Disease caused by L. *interrogans*. The reservoir is found in rodents (rats), as well as in water and soil contaminated with rodent urine. It commonly presents as pneumonia with bilateral infiltrates (pulmonary hemorrhage), but it can also present with jaundice and renal failure, then completing a Weil's syndrome triad. Diagnosis is through serological methods, by sample culture and recently also by PCR. Treatment is with penicillin or tetracycline and there is also a vaccine for cattle (which can occasionally act as reservoir).

Anthrax [7,8]. A rare disease caused by *B. anthracis*, a Gram-positive bacillus, whose reservoir consists of herbivorous animals (lambs, goats, cows) and is transmitted through skin contact with animals (carbuncle) or through inhalation of spores, which causes a pneumonia condition characterized by bilateral alveolar infiltrates or even necrotizing pneumonia, which may present mediastinal widening due to mediastinitis. In 2001 there was a case of bioterrorism in the US, following the mailing of several envelopes containing bacillus spores. Diagnosis is based on blood tests and through sample cultures. Treatment requires high doses of antibiotics, initially in combination with penicillin/tetracyclines and fluoroquinolones. Since this bacillus produces toxins, there is an antitoxin treatment. There is also a vaccine for cattle.

Melioidosis [9]. Disease caused by the Gram-negative bacteria, *B. pseudomallei*. It is found in soil and water in endemic areas in Southeast Asia, as well as in India and China. After pathogen inhalation, pneumonia can present with infiltrates or cavitated lesions. Symptoms can take up months to appear, so the epidemiological study is very important. In the 1960s, several cases were diagnosed after the return home of American soldiers from the Vietnam War. Diagnosis is made by staining and culture. Serological diagnosis is unreliable in endemic areas. Treatment is long-term, with ceftazidime, imipenem, or piperacillin. It is usually resistant to colistin and aminoglycosides.

Q fever [10]. Disease caused by *C. burnetii,* whose reservoir consists of domestic and wild animals, and ornithosis or psittacosis [11] caused by *C. psittaci*, whose reservoir is birds, can both manifest as pneumonia after inhalation of *Coxiella* spores or dust contaminated with bird droppings. The clinical and X-ray picture is usually similar to that found in community pneumonia. The usual diagnostic methods are serological tests, since sample culture is complicated and risky for laboratory personnel. New diagnostic molecular techniques, such as PCR, are being more widely used. The treatment is with macrolides or quinolones.

FUNGI

Histoplasmosis [12]. Disease caused by *H. capsulatum*. It is usually found in soils contaminated with bird and bat droppings, with a high nitrogen content. Often found in endemic areas of Central and South America, Africa, Asia and Australia. Its transmission is by inhalation of conidia, which occurs after turning over large amounts of soil, but a large amount of inoculum is needed to cause pneumonia. 90% of cases are asymptomatic, so calcified pulmonary nodules can be seen as an incidental finding on a chest X-ray, but when the inoculum is sizable, pneumonia symptoms can take shape, presenting pulmonary infiltrates with hilar lymphadenopathies and mediastinal widening. Diagnosis is made by tissue staining, slow-growing culture, serological tests and antigen detection. Treatment is unnecessary in many cases and only in severe forms, azoles or amphotericin B are prescribed.

Coccidiomycosis [13]. Disease caused by *C. immitis,* a fungus that lives on soil, which is more common in dry summers and in endemic desert areas such as Arizona, California or New Mexico. Transmission occurs through inhalation of spores following soil disturbance. Two-thirds of affected patients have few or no symptoms. When the spores affect the lung, they usually manifest radiologically as infiltrates, often involving cavitary lesions and lymphadenopathies. Sometimes these infiltrates do not resolve and X-ray images show persistent solitary nodules in the lung periphery. Diagnosis is through serology, histological (after digestion with potassium hydroxide, or papanicolaou) and by culture. Treatment is not necessary in many cases, and when necessary, azoles or amphotericin B are used.

