

# Pneumonies aiguës communautaires graves

## Actualités / Perspectives

Alexis FERRÉ

*Réanimation-USC, CH de Versailles (78)*



# Conflits/Liens d'intérêts

Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

**Intervenant :** Ferré Alexis

**Titre :** Pneumonies aiguës communautaires graves, Actualités et perspectives

 L'orateur ne souhaite pas répondre

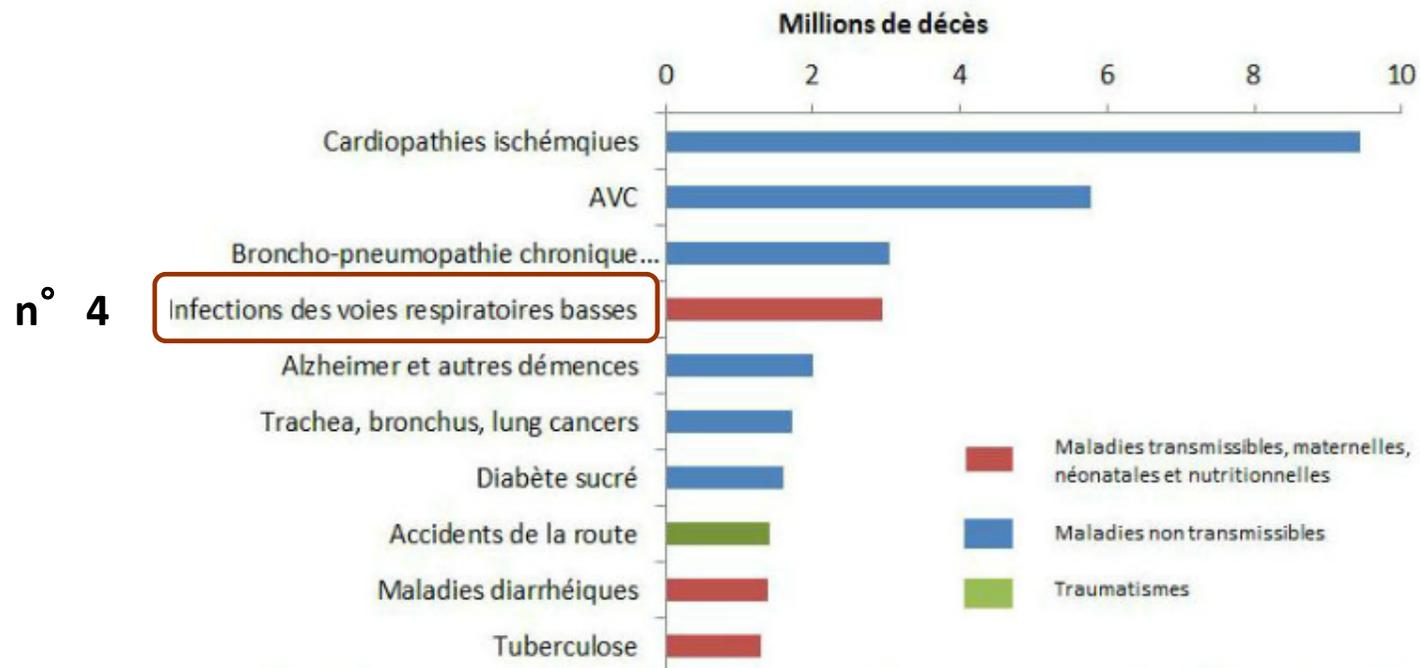
- |   |                              |   |
|---|------------------------------|---|
|  Consultant ou membre d'un conseil scientifique  | <input type="checkbox"/> OUI | <input checked="" type="checkbox"/> NON |
|  Conférencier ou auteur/rédacteur rémunéré d'articles ou documents  | <input type="checkbox"/> OUI | <input checked="" type="checkbox"/> NON |
|  Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations | <input type="checkbox"/> OUI | <input checked="" type="checkbox"/> NON |
|  Investigateur principal d'une recherche ou d'une étude clinique   | <input type="checkbox"/> OUI | <input checked="" type="checkbox"/> NON |

Chapitre 1.

**Etat des lieux**

# Epidémiologie / OMS

## les 10 principales causes de mortalité - 2016



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.

# Epidémiologie en Réa



## The Burden of Community-Acquired Pneumonia Requiring Admission to ICU in the United States

TABLE 1 ] Patient Characteristics on Day of Hospitalization

Characteristics	ICU Admission			P Value
	Early	Late	None	
Total study population, No.	1,275	432	5,742	

Cohorte 2014-2016  
9 hôpitaux  
→ 23% en Réa

TABLE 3 ] Number of Deaths in Patients With Community-Acquired Pneumonia Admitted to the ICU in Louisville and the United States

ICU Admissions and Mortality	Louisville, Kentucky <sup>a</sup>			United States of America <sup>b</sup>
	ICU Admission			
	Early	Late	Total	
Adult patients in the ICU with community-acquired pneumonia, No. (%)	1,275	432	1,707	356,326 <sup>c</sup>
In-hospital deaths <sup>d</sup>	200 (16)	87 (20)	287 (17)	60,576 <sup>c</sup>
15-Day deaths	233 (18)	84 (19)	317 (19)	66,172 <sup>c</sup>
30-Day deaths <sup>d</sup>	319 (25)	140 (33)	459 (27)	96,209 <sup>c</sup>
6-Month deaths <sup>d</sup>	471 (38)	189 (44)	660 (39)	138,968 <sup>c</sup>
1-Year deaths	563 (45)	216 (51)	779 (47)	167,474 <sup>c</sup>

# Définition PAC grave



**BTS guidelines for the management of community acquired pneumonia in adults: update 2009**



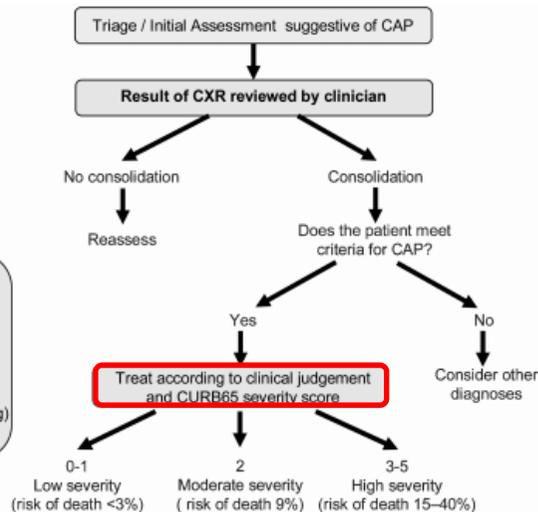
2019

**Diagnosis and Treatment of Adults with Community-acquired Pneumonia**

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

**CURB65 severity score:**  
1 point for each feature present:

- Confusion
- Urea > 7 mmol/l
- Respiratory rate  $\geq$  30/min
- Blood pressure (SBP < 90 or DBP  $\leq$  60mmHg)
- Age  $\geq$  65 years



