Pneumopathies aiguës communautaires (PAC): Les actualités de l’année

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Hôpital Pontchaillou, CHU Rennes
Liens d’Intérêt 2013-2015

• Consultant ou membre d’un conseil scientifique
  Basiléa, The Medicines company, Janssen & Janssen, AstraZeneca, Astellas

• Orateur rémunéré
  AstraZeneca, Astellas, Gilead, MSD

• Subventions pour congrès
  MSD, Pfizer, Janssen & Janssen, AstraZeneca, Astellas
Actualités: ‘Ce qu’on a appris sur les PAC en 2015’

- Epidémiologie
- Prévention
- Stratégies thérapeutiques

NB. Corticoïdes/PAC & Grippe exclus
Middle East Respiratory Syndrome-Coronavirus (MERS-CoV)

- 2012-2015: 1611 cas => 575 décès (35%)
- Y penser si pneumopathie retour péninsule Arabique (< 14 j)
  - Surtout adultes (30-60 ans), hommes
  - Contacts hospitaliers (ou dromadaires)

**Objectifs:** Mettre ‘à jour’ l’épidémiologie des PAC hospitalisées
- Tests diagnostiques ‘modernes’ (PCR, virus)
- Impact de la vaccination systématique des enfants (PCQ conjugué)

**Méthodes:**
- 5 Hôpitaux US (Chicago, Nashville), 2010-2012
- Recrutement actif (18 h/j, 7/7) des PAC hospitalisées
- Tests sang, urine, ECBC, naso/oropharynx, PCR, sérologies (J0, S3-S10)
- Contrôles (hospitalisés sans fièvre ni signe respiratoire)
1. L’adulte

Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults

S. Jain, W.H. Self, R.G. Wunderink, S. Fakhran, R. Balk, A.M. Bramley, C. Reed,

- **Critères inclusions:**
  1. Signe(s) infectieux +
  2. Signe(s) respiratoire(s) aigu(s) +
  3. Anomalies radiologiques confirmées par radiologue thoracique

- **Critères exclusions:**
  - Hospitalisation récente
  - Long séjour
  - Immunodéprimés lourds (VIH CD4 < 200, greffe < 3 mois, neutropénie)

Table 1. Characteristics of Adults with Community-Acquired Pneumonia Requiring Hospitalization.

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<th>Characteristic</th>
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<td>18–49 yr</td>
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<td>517 (22)</td>
</tr>
<tr>
<td>≥80 yr</td>
<td>315 (14)</td>
</tr>
<tr>
<td>Any underlying condition — no. (%)‡</td>
<td>1817 (78)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>968 (42)</td>
</tr>
<tr>
<td>Chronic heart disease</td>
<td>810 (35)</td>
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<tr>
<td>Immunosuppression</td>
<td>685 (30)</td>
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<tr>
<td>Diabetes mellitus</td>
<td>597 (26)</td>
</tr>
<tr>
<td>Status regarding receipt of vaccine or treatment — no./total no. (%)§</td>
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<td>Seasonal influenza vaccination</td>
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<tr>
<td>Pneumococcal vaccination in adults ≥65 yr of age</td>
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<td>Radiographic finding — no. (%)¶</td>
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<tr>
<td>Consolidation</td>
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<td>Alveolar or interstitial infiltrate</td>
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Epidémiologie des PAC  

1. L’adulte

Specific Pathogens Detected

- Patients with a Positive Result (%)
- Viral pathogen only (22%)
- Viral-viral co-detection (2%)
- Bacterial-viral co-detection (3%)
- Bacterial pathogen only (11%)
- Fungal or mycobacterial detection (1%)

No pathogen detected (62%)

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<thead>
<tr>
<th>Pathogen</th>
<th>Patients with Positive Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human rhinovirus</td>
<td>194</td>
</tr>
<tr>
<td>Influenza A or B</td>
<td>132</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>115</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>88</td>
</tr>
<tr>
<td>Respiratory synciyal virus</td>
<td>68</td>
</tr>
<tr>
<td>Parainfluenza virus</td>
<td>67</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>53</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>43</td>
</tr>
<tr>
<td>S. aureus</td>
<td>37</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>32</td>
</tr>
<tr>
<td>Legionella pneumophila</td>
<td>32</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>31</td>
</tr>
<tr>
<td>Other</td>
<td>74</td>
</tr>
</tbody>
</table>

