Disponible en ligne sur
SciVerse ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Médecine et maladies infectieuses

Médecine et maladies infectieuses 42 (2012) 517–524

Short communication

# Pneumococcal infections and adult with risk factors

## *Infections à pneumocoque et populations adultes à risque*

C. Chidiac

*Service des maladies infectious et tropicales, hôpital de the Croix-Rousse, 103, Grande-Rue-de-la-Croix-Rousse, 69317 Lyon cedex 04, France*

Received 8 December 2011; accepted 2 April 2012

**Abstract**

*Streptococcus pneumoniae* is an important bacterium in humans, and is a cause of upper and lower respiratory tract infections, meningitis, bacteremia, and/or invasive infections. An analysis of literature allows identifying the main risk factors; spleen dysfunctions, sickle cell anemia, alcohol abuse, chronic liver disease, cirrhosis, ischemic cardiac diseases, congestive cardiac failure, diabetes mellitus, obesity, chronic lung disease, immunodeficient patients including HIV infection, and old age. *S. pneumoniae* infections are more frequent and more severe in these patients. The pathophysiological mechanisms involved may be associated. These populations at risk should receive anti-pneumococcal vaccination. The availability of a 13 valent conjugate vaccine for adult opens new perspectives, but its clinical effectiveness needs to be proved for these patients at risk.


*Keywords:* *S. pneumoniae*; Risk factor; Invasive infection; Vaccine

**Résumé**

*Streptococcus pneumoniae* est un pathogène important chez l'homme et est source d'infections des voies respiratoires hautes et basses, méningites, bactériémies et/ou infections invasives. L'analyse de la littérature permet d'identifier de nombreux facteurs de risque; dysfonctions spléniques, drépanocytoses, alcoolisme, hépatopathies chroniques, cirrhoses, cardiopathies ischémiques et insuffisance cardiaque, diabète, obésité, pathologie broncho-pulmonaire chronique, immunodépressions dont l'infection à VIH et enfin l'âge avancé. Les infections à *S. pneumoniae* sont plus fréquentes et plus graves chez ces patients. Les mécanismes physiopathologiques sont diversement associés. Ces populations mériteraient de bénéficier d'une couverture vaccinale anti-pneumococcique. La mise à disposition du vaccin conjugué 13 valent pour l'adulte offre des perspectives nouvelles, mais la démonstration de l'efficacité clinique est nécessaire chez ces patients à risque.


*Mots clés :* *S. pneumoniae* ; Facteur de risque ; Infection invasive ; Vaccin

## 1. Introduction

*Streptococcus pneumoniae* is an important bacterium in humans, colonizing the respiratory tract very early in life, and a major etiology of pneumonia, meningitis, and otitis. The defense mechanisms rely on very strong interactions between humoral factors such as antibodies, complement, and phagocytic cells, especially polymorphonuclear cells. Invasive *S. pneumoniae* infections (IPI) are defined by the isolation of *S. pneumoniae* in a normally sterile site, such as blood, CSF, and middle ear fluid [1].

It is difficult to analyze publications on *S. pneumoniae* infections: the relative scarcity of microbiological documentation for community-acquired pneumonia (50% of well-investigated community-acquired pneumonia are not documented), the low percentage of bacteremia (IPI) during *S. pneumoniae* pneumonia. Thus, in the analyzed articles, the difference was not always easy to establish, some studies focusing on IPI, others on community-acquired pneumonia, and others still on documented *S. pneumoniae* pneumonia.

The objective of our review was to describe adult populations at risk of *S. pneumoniae* pneumonia mainly, but also bacteremia, and/or IPI.

The data published for various risk situations was analyzed, and in some cases, the results concerning the vaccinal

*E-mail address:* christian.chidiac@univ-lyon1.fr

0399-077X/$ – see front matter © 2012 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.medmal.2012.04.003

effectiveness of the 23-valent polysaccharidic vaccine (PPV23) or the 7- or 13-valent conjugate vaccine (PCV7 or PCV13).

## 2. The main risk factors

Globally, the incidence of IPI (bacteremia, meningitis, etc.) is considerably higher in people over 65 years (35 to 50/100,000 per year) and in patients presenting with a chronic disease [2].

Table 1, adapted from Feikin, lists the main comorbidities associated to *S. pneumoniae* infections, and illustrates the impact they have on the lethality rate of patients hospitalized for invasive pneumonia [2].

### 2.1. Spleen dysfunction

This term includes asplenism and hyposplenism.

It is a frequent situation in adults. Anatomic or congenital asplenia is rare, the main causes are post-traumatic or curative splenectomy (5000 to 9000 cases/year in France), functional asplenia related to the sickle cell anemia (3000 to 5000 patients), acquired hyposplenia related to portal hypertension, splenic infarct, blood diseases, systemic inflammatory diseases, for a total of 250,000 people in France [3].