**Validated definition includes either one major criterion or three or more minor criteria**

**Minor criteria  $\geq$  3**

- Respiratory rate  $\geq$  30 breaths/min
- $Pa_{O_2}/F_{iO_2}$  ratio  $\leq$  250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (blood urea nitrogen level  $\geq$  20 mg/dl)
- Leukopenia\* (white blood cell count < 4,000 cells/ $\mu$ l)
- Thrombocytopenia (platelet count < 100,000/ $\mu$ l)
- Hypothermia (core temperature < 36°C)
- Hypotension requiring aggressive fluid resuscitation

**ou Major criteria = 1**

- Septic shock with need for vasopressors
- Respiratory failure requiring mechanical ventilation

**Score CURB65**

**Score PSI**

# Pathogènes en Réa

Viral-bacterial coinfection affects the presentation and alters the prognosis of severe community-acquired pneumonia

**Table 2** Microbiological findings of 174 patients with severe CAP

Patients	All patients (n = 174)	Bacterial group (n = 46)	Viral group (n = 53)	Mixed group (n = 45)	No etiology group (n = 30)
<i>S. pneumoniae</i>	40 (23)	19 (41.3)	-	21 (46.7)	-
Other streptococci	6 (3.4)	2 (4.3)	-	4 (8.9)	-
<i>S. aureus</i>	12 (6.9)	6 (13)	-	6 (13.3)	-
<i>L. pneumophila</i>	8 (4.6)	7 (15.2)	-	1 (2.2)	-
<i>C. pneumoniae</i> – <i>M. pneumoniae</i>	6 (3.4)	5 (10.9)	-	1 (2.2)	-
<i>H. influenzae</i>	13 (7.5)	5 (10.9)	-	8 (17.8)	-
Enterobacteriaceae species	11 (6.3)	7 (15.2)	-	4 (8.9)	-
<i>P. aeruginosa</i>	7 (4)	2 (4.3)	-	5 (11.1)	-
Other bacteria	3 (1.7)	1 (2.2)	-	2 (4.4)	-
Mixed flora	10 (5.7)	6 (13)	-	4 (8.9)	-
Picornavirus (rhinovirus)*	22 (12.6)	-	7 (13.2)	15 (33.3)	-
Influenza A	32 (18.4)	-	19 (35.8)	13 (28.9)	-
Influenza B	6 (3.4)	-	4 (7.5)	2 (4.4)	-
Parainfluenza	3 (1.7)	-	2 (3.8)	1 (2.2)	-
Respiratory syncytial virus	9 (5.2)	-	5 (9.4)	4 (8.9)	-
Human metapneumovirus	12 (6.9)	-	6 (11.3)	6 (13.3)	-
Coronavirus	14 (8)	-	7 (13.2)	7 (15.6)	-
Adenovirus	3 (1.7)	-	2 (3.8)	1 (2.2)	-
Bocavirus	1 (0.6)	-	1 (1.9)	0 (0)	-
Cytomegalovirus	1 (0.6)	-	1 (1.9)	0 (0)	-
Herpes simplex virus	3 (1.7)	-	1 (1.9)	2 (4.4)	-
Varicella zoster virus	1 (0.6)	-	1 (1.9)	0 (0)	-

# Synthèse des recommandations ATB

Recommandations hors FDR	Traitement empirique
BTS (UK) 2009	Co-Amoxiclav + Clarithromycine
SPILF-SPLF (France) 2006-2010	C3G + Macrolides ou C3G + FQ (Levoflo)
SEPAR (Espagne) 2010	C3G + Macrolides (Azithro ou Clarithro) ou C3G + FQ (Levoflo)
SSID (Suède) 2017	C3G + Macrolides (Erythro) ou Péni G + FQ
CTS-CMA (Chine) 2018	[Co-Amoxiclav ou C3G] + Macrolides ou [Co-Amoxiclav ou C3G] + FQ
SWAB-NVALT (Pays-Bas) 2018	FQ (Moxiflo) ou C3G + Cipro
IDSA (USA) 2019	C3G + Macrolides (Azithro ou Clarithro) ou C3G + FQ (Levoflo ou Moxiflo)

# Les Fluoroquinolones ?

**Pas de preuve clinique de supériorité en Réa**  
**Pression de sélection / BMR**  
**Alerte ANSM 2019**



Chapitre 2.

**Actualités**

# Evolution épidémiologique en Réa

Evolution over a 15-year period of the clinical characteristics and outcomes of critically ill patients with severe community-acquired pneumonia

**Table 1** Characteristics of the patients with severe community-acquired pneumonia.

	Total n:458	P1 n:124	P2 n:153	P3 n:181	P
Age ( $\pm$ SD)	61.3 (16)	59.5 (18)	63.3(16)	60.6(16)	0.13
Male gender (%)	69.0	70.2	70.6	67	0.21
<b>Severity</b>					
<i>Apache II (mean <math>\pm</math> SD)</i>	19.0 $\pm$ 7.9	20.8 $\pm$ 7.5	18.6 $\pm$ 8.1	18.1 $\pm$ 7.7	0.03
CURB-65 (mean $\pm$ SD)	3.0 $\pm$ 1.1	2.9 $\pm$ 1.1	3.2 $\pm$ 1.0	2.9 $\pm$ 1.1	0.01
$\geq$ 1 major criteria IDSA/ATS (%)	73.0	64.2	72.8	82.5	<0.01
<b>Comorbidities (%)</b>					
COPD	30.8	27.6	34.4	28.0	0.42
Alcoholism	14.4	18.0	11.0	14.4	0.26
Chronic renal failure	4.8	8.9	5.2	1.6	0.01
Cardiovascular disease	21.0	23.4	24.8	16.0	0.10
Cancer	15.3	12.1	15.0	17.7	0.41
Diabetes	24.1	28.5	26.8	17.1	0.04
HIV	8.1	5.6	9.2	8.8	0.50
Immunocompromised	9.6	8.9	7.2	12.2	0.29
Patients with $\geq$ 2 comorbidities	52.3	53.7	54	49.5	0.60
Septic shock (%)	47.2	38.2	44.8	50.0	0.54
Mechanical ventilation (%)	67.2	56.9	63.0	72.0	0.02

P1 (1999-2003), P2 (2004-2008), P3 (2009-2013)

# Evolution des pathogènes

Evolution over a 15-year period of the clinical characteristics and outcomes of critically ill patients with severe community-acquired pneumonia