**Épidémiologie des PAC**

1. L’adulte

**Graphique**: Distribution des pathogènes spécifiques détectés.

- **Patients with a Positive Result (%):**
  - Copathogen
  - Single pathogen

**Pathogènes détectés**:
- Virus pathogen only (22%)
- Viral-viral co-detection (2%)
- Bacterial-viral co-detection (3%)
- Bacterial pathogen only (11%)
- Fungal or mycobacterial detection (1%)

**Pathogènes spécifiques détectés**:
- Human rhinovirus
- Influenza A or B
- *S. pneumoniae*
- Human metapneumovirus
- Respiratory syncytial virus
- Parainfluenza virus
- Coronavirus
- *Mycoplasma pneumoniae*
- *S. aureus*
- Adenovirus
- *Legionella pneumophila*
- Enterobacteriaceae
- Other

Epidémiologie des PAC  

1. L’adulte

Specific Pathogens Detected

- Patients with a Positive Result (%)
  - 194
  - 132
  - 115
  - 88
  - 68
  - 67
  - 53
  - 43
  - 37
  - 32
  - 32
  - 31
  - 74

- Copathogen
- Single pathogen

- Viral pathogen only (22%)
- Viral–viral co-detection (2%)
- Bacterial–viral co-detection (3%)
- Bacterial pathogen only (11%)
- Fungal or mycobacterial detection (1%)

- Human rhinovirus
- Influenza A or B
- S. pneumoniae
- Human metapneumovirus
- Respiratory syncytial virus
- Parainfluenza virus
- Coronavirus
- Mycoplasma pneumoniae
- S. aureus
- Adenovirus
- Legionella pneumophila
- Enterobacteriaceae
- Other

Pathogens Detected, According to Month and Year

All causes of pneumonia

- Human rhinovirus
- Influenza A or B
- Human metapneumovirus
- Respiratory syncytial virus
- S. pneumoniae
- S. aureus
Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults
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• **Et les PAC graves ?** => 3 pathogènes sur-représentés
  – Pneumocoque (8%)
  – *S. aureus* (5%)
  – Entérobactéries (3%)

• **Conclusions: la vraie épidémiologie des PAC (USA, 2010-12)**
  – Rhinovirus = pathogène n°1 (tout âge), **27% des PAC documentées !**
  – Rarement retrouvé chez les contrôles (2%)
  – Pneumocoque ‘minoritaire’ (5% des PAC de l’adulte)
# Community-Acquired Pneumonia Requiring Hospitalization among U.S. Children

Seema Jain, M.D., Derek J. Williams, M.D., M.P.H., Sandra R. Arnold, M.D.,

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Children with Radiographic Evidence of Pneumonia (N=2358)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group — no. (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;2 yr</td>
<td>1055 (45)</td>
</tr>
<tr>
<td>2–4 yr</td>
<td>595 (25)</td>
</tr>
<tr>
<td>5–9 yr</td>
<td>422 (18)</td>
</tr>
<tr>
<td>10–17 yr</td>
<td>286 (12)</td>
</tr>
<tr>
<td>Radiographic finding — no. (%) †</td>
<td></td>
</tr>
<tr>
<td>Consolidation</td>
<td>1376 (58)</td>
</tr>
<tr>
<td>Alveolar or interstitial infiltrate</td>
<td>1195 (51)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>314 (13)</td>
</tr>
<tr>
<td>Intensive care unit admission — no. (%)</td>
<td>497 (21)</td>
</tr>
<tr>
<td>Invasive mechanical ventilation — no. (%)</td>
<td>166 (7)</td>
</tr>
<tr>
<td>Death in the hospital — no. (%)</td>
<td>3 (&lt;1)</td>
</tr>
</tbody>
</table>
Epidémiologie des PAC

2. L’enfant

Chaque barre représenterait la proportion de patients testés et ayant un résultat positif pour le pathogène mentionné.

