Institut Maurice Rapin

CNR des IST bactériennes

Epidémiologie et caractéristiques microbiologiques de l'épidémie à *Mycoplasma pneumoniae*

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CHU BDX CENTRE HOSPITALIER UNIVERSITAIRE BORDEAUX

cnrs

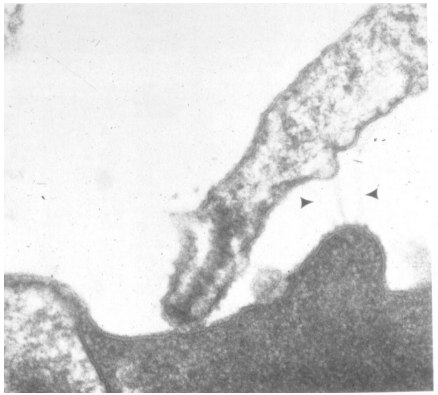
université de BORDEAUX

Conflict of interest disclosure

☑ I have no potential interest to declare

Mycoplasma pneumoniae infections (1)

- **Children+++ and young adults**
- **1st cause of bacterial CAP in children (10-45%)**
- **RTI +++**
  - **Atypical pneumonia (20%)**
  - **Tracheo-bronchitis (80%)**
  - **Asthma ?**
- **Extrarespiratory diseases**
  - **Cutaneous**
    - ✓Skin rash, exanthema, MIRM, Stevens Johnson syndrome
  - **Rheumatologic, cardiac, hematologic**
  - **Neurologic**
    - ✓Meningoencephalitis, peripheral neuropathy, Guillain Barré sd, etc.



***M. pneumoniae* with respiratory epithelial cells (tip adhesion organelle)**

Waites et *al*. Clin Microbiol Rev. 2017

Mycoplasma pneumoniae infections (2)

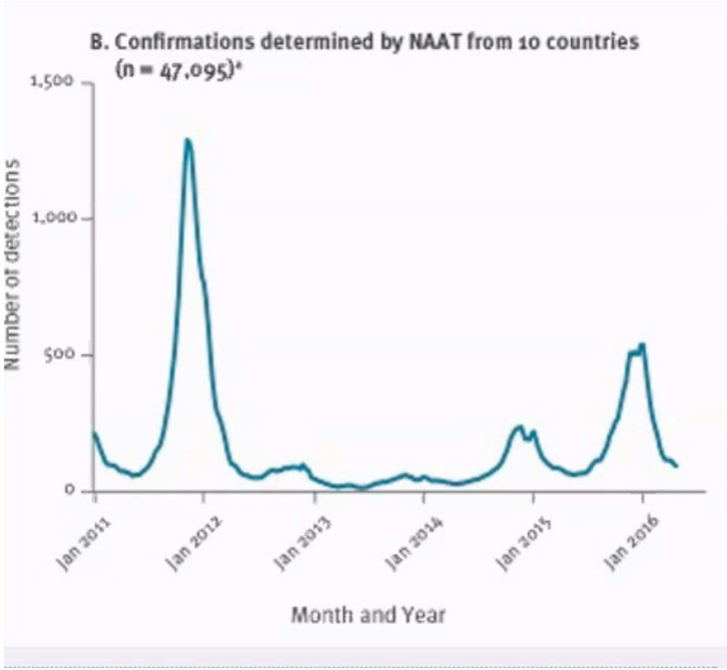
➢ **Extra-respiratory forms:**

- **25 % of infected individuals** (with or without respir. sd)
- **Before or after respiratory syndroms**
- **Autoimmune reactions** (antigenic homology between MP adhesins and eukariotic cell antigens)

- **Asymptomatic carriage, up to 4 months**
  (Spuesens et al, PLoS Med 2013)

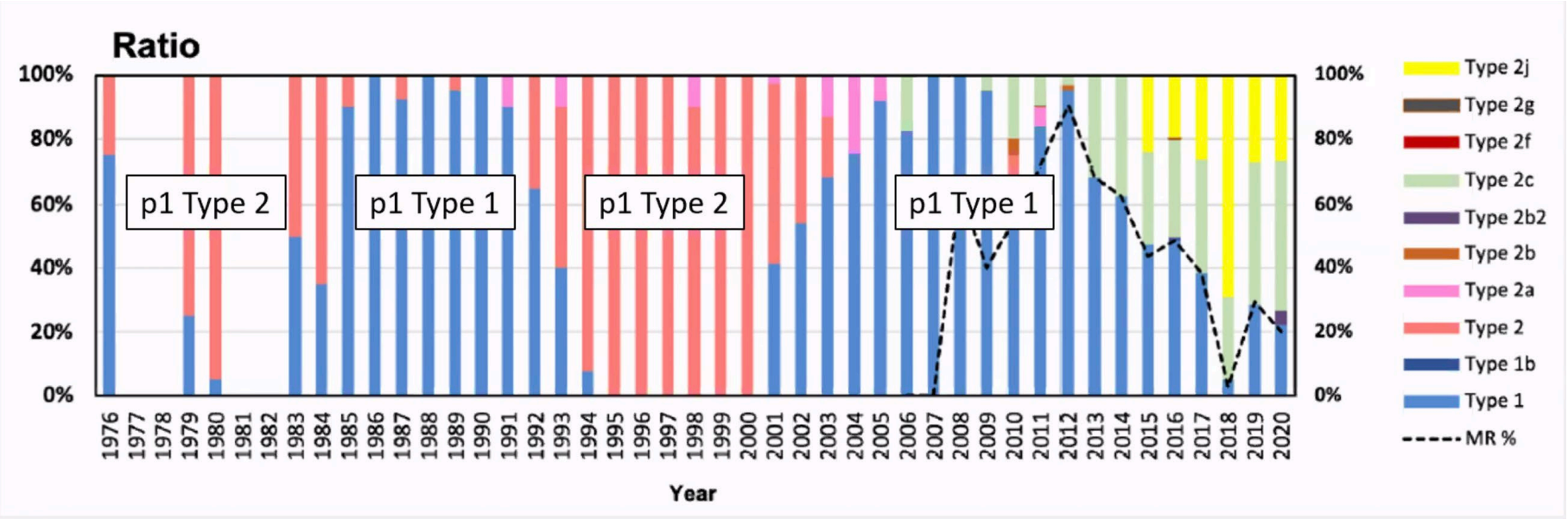
M. pneumoniae epidemiology

- **Endemic with surges**
  - Every 3 to 7 years, lasting ≈18 months
  - 2010-2012 increase in the incidence of Mp infections worldwide
  - Short-course immunity (antigenic variations of the P1 adhesin)