**Table 2** Distribution of etiology of severe community-acquired pneumonia over 15 years.

Pathogen (%)	Total n:458	P1 n:124	P2 n:153	P3 n:181	P
<i>Streptococcus pneumoniae</i>	191 (41.7)	49 (38.7)	73 (47.7)	70 (38.6)	0.18
<i>Legionella pneumophila</i>	29 (6.3)	13 (10.4)	8 (5.2)	8 (4.4)	0.08
Virus <sup>a</sup>	25 (5.4)	5 (4.0)	4 (2.6)	16 (8.8)	0.03
<i>Pseudomonas aeruginosa</i>	12 (2.6)	4 (3.2)	8 (5.2)	-	0.01
<i>Staphylococcus aureus</i>	10 (2.1)	3 (2.4)	4 (2.6)	3 (1.6)	0.80
Enterobacteriaceae	10 (2.1)	4 (3.2)	4 (2.6)	2 (1.1)	0.40
<i>Pneumocystis jiroveci</i>	8 (1.7)	2 (1.6)	2 (1.3)	4 (2.2)	0.80
<i>Haemophilus influenzae</i>	6 (1.3)	2 (1.6)	1 (0.6)	3 (1.6)	0.60
Other Gram positive	4 (0.8)	1 (0.8)	-	3 (1.6)	0.20
Miscellaneous <sup>b</sup>	17 (3.7)	8 (6.4)	5 (3.2)	4 (2.2)	0.10
Polymicrobial	20 (5.4)	1 (0.8)	2 (1.3)	17 (9.3)	<0.001
Unknown origin	126 (27.5)	33 (26.6)	42 (27.4)	51 (28.1)	0.9

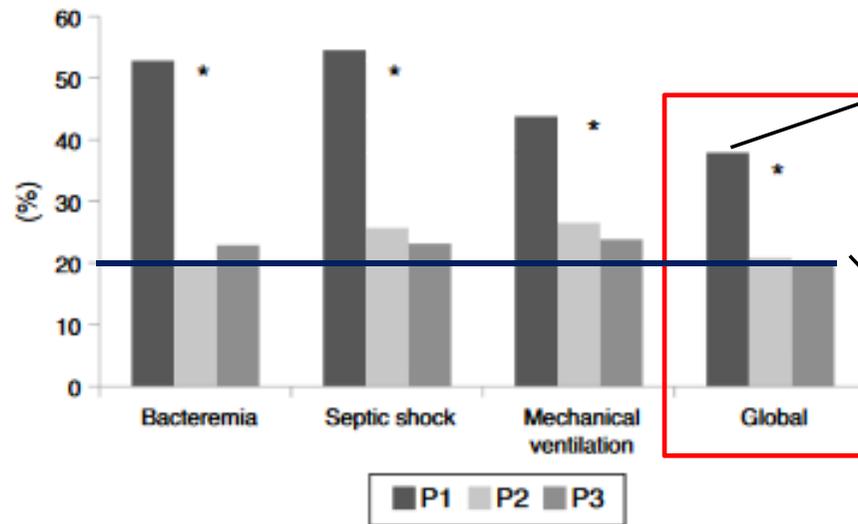
<sup>a</sup> Varicella, Influenza.

<sup>b</sup> *Chlamydomyces* sp., *Fusobacterium* sp., *M. tuberculosis*, *Aspergillus* sp., *Nocardia* sp.

P1 (1999-2003), P2 (2004-2008), P3 (2009-2013)

# Evolution de la mortalité

Evolution over a 15-year period of the clinical characteristics and outcomes of critically ill patients with severe community-acquired pneumonia



**Prognosis and Outcomes of Patients With Community-Acquired Pneumonia**  
 A Meta-analysis Michael J. Fine.  
*JAMA*. 1996;275(2):134-141.  
 ICU, n= 788 → Mortalité 36,5%

-18%

**STREPTOGENE**  
 Mortalité 19%  
 Jean-Pierre Bedos  
*Intensive Care Med* (2018) 44:2162-2173

Figure 2 Evolution of mortality over the three periods.

# Evolution de la mortalité

**Improved survival among ICU-hospitalized patients with community-acquired pneumonia by unidentified organisms: a multicenter case-control study**

Variable	2008–2015 (n = 140)	2000–2002 (n = 193)	p-Value
Intensive care unit mortality	22 (15.7)	52 (26.9)	0.02
Variable	2008–2015 (n = 140)	2000–2002 (n = 193)	p-Value
Previous antibiotic	26 (18.6)	50 (25.6)	0.15
<b>Monotherapy</b>	<b>8 (5.7)</b>	<b>44 (22.8)</b>	<b>&lt;0.01</b>
<b>Combined therapy</b>	<b>132 (94.3)</b>	<b>149 (77.2)</b>	<b>&lt;0.01</b>
<b>Antibiotic initiated 0 to 3 h</b>	<b>102 (72.9)</b>	<b>97 (50.3)</b>	<b>&lt;0.01</b>
Antibiotic initiated 4 to 6 h	25 (17.9)	59 (30.6)	0.01
Antibiotic initiated more than 6 h	13 (9.3)	37 (19.2)	0.01
<b>Adequate treatment according to 2007 IDSA/ATS guidelines</b>	<b>99 (70.7)</b>	<b>93 (48.2)</b>	<b>&lt;0.01</b>

# Facteurs de risque de mortalité

## Improved survival among ICU-hospitalized patients with community-acquired pneumonia by unidentified organisms: a multicenter case-control study

**Table 4** Univariate and multivariate analyses to assess variables associated with changes in intensive care unit (ICU) survival

Variable	Survival (n = 259)	No survival (n = 74)	Univariate analysis: <i>p</i> -value	Multivariate analysis: OR (95 % CI); <i>p</i> -value
Age over 65 years	117 (45.2)	47 (63.5)	<0.01	0.87 (0.43–1.76); 0.71
Alcohol use	44 (17.0)	14 (18.9)	0.73	
Active smoker	111 (43.0)	29 (39.2)	0.60	
Diabetes mellitus	59 (23.2)	19 (26.0)	0.64	
Cardiomyopathy	62 (24.4)	26 (35.6)	0.07	
Chronic obstructive pulmonary disease	88 (34.0)	29 (39.2)	0.41	
Immunosuppression	6 (2.3)	5 (6.8)	0.07	
Need for vasopressors	93 (35.9)	52 (70.3)	<0.01	0.89 (0.40–1.96); 0.77
Invasive mechanical ventilation	128 (49.4)	67 (90.5)	<0.01	0.24 (0.10–0.62); <0.01
Acute kidney injury	58 (22.7)	45 (63.4)	<0.01	0.21 (0.10–0.44); <0.01
Rapid radiographic spread	105 (41.3)	41 (57.7)	0.02	0.58 (0.29–1.16); 0.12
Adequate treatment according to 2007 IDSA/ATS guidelines	164 (63.3)	28 (37.8)	<0.01	2.22 (1.11–4.43); 0.02
Estimated probability of death <sup>a</sup>	26.0 (15.0–42.0)	46.0 (26.5–61.0)	<0.01	0.97 (0.95–0.99); <0.01
Combined therapy	220 (84.9)	61 (82.4)	0.59	
Antibiotic initiated within 3 h	166 (64.1)	33 (44.6)	<0.01	3.48 (1.70–7.15); <0.01

# Diagnostic et imagerie thoracique

- Radiographie standard...
- La TDM thoracique ?
- **L'échographie pulmonaire :**

**Lung Ultrasound Will Soon Replace Chest Radiography in the Diagnosis of Acute Community-Acquired Pneumonia**  
*Curr Infect Dis Rep.* 2016 Dec;18

**Is lung ultrasound the stethoscope of the new millennium? Definitely yes!**  
*Acta Med Acad.* 2016 May;45

**Point-of-Care Lung Ultrasound in Critically ill Patients**

*Rev Recent Clin Trials.* 2018 Jan

**Conclusion:** Bedside lung ultrasound in critically ill patients can serve as a tool to diagnose common lung pathologies, monitor its course and guide clinical management.