VIRUSES

Hantavirus [14]. There are several types of this virus, whose reservoir is found in different types of rodents that act as vectors and its transmission occurs after inhalation of aerosols derived from the urine, feces or saliva of the vector. It is endemic in the US and South America. When it affects the lung, it causes severe bilateral pneumonia (infiltrated interstitial alveoli), often involving hypotension and shock (cardiopulmonary syndrome). Diagnosis is made through serology and PCR techniques. There is no effective antiviral treatment (ribavirin has shown activity in vitro), so mainly supportive measures are used. There is no vaccine.

Viruses that occasionally circulate in the community, such as measles, rubella, chicken pox or syncytial, can also affect health care professionals and cause pneumonia. Among those causing the most impact in recent years and which can be transmitted between humans are the Influenza virus and the coronavirus [1].

Influenza viruses. There are four types of Influenza viruses (A, B, C, D), with A and B being the types that cause seasonal epidemics, and Influenza A viruses the only type known to cause pandemics. These influenza A viruses are classified based on surface proteins hemagglutinin (H) and neuraminidase (N). There are 18 hemagglutinin and 11 neuraminidase subtypes. In Figure 1, you can see the successive flu pathogens that have affected the human population. The H5 lineage of the Influenza virus is the one causing the most concern in recent years, given that it affects millions of birds and has the potential to be transmitted to humans (figure 1)

Coronavirus. There are 7 types of coronaviruses that infect humans (see figure 2). The first four are very common and

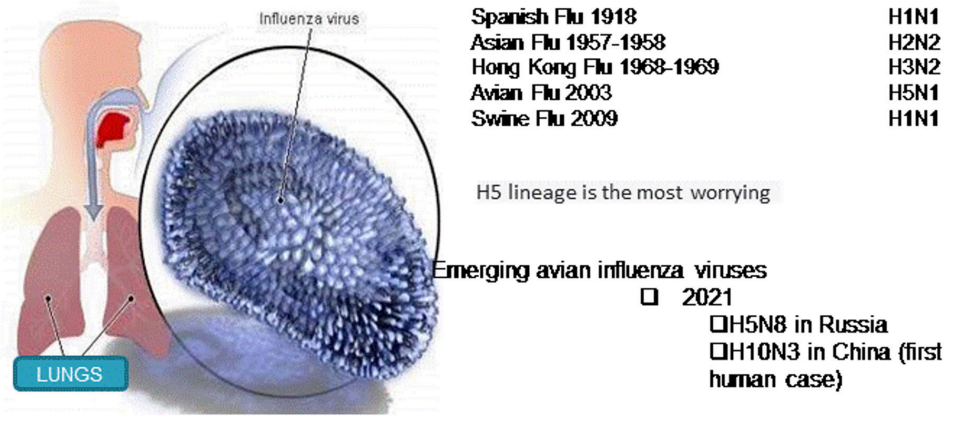
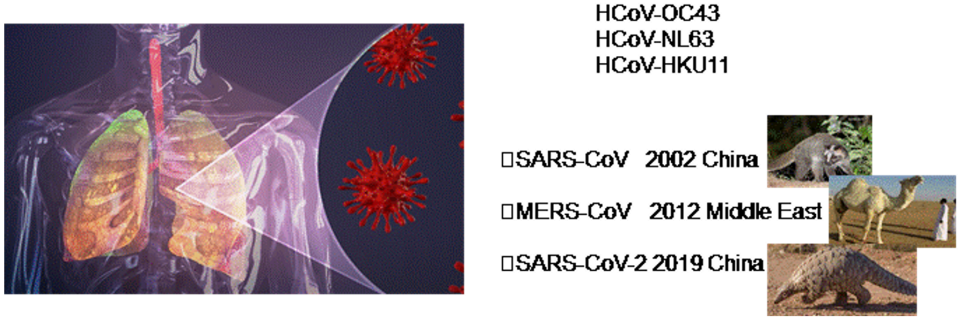


Figure 1 Influenza viruses that affect humans



* HCoV: Human Coronavirus .HCoV-229, HCoV-OC43, HCoV-NL63, HCoV-HKU11, Common coronaviruses that infect humans

*SARS-CoV: Severe Acute Respiratory Sindrome Coronavirus; MERS-CoV : Middle East respiratory Syndrome Coronavirus; SARS- CoV2; Severe Acute Respiratory Sindrome related coronavirus type 2; types of coronavirus that have appeared more recently

Figure 2 Coronaviruses that affect humans.