Pathogen Detected

- **RSV**: 622 patients
- **HRV**: 606 patients
- **HMPV**: 285 patients
- **AdV**: 248 patients
- **M. pneumoniae**: 178 patients
- **P1V**: 151 patients
- **Flu**: 149 patients
- **CoV**: 110 patients
- **S. pneumoniae**: 79 patients
- **Other**: 81 patients

Epidémiologie des PAC  2. L’enfant

Epidémiologie des PAC  2. L’enfant

NB: Couverture vaccinale PCQ conjugué 3 doses (19 Mo) = 87%
Epidémiologie des PAC  

2. L’enfant

2. L’enfant

Epidémiologie des PAC

Graphique montrant l'épidémiologie des PAC, avec des ondes de fréquences élevées de RSV, HMPV et Adenovirus.
Prévention des PAC => Vaccin PCQ conjugué après 65 ans

- **Rationnel**
  - Vaccin PCQ conjugué + efficace que le PS chez enfants et IDP
  - Sujet âgé = FDR d’infection invasive à PCQ / IDP ⇔ âge

- **Méthodes**
  - Essai randomisé, double aveugle, PCV13 vs. placebo, n > 82 000
  - Âge > 65 ans, suivi moyen 4 ans (2008-2013)
  - Test Ag U PCQ avec diagnostic de sérotype
Prévention des PAC => Vaccin PCQ conjugué après 65 ans

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<th>End Point and Analysis</th>
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<td>1534</td>
<td>747</td>
<td>787</td>
<td>5.1 (-5.1 to 14.2)</td>
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<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From confirmed vaccine-type pneumococcal community-acquired pneumonia or vaccine-type invasive pneumococcal disease</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>0 (-1279.6 to 92.8)</td>
</tr>
<tr>
<td>From confirmed pneumococcal community-acquired pneumonia or invasive pneumococcal disease</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>14.3 (-197.9 to 76.2)</td>
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Bons résultats
- **Efficacité vaccinale** sur les pneumonies à PCQ de sérotype vaccinal = 46% (22-62%) (P<0,001)
- **Efficacité vaccinale** sur les infections invasives à PCQ de sérotype vaccinal = 75% (41-91%) (P<0,001)
- Pas de réduction d’efficacité jusqu’à 4 ans
- Tolérance OK (n=42 240)

Moins bons
- Pas d’impact sur l’incidence des PAC, ni sur le décès
- Il faut vacciner 1030 sujets pour éviter une PAC en 4 ans, et 2050 sujets pour éviter une infection invasive à PCQ
Prévention des PAC => Vaccin PCQ conjugué après 65 ans

• L’efficacité du PCV13
  – Nourrissons tous vaccinés aux Pays-Bas depuis 2006
  – Effet ‘troupeau’
  – Baisse d’incidence des PAC à PCQ de sérotype vaccinal

• Polémique sur son prix
  – 55 € en France
  – 150 USD aux USA
  – 10 USD les 3 doses dans les PED

Antibiothérapie des PAC

- **Objectifs:** Comparaison de 3 ‘stratégies’ d’ATB empirique
  - Bêta-lactamine
  - Bêta-lactamine + macrolide
  - Fluoroquinolone

- **Méthodes:** Essai ‘pragmatique’
  - Adultes, PAC => hospitalisation (pas en réanimation)
  - Critère principal = mortalité J90
  - Etude non-infériorité (marge IC90 < 3%)

Antibiothérapie des PAC

- Randomisation en cluster (à l’échelle de l’hôpital) avec cross over

• Résultats:
  – PCQ (16%), *H. influenzae* (7%), atypiques (2%)
Antibiothérapie des PAC

• Résultats:
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Table 2. Baseline Characteristics of Patients in the Intention-to-Treat Population.*