Beeton et al, Euro Surv 2020

P1 adhesin changes over time

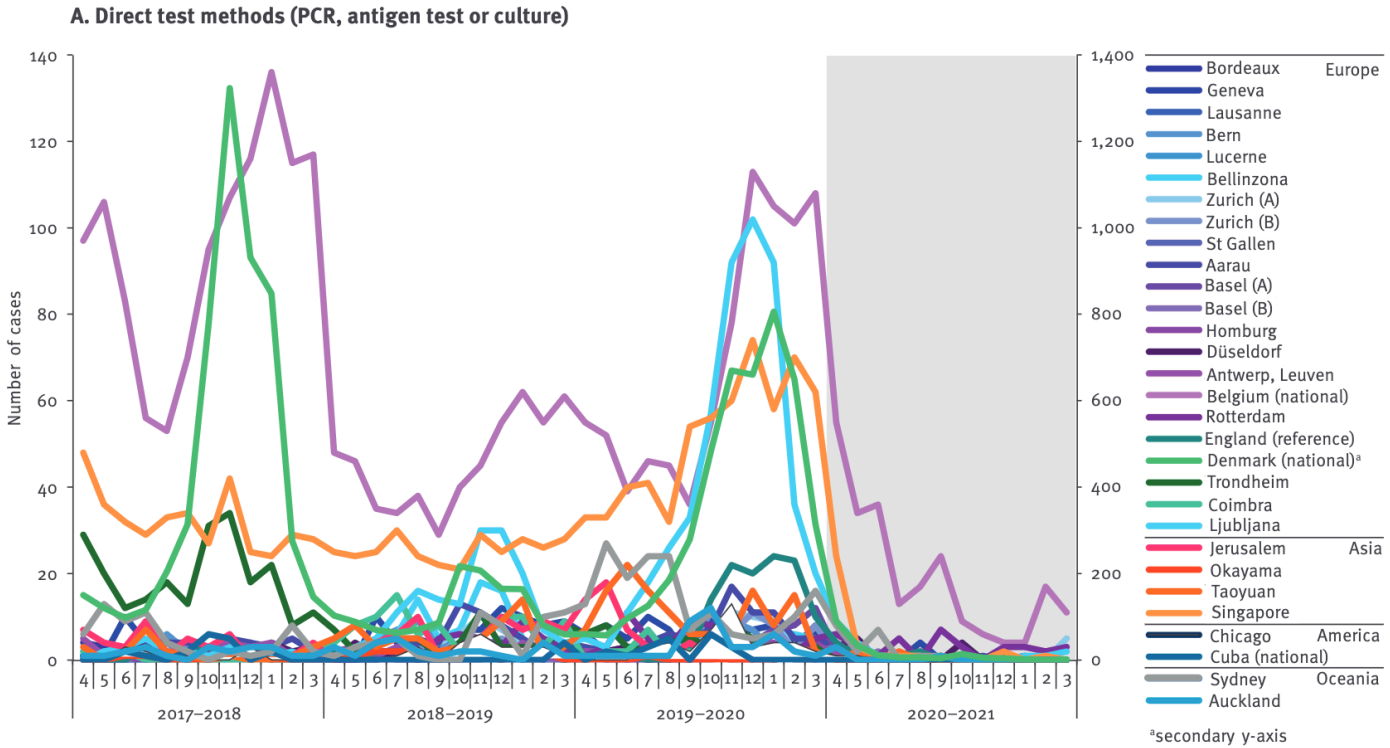


Kenri et al, Front Microbiol 2023

M. pneumoniae epidemiology: 2017-2021

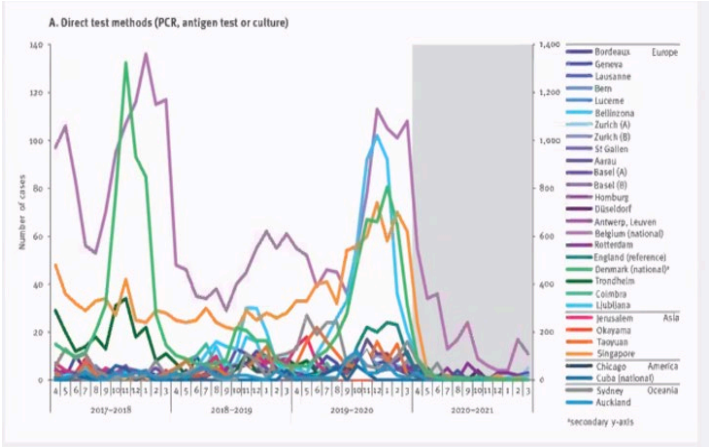
FIGURE 2

Global detection of *Mycoplasma pneumoniae*, April 2017–March 2021 (n = 30,617)



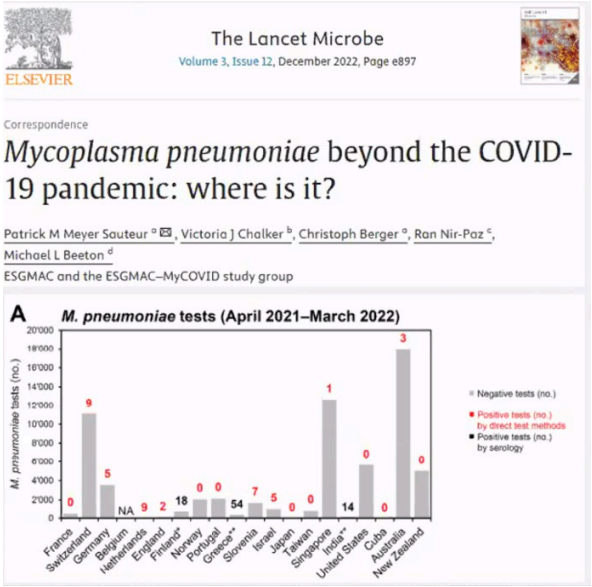
Meyer Sauteur et al, Lancet Microbe 2022

Impact of non-pharmaceutical interventions (NPS) on *M. pneumoniae* epidemiology: 2020-2022