* HCoV: Human Coronavirus .HCoV-229, HCoV-OC43, HCoV-NL63, HCoV-HKU11, Common coronaviruses that infect humans
*SARS-CoV: Severe Acute Respiratory Sindrome Coronavirus; MERS-CoV : Middle East respiratory Syndrome Coronavirus; SARS-CoV2; Severe Acute Respiratory Sindrome related coronavirus type 2; types of coronavirus that have appeared more recently

often cause colds. However, the other three (SARS-CoV, MERS-CoV and SARS-CoV-2) can cause pneumonia and significant mortality rates, especially the first two, while SARS-CoV-2 has also shown a great ease of transmission.

The huge socio-sanitary repercussions that COVID-19, caused by SARS-CoV-2, has had worldwide, has once again raised our interest in a better understanding and control of emerging zoonotic infections. The risks of zoonoses are accentuated with globalization, wich has enabled its rapid expansion throughout the world. The "posthoc" analysis of recent epidemics such as bird flu or COVD-19, showed that the viruses were already circulating in the population weeks before the first case was diagnosed. This shows our need for earlier detection of future emerging zoonoses [15,16].

THERAPEUTIC DIAGNOSTIC APPROACH

A good clinical history is always very important in medicine, but in work-related or occupational diseases it is the key to indicating a possible diagnosis and being able to order the relevant diagnostic tests.

The diagnostic methods used are the same as those used for community pneumonia, among them:

- Cultures, which can be more or less complex and sometimes slow-growing, making it possible to study sensitivity to antimicrobials
- Histopathological staining techniques, especially when fungi are suspected
- Serology methods (IFI, ELISA)
- Rapid antigen tests
- Nucleic acid amplification tests (PCR), which have revolutionized the diagnosis of infectious diseases

As for therapeutic approaches, like in all work-related diseases, the most important measures are avoidance and protection. Vaccines play a major role in preventing the disease. Once the infection is established, we have at our disposal, as in other types of pneumonia, drug treatments with antibiotics, antifungals and antivirals. As adjuvant therapy, we must consider immunomodulatory drug treatment, which was tried during the recent COVD-19 pandemic. In cases when we do not have very effective therapeutic measures, we will need to resort to life support measures.

CONCLUSIONS

Some of the occupational origin bacterial and fungal pneumonias that were prevalent historically have been decreasing in recent years, due to improvements in prevention. However, social and demographic changes in the last two decades have meant that zoonotic infections, and especially viruses, have become the main cause of new infections or at least had a large increase in incidence.

Human health and that of animals are closely linked, so collaboration between veterinarians and doctors, together with the necessary environmental respect and conservation, plus the appropriate public policies are essential to avoid the negative effects that the development of these zoonoses and communicable diseases can give rise to. To this effect there is a WHO-supported initiative called "One Health" [17,18], which establishes a global collaborative approach to understand the interrelated challenges that human and animal health will face in this promising future.

Among the measures aimed at preventing and/or controlling epidemics/pandemics, we should consider the implementation of strategies based on "early warning" and "rapid response" mechanisms, as well as the development of rapid diagnostic technologies. One of the most important tools we currently have in the diagnostic study of these zoonoses and other infections, is the use of molecular biology techniques applied to the understanding of epidemiology. For an optimal response we should have human resources available, but also specialized laboratories with good communication networks between them and with health care facilities. On the other hand, the use of new technologies such as *big data* and *artificial intelligence* [19] can help us monitor these infections, create predictive algorithms, and discover or develop new treatments.

CONFLICTS OF INTEREST

Authors declare no conflicts of interest

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