These anatomic or functional asplenia expose to infections with a rapid onset, and death within a few hours. The incidence of these infections is 50 to 500 times higher than those observed in the global population, the mortality rate is 50 to 100 times higher than that of controls.

Thus, Bisharat in his study reported a 55% mortality rate for splenectomized patients in case of *S. pneumoniae* infection [4].

More than 80% of severe infections occur early in splenectomized patients, within 2–3 years after surgery [5].

IPI may nevertheless occur up to 30 years after splenectomy and the infectious risk could persist all life long [6].

Table 1
Death rate of hospitalized patients for invasive *S. pneumoniae* pneumonia according to comorbidities (1995–1997).
*Taux de létalité des patients hospitalisés pour pneumonie à S. pneumoniae invasive selon les comorbidités (1995–1997).*

| Comorbidities | *N* death/total Non adjusted death rate | RR (CI 95%) |
|---|---|---|
| None | 44/757 (6) | Reference |
| Hepatic cirrhosis | 20/59 (34) | 5.8 (3.7–9.2) |
| Congestive cardiac insufficiency | 70/255 (27) | 4.7 (3.3–6.7) |
| Renal insufficiency | 40/164 (24) | 4.2 (2.8–6.2) |
| Solid tumor | 45/210 (21) | 3.7 (2.5–5.4) |
| Ischemic cardiac disease | 29/156 (19) | 3.2 (2.1–5.0) |
| Asplenia | 3/16 (19) | 3.2 (1.1–9.3) |
| Diabetes mellitus | 43/254 (17) | 2.9 (2.0–4.3) |
| COPB | 60/372 (16) | 2.8 (1.9–4.0) |
| Immunosuppressive treatment | 23/157 (15) | 2.5 (1.6–4.1) |
| AIDS | 28/207 (14) | 2.3 (1.5–3.6) |
| Malignant blood disease | 10/77 (13) | 2.2 (1.2–4.3) |
| Asthma | 12/159 (8) | 1.3 (0.7–2.4) |
| HIV infection (non AIDS) | 13/206 (6) | 1.1 (0.6–2.0) |

According to Fekin DR [2].

*S. pneumoniae* could be implicated in 50 to 90% of identified infections (etiological diagnosis or reported pneumonia?). It is the most frequent bacterium, responsible for 60% of deaths [7].

### 2.2. Sickle cell anemia

Bacterial infections are a major cause of morbidity and mortality in young children presenting with sickle cell anemia.

Functional asplenia, a decreased capacity for opsonization due to abnormalities of B-lymphocytes and alternative pathway of the complement result in the incapacity to eliminate *S. pneumoniae* from the blood.

*S. pneumoniae* is the most frequently isolated bacterium, especially before 6 years of age, reaching a rate of 66% in an American multicentric prospective study [8].

Septicemia is characterized by a rapid onset and a severe outcome, the frequency of disseminated intravascular coagulation (DIC) and shock, and a high lethality rate (11 to 24% in developed countries before introduction of antibiotic prophylaxis) [9].

The susceptibility to infections is observed especially in homozygote sickle cell patients, but also in those chez presenting with β-thalasso-sickle cell anemia and double heterozygous SC. The incidence of bacteremia ranges around 8 child-years for homozygotes, and around 100 child-years for patients presenting with double heterozygous SC. *S. pneumoniae* and *Salmonella* are the most frequently isolated bacteria. The incidence of severe bacterial infections is especially high before 3 years of age in sickle cell patients if there is no antibiotic prophylaxis [10].

The infectious risk remains all life long in sickle cell patients. In adults, the alteration of splenic functions (splenic infarct, fibrosis,) is associated to functional abnormalities of non-specific immunity (complement, immunoglobulins, leucocytes, monocytes, etc.). *S. pneumoniae* is an important cause of bacteremia, lung infections are frequents [11].

The risk associated with splenectomy, increasing with age are reported in Table 2 adapted from Holdsworth [7].

Table 2
Post-splenectomy *S. pneumoniae* infections. Frequency of first episode occurrence according to age.
*Infections à S. pneumoniae post splénectomie. Fréquence de survenue du premier épisode selon l'âge.*

| Age | All infections | *S. pneumoniae* infections | |
|---|---|---|---|
| | | *N* | % |
| <5 | 62 | 24 | 38.7 |
| 6–10 | 49 | 28 | 57.1 |
| 11–15 | 34 | 20 | 58.8 |
| 16–20 | 18 | 4 | 22.2 |
| 21–30 | 31 | 22 | 71.0 |
| 31–40 | 25 | 20 | 80.0 |
| 41–50 | 23 | 15 | 65.2 |
| 51–60 | 17 | 9 | 52.9 |
| >61 | 22 | 18 | 81.8 |
| Total | 281 | 160 | |

According to Holdsworth RJ [7].