# Echographie pulmonaire

## Relevance of Lung Ultrasound in the Diagnosis of Acute Respiratory Failure\* The BLUE Protocol (CHEST 2008; 134:117-125)

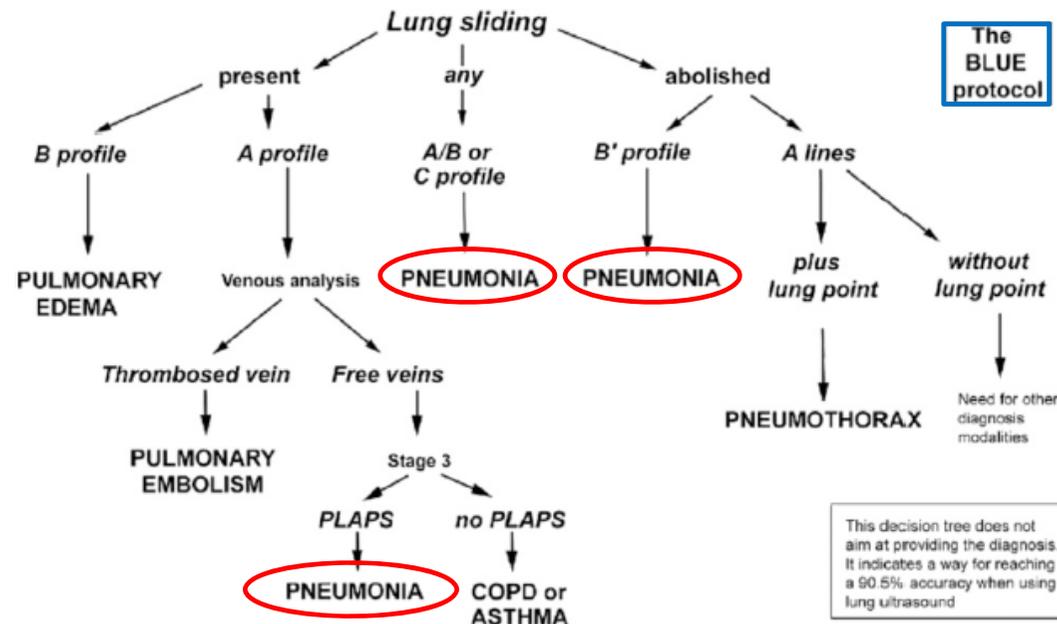


FIGURE 7. A decision tree utilizing lung ultrasonography to guide diagnosis of severe dyspnea.

# Echographie pulmonaire

**Effectiveness of lung ultrasonography for diagnosis of pneumonia in adults: a systematic review and meta-analysis**

*J Thorac Dis*, 2016 Oct;8

**Lung ultrasound for the diagnosis of pneumonia in adults: A meta-analysis**

*Medicine (Baltimore)*, 2017

**Systematic review and meta-analysis for the use of ultrasound versus radiology in diagnosing of pneumonia**

*Crit Ultrasound J*, 2017 Dec;9

**Echo > radio**  
**Echo = TDM ?**

**Impact pronostic ?**

# Tests diagnostiques

2015 - Annotated **BTS** Guideline  
for the management of CAP in adults (2009)  
Summary of recommendations

Management of community-acquired pneumonia  
in immunocompetent adults: updated **Swedish**  
guidelines 2017

What microbiological investigations should be performed in hospital?

high severity CAP

Blood cultures

Sputum cultures

Other tests for *Streptococcus pneumoniae*

25. Pneumococcal urine antigen tests

Tests for Legionnaires' disease

28. Legionella urine antigen tests

Tests for *Mycoplasma pneumoniae*

33. Where available, PCR of respiratory tract samples

Tests for *Chlamydia* species

36. *Chlamydia* antigen and/or PCR detection tests should be available

PCR and serological tests for other respiratory pathogens    grippe/épidémie +++

38. Where PCR for respiratory viruses and atypical pathogens is readily available or obtainable

à considérer

Autres techniques : Filmarray© Pneumonia Panel plus (FA-PP) → impact clinique et rapport coût-efficacité ?

# Adjuvant : La corticothérapie ?

- **Objet du débat = PAS dans le choc septique et le SDRA ?**

-2/3 choc septique = origine pulmonaire

-2/3 SDRA = pneumonie

- **Effet propre des CTC pour les pneumonies ?**

- **Les objectifs Réa « forts » de la CTC ?**

-durée de VM

-durée de séjour ICU / hôpital

-mortalité...?

- **Analyse littérature difficile**

sévérité/cours, mortalités variables, effectifs faibles, CIP ≠ Revues

**Major criteria**  
Septic shock with need for  
vasopressors  
Respiratory failure requiring mechanical  
ventilation

LUNG SAFE

JAMA. 2016;315(8)

# La corticothérapie

## Etudes positives ?

Effect of Corticosteroids on Treatment Failure Among Hospitalized Patients With Severe Community-Acquired Pneumonia and High Inflammatory Response  
A Randomized Clinical Trial  
Antoni Torres,  
JAMA. 2015;313(7):  
decreased treatment failure (composite)

- 3 centres, 8 ans... 120 patients
- Plus de choc et VM gpe placebo
- Plus docu microbio gpe CTC
- ATB < 4h : 80% CTC vs 60% placebo
- 0% décès choc/DMV gpe CTC vs 56%

Corticosteroid Therapy for Patients Hospitalized With Community-Acquired Pneumonia  
A Systematic Review and Meta-analysis  
Siemieniuk,  
Ann Intern Med. 2015;163:519-528.  
may reduce mortality by approximately 3%,  
need for mechanical ventilation by approximately 5%,  
hospital stay by approximately 1 day.