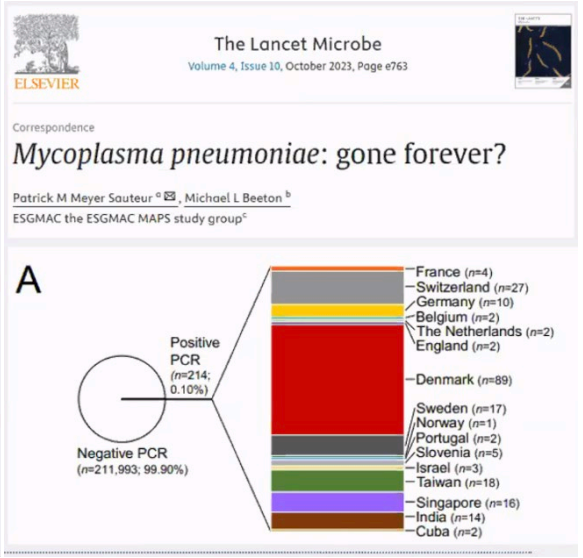
Meyer Sauteur et al, Euro Surv 2022

1st year after NPIs



Meyer Sauteur et al, Lancet Microbe 2022

2nd year after NPIs



Meyer Sauteur et al, Lancet Microbe 2023

3rd year after NPIs

Health warning

World Health Organization

Health Topics | Countries | Newsroom | Emergencies

Home / News / WHO statement on reported clusters of respiratory illness in children in northern China

WHO statement on reported clusters of respiratory illness in children in northern China

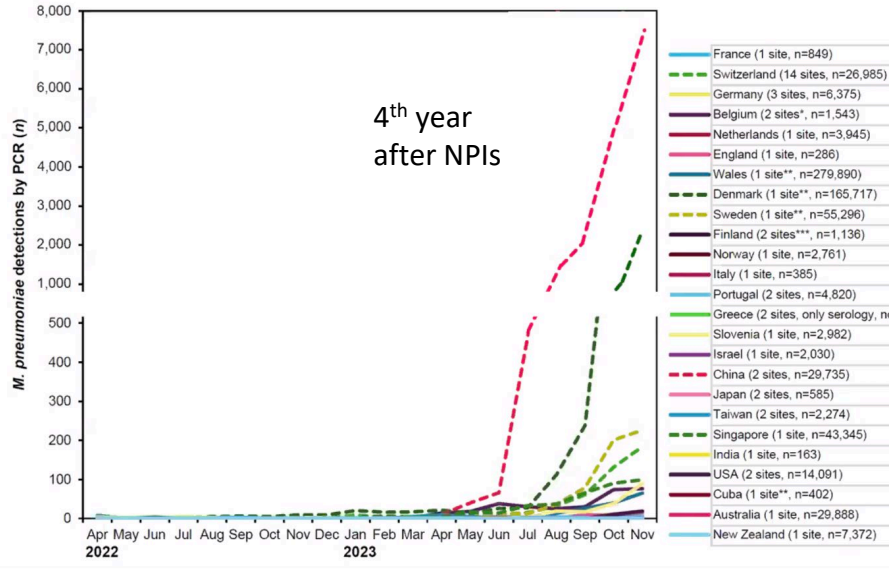
22 November 2023 | Statement | Geneva, Switzerland |Reading time: 1 min (342 words)

WHO has made an official request to China for detailed information on an increase in respiratory illnesses and reported clusters of pneumonia in children.

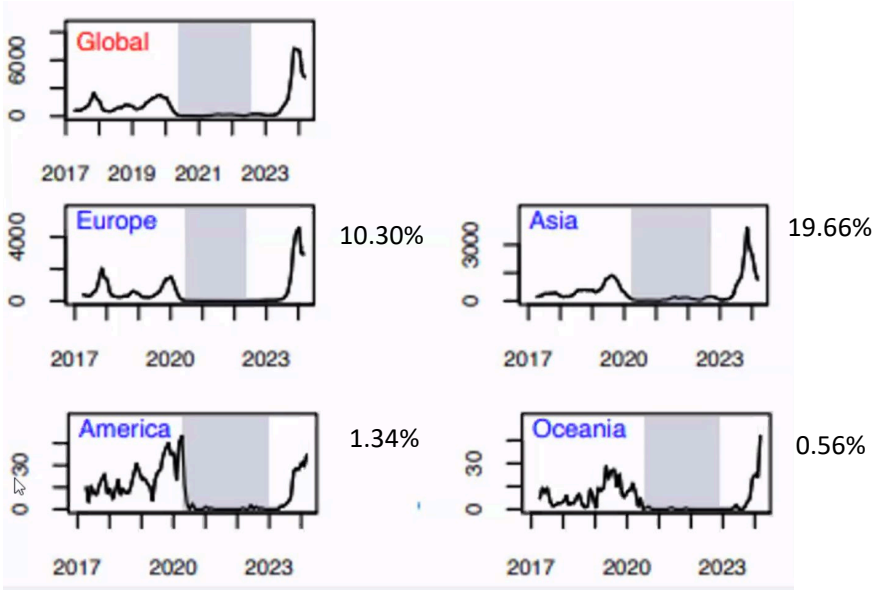
At a press conference on 13 November 2023, Chinese authorities from the National Health Commission reported an increase in incidence of respiratory diseases in China. Chinese authorities attributed this increase to the lifting of COVID-19 restrictions and the circulation of known pathogens such as influenza, *mycoplasma pneumoniae* (a common bacterial infection which typically affects younger children), respiratory syncytial virus (RSV), and SARS-CoV-2 (the virus that causes COVID-19). Authorities stressed the need for enhanced disease surveillance in healthcare facilities and community settings, as well as strengthening the capacity of the health system to manage patients.

https://www.who.int/news/item/22-11-2023-who-statement-on-reported-clusters-of-respiratory-illness-in-children-in-northern-china
https://www.santepubliquefrance.fr/les-actualites/2023/augmentation-des-infections-a-mycoplasma-pneumoniae-en-france