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<th>Beta-Lactam (N=656)</th>
<th>Beta-Lactam–Macrolide (N=739)</th>
<th>Fluoroquinolone (N=888)</th>
</tr>
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<tr>
<td>Median age (interquartile range) — yr</td>
<td>70 (60–79)</td>
<td>70 (59–80)</td>
<td>71 (59–79)</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>381 (58.1)</td>
<td>431 (58.3)</td>
<td>505 (56.9)</td>
</tr>
<tr>
<td>Median duration of symptoms (interquartile range) — days</td>
<td>3 (1–7)</td>
<td>3 (1–7)</td>
<td>3 (1–7)</td>
</tr>
<tr>
<td>Received antibiotics before admission — no./total no. (%)</td>
<td>219/637 (34.4)</td>
<td>227/721 (31.5)</td>
<td>303/873 (34.7)</td>
</tr>
<tr>
<td>Current smoker — no./total no. (%)</td>
<td>109/627 (17.4)</td>
<td>154/723 (21.3)</td>
<td>196/872 (22.5)</td>
</tr>
<tr>
<td>Past smoker — no./total no. (%)</td>
<td>379/627 (60.4)</td>
<td>398/723 (55.0)</td>
<td>490/872 (56.2)</td>
</tr>
<tr>
<td>Received influenza vaccination — no./total no. (%)</td>
<td>453/624 (72.6)</td>
<td>466/700 (66.6)</td>
<td>572/847 (67.5)</td>
</tr>
<tr>
<td>Received pneumococcal vaccination — no./total no. (%)</td>
<td>16/594 (2.7)</td>
<td>18/671 (2.7)</td>
<td>13/822 (1.6)</td>
</tr>
<tr>
<td>PPSV23</td>
<td>19/656 (2.9)</td>
<td>7/739 (0.9)</td>
<td>10/888 (1.1)</td>
</tr>
<tr>
<td>PCV13</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Respect des consignes de randomisation

- **BL:**
  - amox/clav 48%
  - amox 30%
  - ceftriaxone 20%

- **Macrolides:**
  - érythro 35%
  - clarithro 30%
  - azithro 25%

- **FQ:**
  - moxiflo 60%
  - lévoflo 25%
Antibiothérapie des PAC

• Résultats:
  – Non-infériorité démontrée de la monothérapie BL

Antibiothérapie des PAC

• Résultats:
  – Analyses de sensibilité
Antibiothérapie des PAC

• Résultats:

  – Selon sévérité

<table>
<thead>
<tr>
<th>Level of Risk</th>
<th>Beta-Lactam</th>
<th>Beta-Lactam Macrolide</th>
<th>Fluoroquinolone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adherence</td>
<td>Mortality</td>
<td>Adherence</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>no./total no. (%)</td>
<td>%</td>
</tr>
<tr>
<td>CURB-65 score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2</td>
<td>72.5</td>
<td>45/562 (8.0)</td>
<td>73.4</td>
</tr>
<tr>
<td>&gt;2</td>
<td>64.1</td>
<td>14/92 (15.2)</td>
<td>69.2</td>
</tr>
<tr>
<td>PSI risk class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I or II</td>
<td>65.1</td>
<td>3/194 (1.5)</td>
<td>73.6</td>
</tr>
<tr>
<td>III or IV</td>
<td>74.5</td>
<td>41/415 (9.9)</td>
<td>73.6</td>
</tr>
<tr>
<td>V</td>
<td>68.9</td>
<td>15/45 (33.3)</td>
<td>55.9</td>
</tr>
</tbody>
</table>

Table 1. Antibiotic Adherence and 90-Day Mortality for CURB-65 and PSI Risk Strata.*
• Conclusions
  
  – Pour les adultes avec PAC nécessitant une hospitalisation (hors réa)
  – La monothérapie par BL fait au moins aussi bien que BL + M, ou FQ ‘anti-pneumococciques’
  – Y compris formes graves (PSI V ou CURB-65 > 2)
Actualités PAC 2015: Conclusions

• Epidémiologie
  – **Rhinovirus**: net 1er chez l’adulte, 1er ex-aequo (avec VRS) chez l’enfant
  – Le **PCQ en perte de vitesse**: 5% des PAC de l’adulte (enfant 3%)
  – **M. pneumoniae**: 8% (enfant), 2% (adulte)
  – **C. pneumoniae**: une blague ?

• Vaccin conjugué PCV13 c/o âge > 65 ans
  – **Efficacité vaccinale 46%** sur PCQ sérotypes vaccinaux (**13% des PAC**)

• Traitement PAC adultes hospitalisés hors réa
  – Monothérapie amox ou amox/clav
• Merci de votre attention !