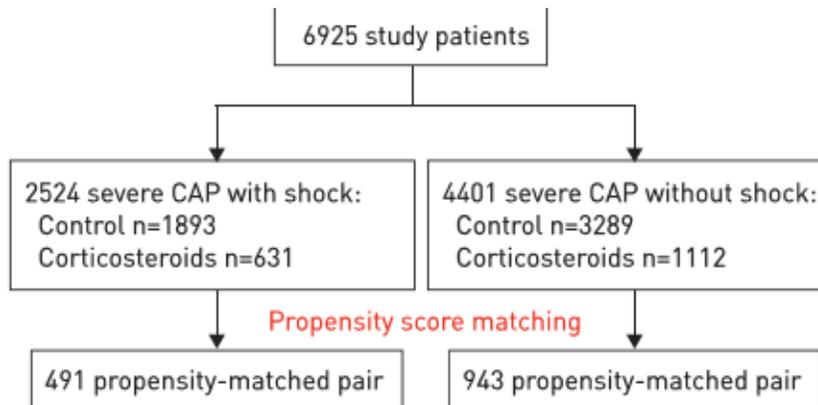
- 13 RCT
- 2005 patients

In summary, although the subgroup effect may be real and there may be a mortality benefit with adjunctive corticosteroids restricted to those with severe pneumonia, established criteria for evaluating subgroup analyses suggest that the apparent effect is probably spurious (52, 53).

# La corticothérapie

Etude négative

## Low-dose corticosteroid use and mortality in severe community-acquired pneumonia patients



- **Pneumonie SANS choc**  
→ Aucune différence
- **Pneumonie AVEC choc**  
→ En faveur CTC  
Cohérent avec littérature

# La corticothérapie

Recommandations hors choc	Corticothérapie systémique
BTS (UK) 2009	NON
SPILF-SPLF (France) 2010	NA
SEPAR (Espagne) 2010	NA
SSID (Suède) 2017	NON (à discuter en Réa)
CTS-CMA (Chine) 2018	NON
SWAB-NVALT (Pays-Bas) 2018	NON
IDSA (USA) 2019	NON

# La corticothérapie

## *ClinicalTrials.gov*

### Community-Acquired Pneumonia : Evaluation of Corticosteroids (CAPE\_COD)

→ Pneumonies graves en Réanimation

ClinicalTrials.gov Identifier: NCT02517489

Recruitment Status ⓘ : Recruiting

Estimated Enrollment ⓘ : 1200 participants

Hydrocortisone will be given in a double-blind fashion for 8 or 14 full days.

Placebo will be given in a double-blind fashion for 8 or 14 full days.

Primary Outcome Measures ⓘ :

1. Day 28 all causes mortality [ Time Frame: at day 28 ]
2. Day 21 failure [ Time Frame: at day 21 ]

\* Amendement récent : On the sub-group of patients included with COVID19

Chapitre 3.

**Les virus**

# Pneumonies virales

## Viral pneumonia

*Olli Ruuskanen, Elina Lahti, Lance C Jennings, David R Murdoch*

About 200 million cases of viral community-acquired pneumonia occur every year—100 million in children and 100 million in adults. Molecular diagnostic tests have greatly increased our understanding of the role of viruses in pneumonia, and findings indicate that the incidence of viral pneumonia has been underestimated.

### Panel: Viruses linked to community-acquired pneumonia in children and adults

- Respiratory syncytial virus
- Rhinovirus
- Influenza A, B, and C viruses
- Human metapneumovirus
- Parainfluenza viruses types 1, 2, 3, and 4
- Human bocavirus\*
- Coronavirus types 229E, OC43, NL63, HKU1, SARS
- Adenovirus
- Enteroviruses
- Varicella-zoster virus
- Hantavirus
- Parechoviruses
- Epstein-Barr virus
- Human herpesvirus 6 and 7
- Herpes simplex virus
- Mimivirus
- Cytomegalovirus†
- Measles†

\*Mostly in children. †Mostly in developing countries.

# Pneumonies virales

Viral-bacterial coinfection affects the presentation and alters the prognosis of severe community-acquired pneumonia

Voiriot *et al. Critical Care* (2016) 20:375

**Table 2** Microbiological findings of 174 patients with severe CAP

Patients	All patients (n = 174)	Bacterial group (n = 46)	Viral group (n = 53)	Mixed group (n = 45)	No etiology group (n = 30)
<i>S. pneumoniae</i>	40 (23)	19 (41.3)	-	21 (46.7)	-
Other streptococci	6 (3.4)	2 (4.3)	-	4 (8.9)	-
<i>S. aureus</i>	12 (6.9)	6 (13)	-	6 (13.3)	-
<i>L. pneumophila</i>	8 (4.6)	7 (15.2)	-	1 (2.2)	-
<i>C. pneumoniae</i> – <i>M. pneumoniae</i>	6 (3.4)	5 (10.9)	-	1 (2.2)	-
<i>H. influenzae</i>	13 (7.5)	5 (10.9)	-	8 (17.8)	-
Enterobacteriaceae species	11 (6.3)	7 (15.2)	-	4 (8.9)	-
<i>P. aeruginosa</i>	7 (4)	2 (4.3)	-	5 (11.1)	-
Other bacteria	3 (1.7)	1 (2.2)	-	2 (4.4)	-
Mixed flora	10 (5.7)	6 (13)	-	4 (8.9)	-
Picornavirus (rhinovirus) <sup>a</sup>	22 (12.6)	-	7 (13.2)	15 (33.3)	-
Influenza A	32 (18.4)	-	19 (35.8)	13 (28.9)	-
Influenza B	6 (3.4)	-	4 (7.5)	2 (4.4)	-
Parainfluenza	3 (1.7)	-	2 (3.8)	1 (2.2)	-
Respiratory syncytial virus	9 (5.2)	-	5 (9.4)	4 (8.9)	-
Human metapneumovirus	12 (6.9)	-	6 (11.3)	6 (13.3)	-
Coronavirus	14 (8)	-	7 (13.2)	7 (15.6)	-
Adenovirus	3 (1.7)	-	2 (3.8)	1 (2.2)	-
Bocavirus	1 (0.6)	-	1 (1.9)	0 (0)	-
Cytomegalovirus	1 (0.6)	-	1 (1.9)	0 (0)	-
Herpes simplex virus	3 (1.7)	-	1 (1.9)	2 (4.4)	-
Varicella zoster virus	1 (0.6)	-	1 (1.9)	0 (0)	-

53%

# Pneumonies virales

Viral-bacterial coinfection affects the presentation and alters the prognosis of severe community-acquired pneumonia

Voiriot et al. *Critical Care* (2016) 20:375

**Table 3** Multivariate analysis of the risk factors for complicated course in 174 patients with severe CAP

Variables	OR	95 % CI	<i>p</i> value
Microbiological diagnosis			
Bacterial pneumonia	Ref	...	
Viral pneumonia	0.69	0.24–1.95	0.48
Mixed pneumonia	3.15	1.12–8.83	0.03
No etiology pneumonia	1.29	0.40–4.21	0.67
Coronary artery disease	3.52	1.22–10.15	0.02
Shock on ICU admission	4.63	1.56–13.74	0.006
Lactate dehydrogenase > 245 U/L	4.27	1.55–11.78	0.005
PSI class IV-V at hospital referral	4.67	1.96–11.12	0.0005

CAP community-acquired pneumonia, ICU intensive care unit, OR odds ratio, PSI Pneumonia Severity Index, Ref reference, 95 % CI = 95 % confidence interval

# Pneumonies virales

→ En dehors de la grippe : **Mythe ou réalité ?**

Colonisation vs infection ?