M. pneumoniae epidemiology: 2022-2024
ESGMAC-MAPS study



Meyer Sauteur et al., Lancet Microbe 2023



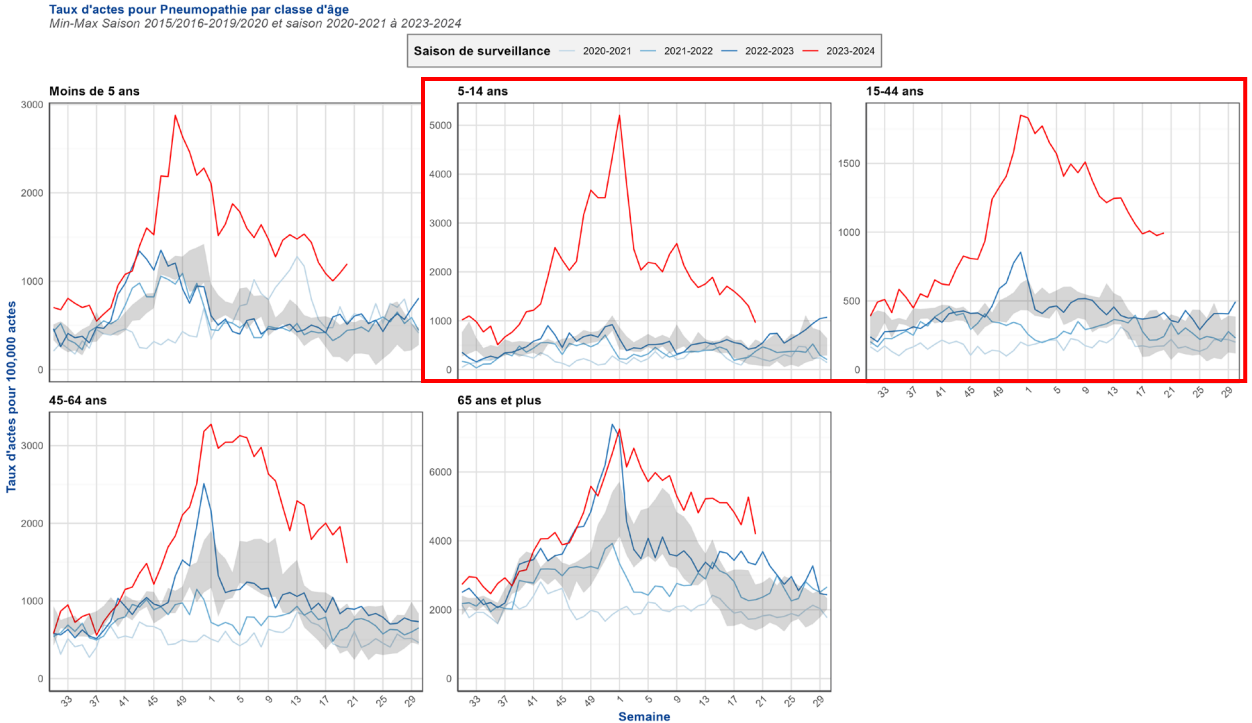
Meyer Sauteur et al., Lancet Microbe in press

ESGMAC
(ESCMID study group)

Surveillance syndromique SurSaUD® en ville (réseau SOS Médecins)

Santé publique France

Part hebdomadaire des actes pour toutes pneumopathies pour 100 000 actes chez SOS Médecins, par classe d'âge, semaines 26/2015 à S20/2024, réseau SOS Médecins

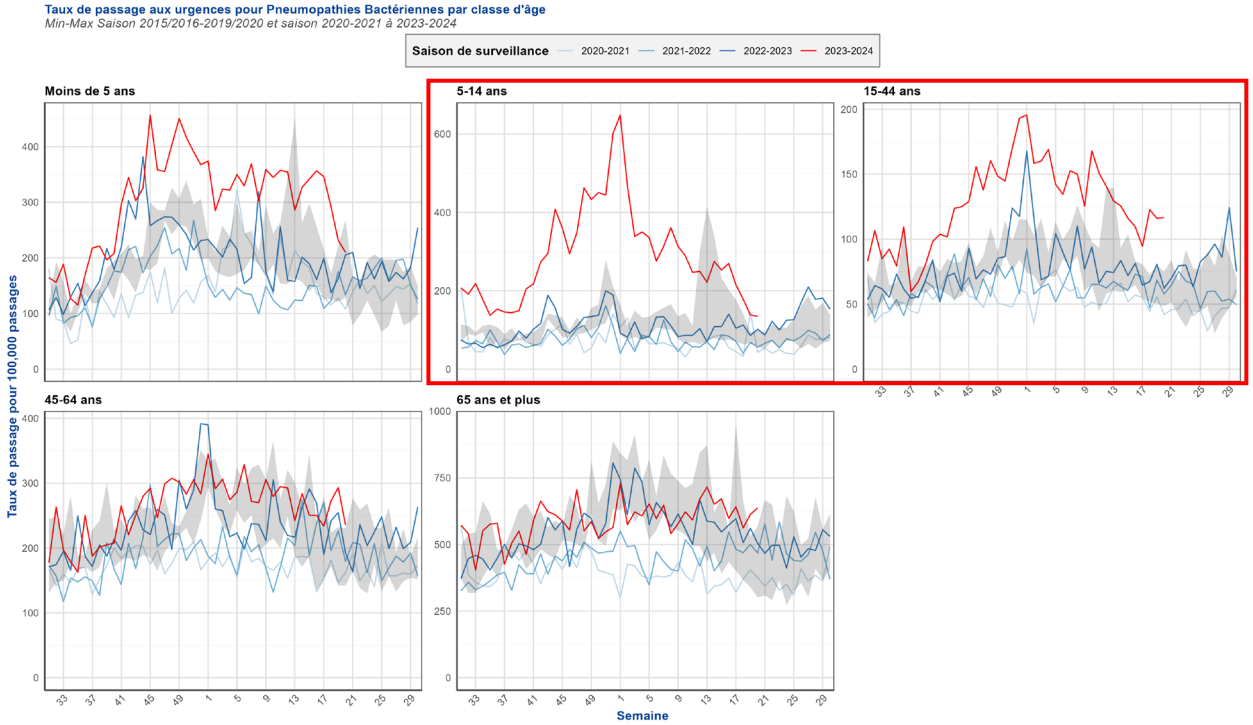


D. Viriot, JNI 2024

Surveillance syndromique SurSaUD® à l'hôpital (réseau Oscour®)

Santé publique France

Part hebdomadaire des passages pour pneumopathie bactérienne pour 100 000 passages aux urgences par classe d'âge, semaines 26/2015 à S20/2024, réseau Oscour®

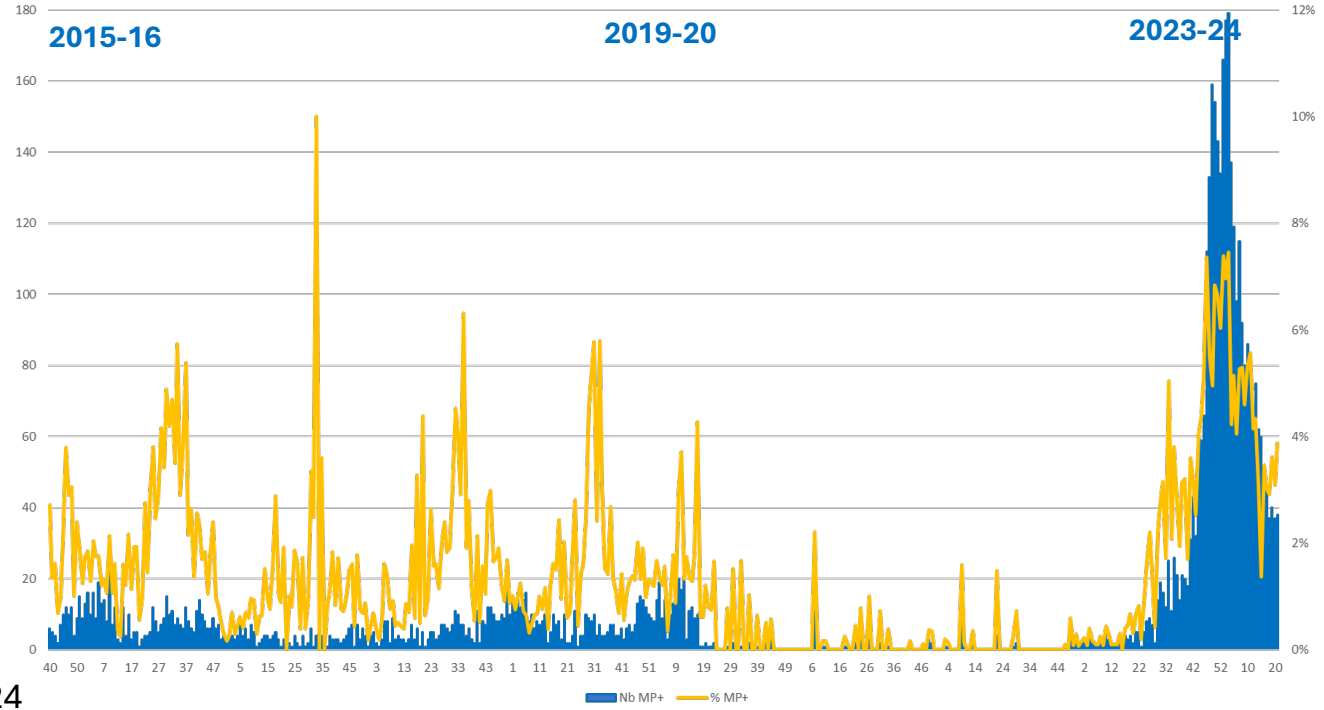


D. Viriot, JNI 2024

Suivi des taux de détection de *M. pneumoniae* l'hôpital (réseau de laboratoires RENAL)

Santé publique France

Nombre et taux hebdomadaire de détection par PCR de Mycoplasma pneumoniae tous âges confondus, semaines 40/2015 à 20/2024, réseau de laboratoires hospitaliers RENAL

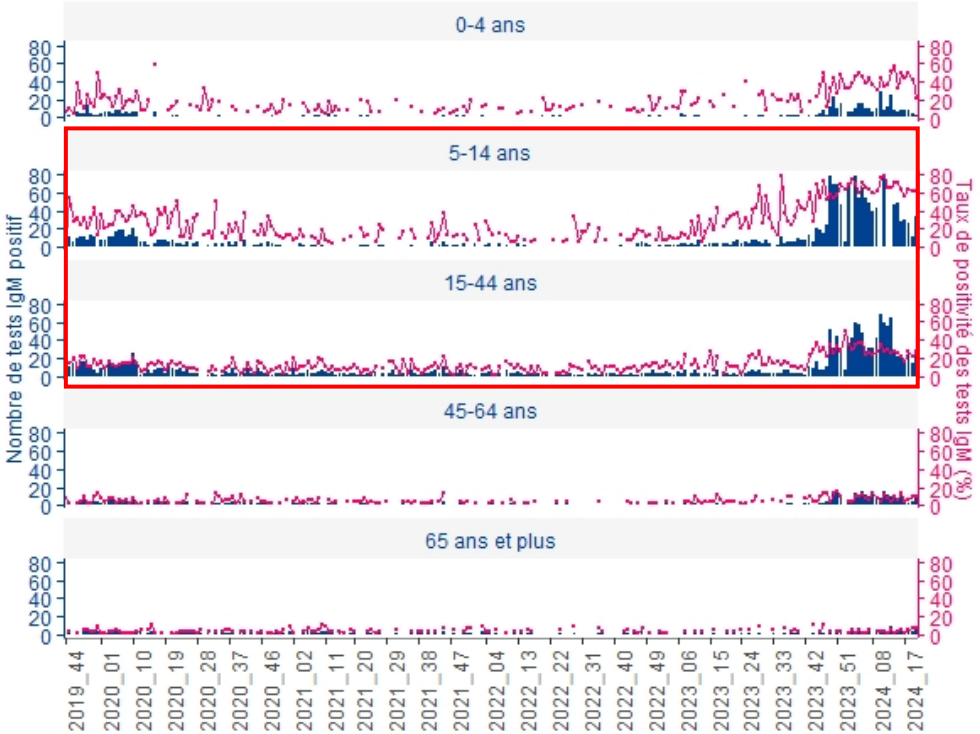


D. Viriot, JNI 2024

Suivi des données sérologiques en ville (réseau de laboratoires 3Labos)

Santé publique France

Nombre de tests IgM positifs à *Mycoplasma pneumoniae* et taux de positivité par classe d'âge en ville, semaines 44/2019 à 20/2024, données Eurofins-Biomnis, réseau de laboratoires 3Labos



D. Viriot, JNI 2024

HAUTE AUTORITÉ DE SANTÉ

RECOMMANDER LES
BONNES PRATIQUES

FICHE

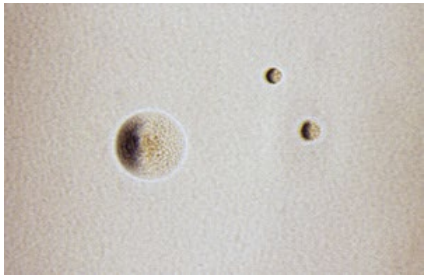
Réponse rapide sur la prise en charge diagnostique et thérapeutique des pneumonies atypiques à *Mycoplasma pneumoniae* en ambulatoire chez l'enfant et l'adulte

Validée par le Collège le 21 décembre 2023

Diagnostic des infections à *M. pneumoniae*

- **Diagnostic direct**

  - Culture très rarement faite, fastidieuse (lab expert)



- Tests d'amplification d'acides nucléiques (TAAN) +++

plus sensibles que la sérologie au stade précoce d'infection

New « gold standard », non remboursé

M. pneumoniae: diagnostic par TAAN

- **Echantillons**
  - ORL: écouvillon nasopharyngé, oropharyngé
  - Respiratoires: expectoration, asp trachéales, LBA (rarement validés par les kits commerciaux)
  - Autres: LCS, liq ponction, prel cutanés etc.