17-53% de virus selon les séries de Réanimation

Critical care management of adults  
with community-acquired severe respiratory  
viral infection

Yaseen M. Arabi<sup>1,2,3\*</sup>, Robert Fowler<sup>4,5,6</sup> and Frederick G. Hayden<sup>7</sup>

- « **Supportive care ICU** »
- Traitement antiviral : grippe
- Traitements adjuvants : aucune preuve, non recommandés (macrolides, CTC, COX2-i, Sirolimus, Statines, immunothérapie, vit C)

# Screening viral des PAC graves

- **Selon les techniques disponibles /labo**
- **PCR mutliplex**
  
- **Objectif thérapeutique /épidémique : grippe**
- **Objectif diagnostique/épidémiologique : autres virus**
  
- **Impact pronostique ?**
  - même pour le traitement antiviral de la grippe grave...?
- **Co-infections bactériennes**
  - 15-30% selon les séries

# Epidémies

- **Epidémies du 20<sup>ème</sup> et du 21<sup>ème</sup> siècles**

- grippe espagnole H1N1 en 1918-1919 ( $40 \cdot 10^6$  décès)

- grippe asiatique H2N2 en 1957-58 ( $2 \cdot 10^6$  décès)

- grippe de Hong-Kong H3N2 en 1968-69 ( $1 \cdot 10^6$  décès)

- grippe H1N1 – pdm2009 (Réa : jeune, femmes enceintes, obèses)

- SARS-CoV en 2002-03 (létalité 10%)

- MERS-CoV en 2012 (létalité 30%)

# Epidémies



du 21  
8-1919  
58 (2.  
1968-  
jeune  
10%)  
(%)



# Epidémies

- **Epidémies du 20<sup>ème</sup> et du 21<sup>ème</sup> siècles**

- grippe espagnole H1N1 en 1918-1919 ( $40 \cdot 10^6$  décès)

- grippe asiatique H2N2 en 1957-58 ( $2 \cdot 10^6$  décès)

- grippe de Hong-Kong H3N2 en 1968-69 ( $1 \cdot 10^6$  décès)

- grippe H1N1 – pdm2009 (Réa jeune, femmes enceintes, obèses)

- SARS-CoV en 2002-03 (létalité 10%)

- MERS-CoV en 2012 (létalité 30%)

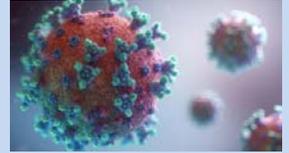
→ **Est-ce le vrai enjeu du 21<sup>ème</sup> siècle ? Le contrôle épidémique...**

→ **Co-infections bactériennes**

→ **Peu/pas de traitements / apparition de résistances ?**

# Le SARS-CoV2...

01/09/2020



© Fusion Medical Animation on Unsplash

## -Monde :



## -France :



# Le SARS-CoV2 en Soins critiques

	Auld (32452888) Crit Care 05/2020 N=217 - USA	Cummings (32442528) Lancet 06/2020 N=257 - NYC	Grasselli (32667669) JAMA Int Med 07/2020 N=3988 - Italie	Karagiannidis (32735842) Lancet Resp Med 07/2020 N= 1727- Allemagne
<b>Age *</b>	<b>64 ans</b> [54-73]	<b>62 ans</b> [51-72]	<b>63 ans</b> [56-69]	<b>71 ans</b> [60-79]
<b>Genre M</b>	55%	67%	80%	66%
<b>Ethnie « Noire »</b>	70%	19% (62% Hispanic)	NA	NA
<b>IMC* kg.m<sup>2</sup></b>	30 [26-35]	30,8 (7,7)	NA	Obésité 13%
<b>HTA</b>	62%	63%	41%	62%
<b>Diabète</b>	45%	36%	13%	39%
<b>IRC</b>	27%	14%	2%	24%
<b>Insuf cardiaque</b>	19%			30%
<b>CM ischémique</b>	14%	19%	13%	NA
<b>BPCO</b>	10%	9% (+PID)	2%	
<b>Asthme</b>	9%	8%	NA	19%

\* Mean (SD) or median [IQR]

# Le SARS-CoV2 en Soins critiques

	Auld (32452888) Crit Care 05/2020 N=217 - USA	Cummings (32442528) Lancet 06/2020 N=257 - NYC	Grasselli (32667669) JAMA Int Med 07/2020 N=3988 - Italie	Karagiannidis (32735842) Lancet Resp Med 07/2020 N= 1727- Allemagne
SOFA*	7 [5-11]	11 [8-13]	NA	NA
Délai admission Réa / symptômes*	NA	5 jours [2-7]	10 jours [6-14]	NA
VM invasive Durée de VM*	76% 9 jours [4-13]	79% 18 jours [9-28]	87% 10 jours [6-17]	100% 10 jours [4,3-19,3]
Catécholamines	66%	66%	NA	NA
EER	29%	31%	NA	27%
NO inhalé	10%	11%	NA	NA
DV / ECMO	NA / 2% (0% décès)	17% / 3%	NA / 1,7% (60% décès)	NA / 7%
Durée séjour Réa*	9 jours [5-15]	NA	12 jours [6-21]	NA
Durée séjour H*	15 jours [9-24]	NA	28 jours [15-48]	21 jours [10-37]
<b>Mortalité Réa</b>	<b>29%</b> (-14)	NA	<b>44%</b> (-91)	NA
<b>Mortalité H</b>	<b>32%</b> (-19)	<b>39%</b> (-94)	<b>48%</b> (-501)	<b>53%</b>

\* Mean (SD) or median [IQR]

# Le SARS-CoV2 en Soins critiques

Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study

	Univariable HR (95% CI)	Multivariable HR (95% CI)
Age (per 10-year increase)	1.49 (1.29-1.73)	1.31 (1.09-1.57)
Male sex	0.85 (0.57-1.27)	1.13 (0.71-1.81)
Symptom duration before hospital presentation (per day)	0.98 (0.93-1.02)	1.01 (0.96-1.05)
Hypertension	2.24 (1.40-3.59)	1.58 (0.89-2.81)
Chronic cardiac disease*	2.21 (1.44-3.39)	1.76 (1.08-2.86)
Chronic obstructive pulmonary disease or interstitial lung disease	3.15 (1.84-5.39)	2.94 (1.48-5.84)
Chronic kidney disease	1.50 (0.92-2.45)	..
Diabetes	1.65 (1.11-2.44)	1.31 (0.81-2.10)
Body-mass index $\geq 40$	0.76 (0.40-1.47)	..
Interleukin-6 (per decile increase)	1.12 (1.04-1.21)	1.11 (1.02-1.20)
D-dimer (per decile increase)	1.18 (1.10-1.27)	1.10 (1.01-1.19)

HR=hazard ratio. \*Coronary artery disease or congestive heart failure.