- **Méthodes**
  - PCR en temps réel, LAMP, NASBA
  - Cibles: adhésine P1, ARNr 16S, toxine CARDS
  - Simplex, multiplex (virus et autres bactéries atypiques)

M. pneumoniae: diagnostic par TAAN

- **CHU de Bordeaux**

- qPCR maison simplex sur LC 480 (Roche), extraction (MagnaPure 96-Roche, EZ2-Qiagen), CI extraction et amplification

- qPCR Bacterial Respiratory ELITe MGB panel sur l'Ingenius, ELITechGroup (série 12):
MP, *C. pneumoniae*, *L. pneumophila*

- N134 (RIHN250), 62,5€

Commercial molecular assays for *M. pneumoniae* detection

Table 3.14.3–1 Examples of commercial NAATs for detection of *M. pneumoniae*[a]

Product	Manufacturer, platform	Method	Pathogen(s) detected (no.)	*M. pneumoniae* gene target	Time to result (h); sample throughput	Regulatory status
Film Array RP	bioMérieux/Biofire Diagnostics, Torch	PCR	*M. pneumoniae*, *C. pneumoniae*, *B. pertussis*, several respiratory viruses (20)	CARDS toxin	~1; cartridge assay, 12 per tower	FDA cleared, CE-IVD
ePlex RPP	GenMark Diagnostics, ePlex instrument	PCR	*M. pneumoniae*, *C. pneumoniae*, several respiratory viruses (17)	P1 adhesin	~1.5; cartridge assay, 6 per tower	FDA cleared, CE-IVD
Nx TAG RPP	Luminex Corporation, MagPix	PCR	*M. pneumoniae*, *C. pneumoniae*, several respiratory viruses (20)	P1 adhesin	~4; 96-well plate	FDA cleared, CE-IVD
Mycoplasma direct	Meridian Bioscience, Alethia	LAMP	*M. pneumoniae* (1)	repMp4	~1; 10 per run	FDA cleared, CE-IVD
MGB Alert *M. pneumoniae*	ELITechGroup, InGenius	PCR	*M. pneumoniae* (1)	Protease-like protein	~3; 12 per run	RUO

[a]PCR, polymerase chain reaction; LAMP, loop-mediated isothermal amplification; FDA, U.S. Food and Drug Administration; CE-IVD, approved Communauté Européenne marking for *in vitro* diagnostic medical devices.

Bébéar C. Diagnostic of human mycoplasmas and ureaplasmas from clinical specimens by culture and PCR. Clinical Microbiology Procedures Handbook 5th edition ASM Books, Wiley, 2023.

M. pneumoniae : diagnostic sérologique

- **Diagnostic rétrospectif**
  - **Peu utile dans le diagnostic de l'infection aiguë (⬆️ IgM 10eme jour infection)**
  - **le seul remboursé (B50)**
  - **Sang, pas dans le LCS**

- **Méthodes**
  - **Immunoenzymatiques (plaques, membranes) +++**
  - **Performances variables**
  - **2 sérums collectés à 15 j d'intervalle +++**
  - **IgM, IgG**
  - **Séroconversion, ⬆️ significative du tx AC**
  - **CHU Bdx: Kit Diasorin, XL Liaison**

Diagnostic des infections à *M. pneumoniae*

• **TAAN plus sensibles que la sérologie et la culture dans la phase précoce de l'infection.**

• **Sérologie encore très réalisée malgré un intérêt limité dans le diagnostic de l'infection aiguë à *M. pneumoniae*, seul examen remboursé. Utile dans les études épidémiologiques.**

➡ **La plupart des cas détectés par combinaison TAAN et détection d'IgM.**

M. pneumoniae and antibiotics

- **Intrinsic resistance to ATB targeting the cell wall (β-lactams +++)**

- **Active antibiotics**
  - **Macrolides and related: macrolides, lincosamides, streptogramin combinations, ketolides (MLSK)**
  - **Tetracyclines**
  - **Fluoroquinolones**

☞ Macrolides and related antibiotics = 1st line treatment for *M. pneumoniae* infections

Antibiotic susceptibility testing in *M. pneumoniae*

- **Not in routine (fastidious growth)**
  No commercialized kit or test

- **CLSI recommendations**
  M43-A 31(19), 2011

- **Phenotypic techniques**
  No agar diffusion

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria S*	I*	R*
Quinolones				
	Levofloxacin	≤1	–	–
	Moxifloxacin	≤0.5	–	–
Tetracyclines				
	Tetracycline	≤2	–	–
Macrolides				
	Erythromycin	≤0.5	–	≥1
	Azithromycin	≤0.5	–	≥1

*Abbreviations: S, susceptible; I, intermediate; R, resistant.

M43-A, 2011. *CLSI*

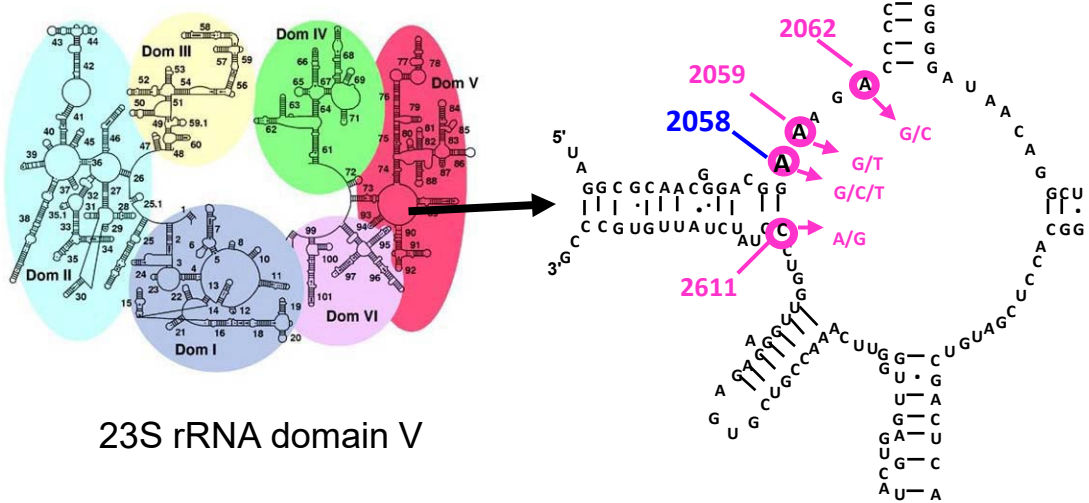
- **Molecular techniques to detect macrolide resistance directly from specimens**

Acquired antimicrobial resistance in *M. pneumoniae*

Antimicrobial Class	Resistance		Mechanism	MIC range for Resistant Isolates (µg/ml)
	In vitro	*In vivo*		
MLSK	Yes	Yes	23S rRNA mutations at positions 2611, 2058, 2059 and 2062 Mutations, insertions or deletions in L4 and L22 ribosomal proteins (*in vitro* only)	64 - >256 (erythromycin)
Tetracycline	Yes	No	16S rRNA mutations at position 968 and 1193 (*in vitro* only)	2
Fluoroquinolones	Yes	No	Mutations in *gyrA*, *gyrB*, *parC* or *parE* genes of QRDRs [c]	2 - 16 (levofloxacin)

Macrolide resistance in *M. pneumoniae*

- **Mutations in 23S rRNA** (1 copy in *M. pneumoniae*)



23S rRNA domain V

- **Predominance of A2058G then A2059G** (***E. coli*** **numbering)**
  - **MLSB phenotype for A2058G/C, A2059G**
  - **C2611A/G: lower MICs increases**
  - **Very rare cases of A2062G/C : sole resistance to 16-member macrolides and pristinamycin**

Molecular diagnostic of MP macrolide resistance

- **Real-time (RT)-PCR (FRET) with melting curve analysis**

  → **Mutated strains: lower Tm**

  → **Directly from clinical specimens**

Mutation	Tm (°C)
WT	60
A2058C	**55**
A2058G/A2059G	**50**

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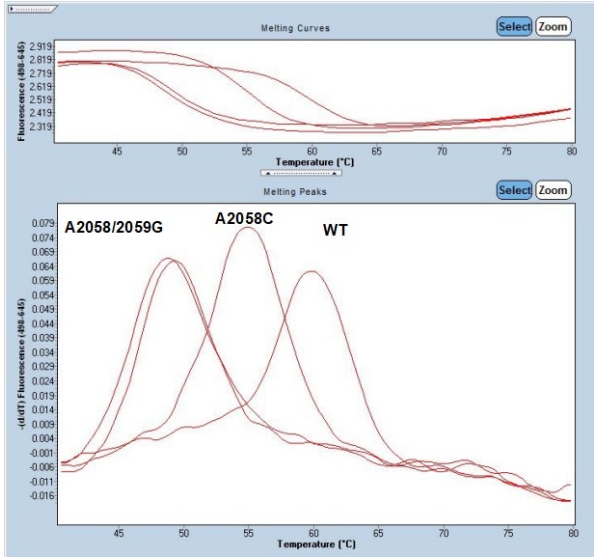

- **Other molecular methods:** **HRM RT-PCR, Sanger sequencing, pyrosequencing, NGS…**
- **A few commercial assays**

Peuchant et al., J Antimicrob Chemother, 2009
Bébéar et al., Future Microbiol, 2011, Pereyre Front Microbiol 2016, Waites, Clin Microb Rev 2017

Molecular diagnostic of MP macrolide resistance

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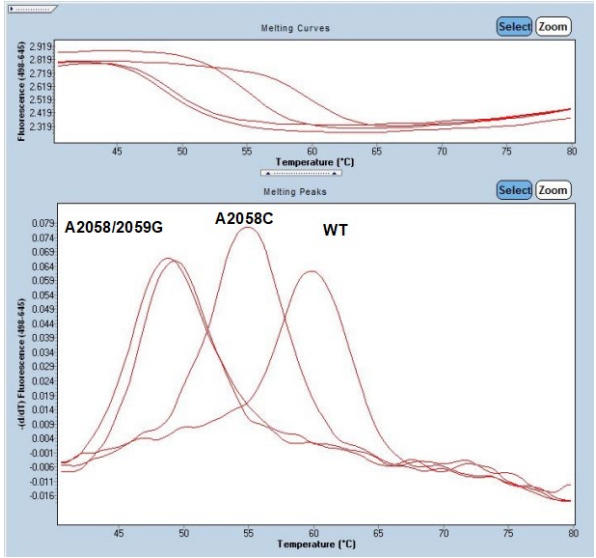

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  ☞ **Poster A. Silvant P157**

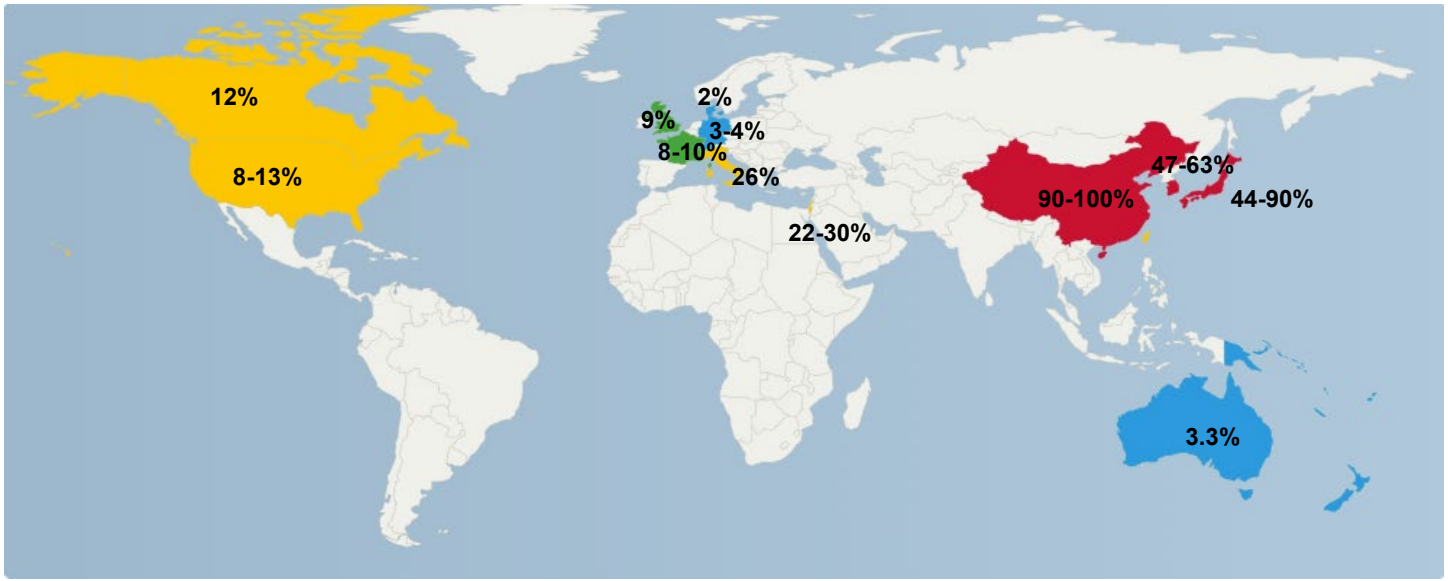
Peuchant et al., J Antimicrob Chemother, 2009
Bébéar et al., Future Microbiol, 2011, Pereyre Front Microbiol 2016,
Waites, Clin Microb Rev 2017