**Table 4: Risk factors for in-hospital mortality**

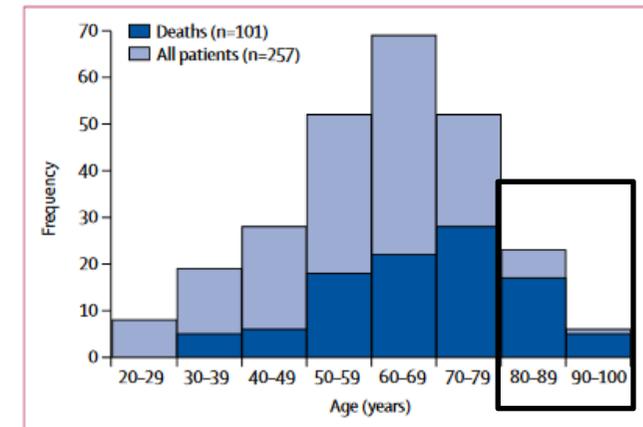
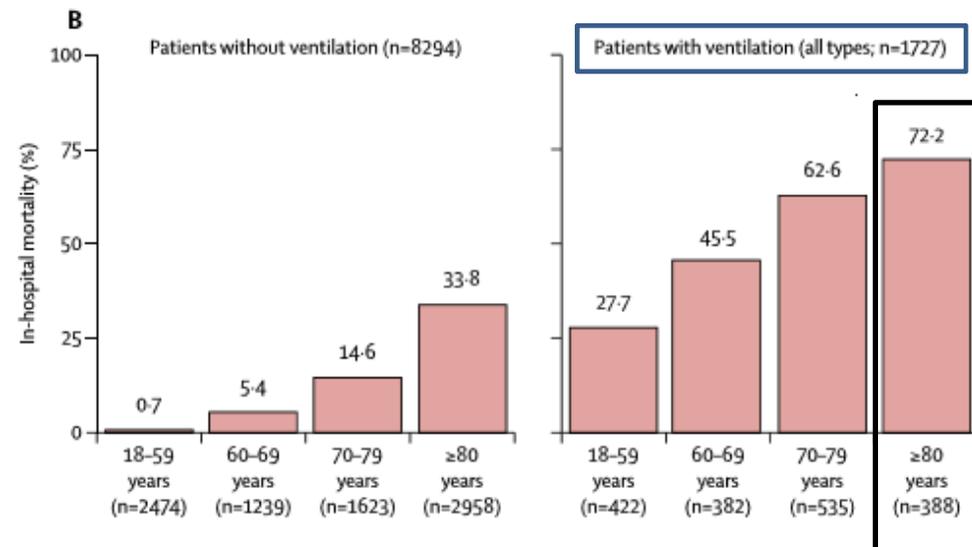


Figure 2: Age distribution of critically ill patients with COVID-19

# Le SARS-CoV2 en Soins critiques

Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study



Christian Karagiannidis

Lancet Respir Med 2020

Published Online

July 28, 2020

# Le SARS-CoV2 au CHV



Cohorte française **COVID-ICU** en cours...  
Environ **1100** /4500 patients

- En Réa au CHV :
    - 104 pneumonies à *Pneumocoque* en 8 ans
    - 101 *Grippes* grave en 5 ans
    - **101** COVID-19 en 2 mois...
- 20 lits de réa + 8 lits d'USC  
→ 43 lits de Réa + 6 lits USI pour le SARS-CoV2

# Le SARS-CoV2 au CHV

Tableau 1. Caractéristiques patients Soins Critiques SARS-CoV2 au CHV		
N = 101	N(%) ou Médiane [IQ]	Range
Âge (années)	62 [54-73]	21-88
Sexe masculin	72 (71,3%)	
Tabagisme actif / sevré	5 (5%) / 29 (28,7%)	
Indice de Masse Corporelle (cm/kg2)	27,8 [24,8-32]	17-54,3
<b>Comorbidités</b>		
Cardiopathie ischémique	8 (7,9%)	
HTA	48 (47,5%)	
Diabète	25 (24,8%)	
Immunodépression	9 (8,9%)	
Obésité (IMX > 30)	36 (35,6%)	
BPCO/Asthme/DBD	15 (14,9%)	
Aucune	35 (34,7%)	
<b>Provenance</b>		
SAMU	8 (7,9%)	
SAU	38 (37,6%)	
Salle CHV	42 (41,6%)	
Extérieur (SAU, salle, Réa)	13 (12,9%)	
<b>Données Réa</b>		
Délai admission Réa /symptômes	9 [7-12]	1-20
Délai admission Réa / hospitalisation	1 [0-3]	0-17
IGS2	39 [34-47]	6-91
Co-infection pulm. Initiale à l'admission en Réa	5 (5,8%)	
Catécholamines	81 (80,2%)	
EER	14 (13,9%)	
<b>Données bio admission en Réa avec n(%)</b>		
Lactate (mmol/L), n = 101 (100%)	1,4 [1,2-2]	0,28-10,7
LDH (UI/L), n = 99 (98%)	802 [644-1073]	296-1699
Lymphocytes (G/L), n = 100 (99%)	0,8 [0,5-1]	0,21-5,11
PCT (ng/mL), n = 71 (70,3%)	0,4 [0,2-1]	0,06-61,33
Créatininémie (µmol/L), n = 101 (100%)	71 [59-93]	28-523
Troponine (ng/mL), n = 79 (78,2%)	0,013 [0,009-0,024]	0,003-1,37
NT-proBNP (pg/mL), n = 39 (38,6%)	455 [137-1097]	30-8535

Tableau 2. Données ventilatoires et outcome Soins Critiques SARS-CoV2 CHV		
N = 101	N(%) ou Médiane [IQ]	Range
<b>Données ventilatoires Soins Critiques</b>		
VS (N = 17)	succès	7 (41,2%)
	échecs (IOT > 24h de VS en Réa)	10 (58,8%)
VNI (N = 2)	succès	1 (50%)
	échecs (IOT)	1 (50%)
ONHD (N=21)	succès (dont 3 enUSIC)	7 (33,3%)
	échecs (dont 2 hors CHV) (IOT)	14 (66,7%)
VM invasive		86 (85,1%)
<b>Données ventilatoires sous VM invasive</b>		
Délai IOT en Réa (jours)		0 (0-0)
Décub. ventral	nb patients avec au moins 1 séance	52 (60,5%)
	nb séances / patient ayant eu du DV	4 (3-8)
Administration de NO inhalé chez intubés		13 (15,1%)
Recours ECMO chez intubés		6 (7%)
Réintubations chez intubés		14 (16,3%)
Trachéotomie sevrage chez intubés		14 (16,3%)
Nb patients avec PAVM chez intubés		41 (47,7%)
Rescue CTC et délai / admission Réa (jours)		17 (19,8%) - 13 [9-23]
Durée de ventilation chez intubés (jours)		20 [11,5-33]
<b>Outcome Soins critiques</b>		
Durée séjour (is)	Réa	19 [12-36]
	hospi post Réa (hors SSR)	9 [6,8-12]
	SSR	26 [16,3-40]
Mortalité en Réa		25 (24,8%)
Mortalité Réa chez ventilés (VM invasive), n = 86		24 (27,9%)
Mortalité Réa /âge < 40 ans, n =3		0 (0%)
	40-49 ans, n =14	2 (14,3%)
	50-59 ans, n = 26	3 (11,5%)
	60-69 ans, n = 22	3 (13,6%)
	70-79 ans, n = 28	9 (32,1%)
	≥ 80 ans, n = 8	8 (100%)
Mortalité Réa > 65 ans, n = 40		15 (37,5%) = 68% des décès de Réa

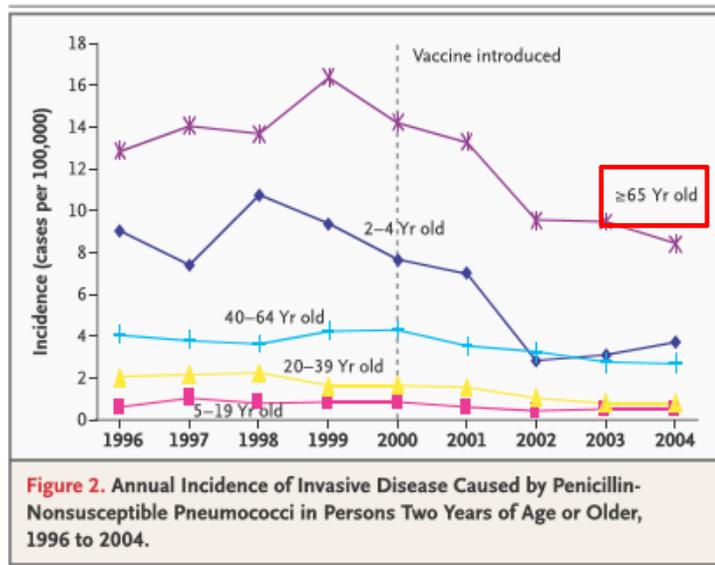
Chapitre 4.

**Perspectives**

# Facteurs d'influence sur la mortalité

## -Rôle de la vaccination

Effect of Introduction of the Pneumococcal Conjugate Vaccine on Drug-Resistant *Streptococcus pneumoniae*



« Herd immunity »

Moe H. Kyaw,  
N Engl J Med 2006;354:1455-63.

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults = CAPITA study

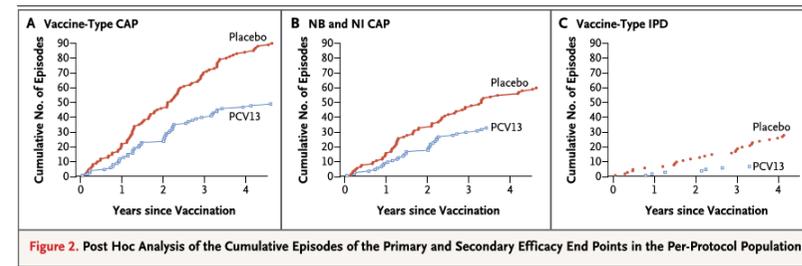


Table 3. Safety Outcomes.\*

Event	Safety Subgroup		All Participants		P Value†
	PCV13 (N=1006)	Placebo (N=1005)	PCV13 (N=42,237)	Placebo (N=42,255)	
Death			3006 (7.1)	3005 (7.1)	0.98

M.J.M. Bonten,  
N Engl J Med 2015;372:1114-25.

# Facteurs d'influence sur la mortalité

-Rôle de la vaccination

**-Rôle des campagnes d'information/sensibilisation**

World Sepsis Day



# Facteurs d'influence sur la mortalité

- Rôle de la vaccination
- Rôle des campagnes d'information/sensibilisation (World SD)

## -Suivi/adhésion des recommandations



British Thoracic Society

National Audit Report: Adult Community Acquired Pneumonia Audit 2018-2019

National Audit Period: 1 December 2018 – 31 January 2019

Professor Wei Shen Lim and Dr Hannah Lawrence

### National Improvement Objectives:

1. Demonstrate continued improvement in the proportion of adults with CAP who receive the first dose of antibiotic therapy within 4 hours of admission. (Target in 3 years: 85%)
2. Demonstrate improvement in the proportion of adults with high severity CAP administered combination  $\beta$ -lactam and macrolide antibiotic therapy. (Target in 3 years: 85%)
3. Demonstrate an improvement in the proportion of coded cases of pneumonia, who have CXR confirmed pneumonia. (Target in 3 years: 85%)

Timeframe: to be achieved by the next re-audit

# Facteurs d'influence sur la mortalité

- Rôle de la vaccination
- Rôle des campagnes d'information/sensibilisation (World SD)
- Suivi/adhésion des recommandations (audit BTS)

## **-En Réanimation**

- \* Suivi/adhésion des recommandations « sepsis/choc »
- \* Amélioration des modalités de VM invasive « SDRA »

Surviving Sepsis Guidelines  
A Continuous Move Toward Better Care of Patients  
With Sepsis

An Official American Thoracic Society/European Society of Intensive  
Care Medicine/Society of Critical Care Medicine Clinical Practice  
Guideline: Mechanical Ventilation in Adult Patients with Acute  
Respiratory Distress Syndrome

## Et dans le reste du monde ?

- **Intérêt majeur dans les pays dits « émergents »**
  - campagnes d'information
  - campagnes de vaccination
  - accès aux soins / aux ATB

- **On estime que la pneumonie cause 15% du nombre total de décès d'enfants de moins de 5 ans. 922 136 enfants de moins de 5 ans sont morts de pneumonie en 2015.**

# Enjeu = futures épidémies virales ?

- **Moyens de contrôle ?**
  - flux humains / économie-tourisme
  - flux animaliers / agriculture
  - impact écologique sur les maladies épidémiques
  
  - système de vigilance / d'alerte sanitaire
  - coopération mondiale
  - vitesse de réactivité / mise en place du contrôle
  - anticipation / surveillance

# L'avenir ?

1. **Antiviraux / Vaccination**
2. **Diagnostic : écho pulmonaire / tests rapides ?**
3. **Encore mieux faire / recommandations – ATB précoces !**
4. **Traitements adjuvants des PAC graves**  
-anti-inflammatoires : Corticoïdes ?  
-immunomodulateurs, à suivre
5. **Alternatives à la VM invasive ?**  
**Oxygénothérapie à haut débit... à suivre (SARS-CoV2 ?)**
6. **Traitement optimisé /personnalisé en Réanimation**  
**Choc septique / SDRA / PK-PD / immunopathologie**

*ClinicalTrials.gov*

47 Studies found for: **High flow oxygen** |  
**Pneumonia**

685 Studies found for: **septic shock**

1040 Studies found for: **ARDS** | **Adult,**