Consequences of macrolide resistance in *M. pneumoniae* clinical isolates

- **Need for macrolide resistance detection?**
  - **Depends on clinical outcomes, macrolide resistance rates**
  - **If rate >10% : molecular detection on all Mp-positive specimens**
    - ✓ Non-macrolide treatment promptly started if macrolide-resistant genotype identified
  - **If rate <10% : molecular detection in case of treatment failure**

- **For severe *M. pneumoniae* cases (in-patients)**

MP macrolide resistance worldwide 2010-2015



Data collated from the literature between 2010-2015

< 5%
5-10%
10-50%
>50%

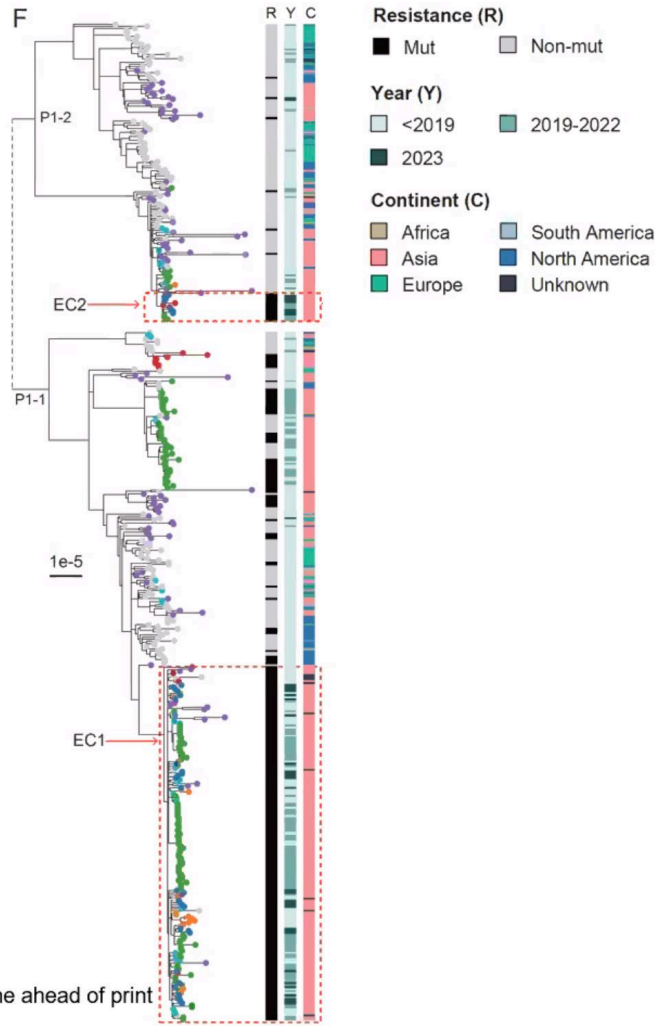
☞ **High macrolide resistance rates certainly associated with antibiotic selective pressure because of extensive macrolide use**

Adapted from *Pereyre et al. Frontiers Microbiol. 2016*

Phylogeny (China)

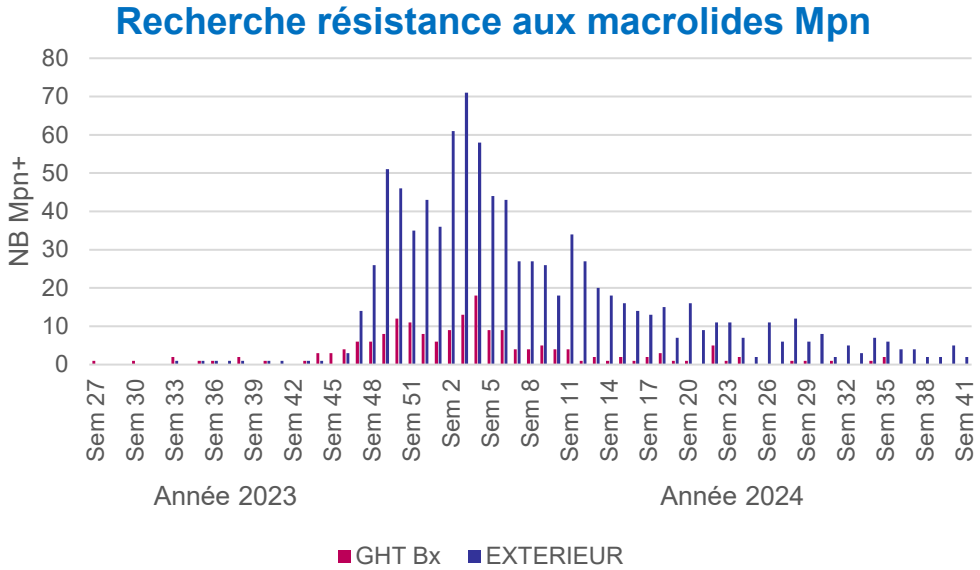
M. pneumoniae surge in China, 2023

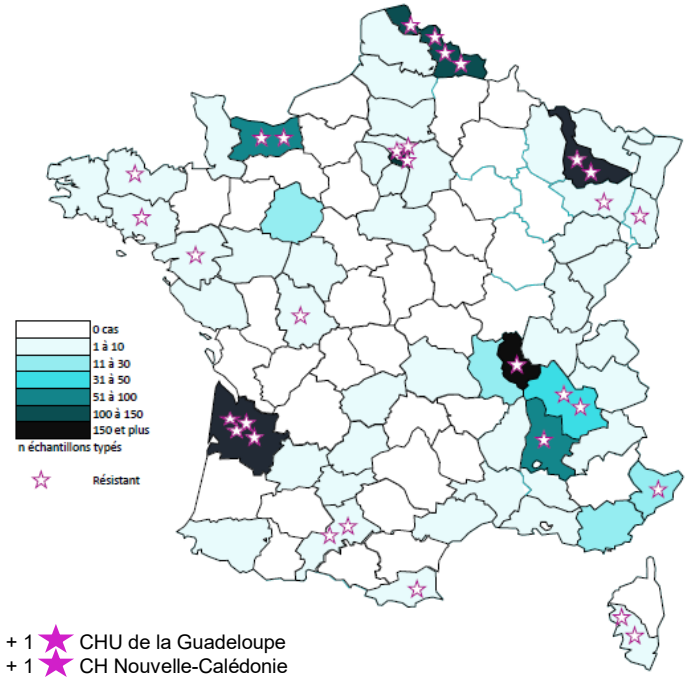
- type P1-1
- Macrolide-resistant



Li et al. **Lancet Microbe** 2024; online ahead of print

Evolution de la résistance aux macrolides en France





+ 1 ★ CHU de la Guadeloupe
+ 1 ★ CH Nouvelle-Calédonie
+ 2 prélèvements WT CH Ouest-Réunion

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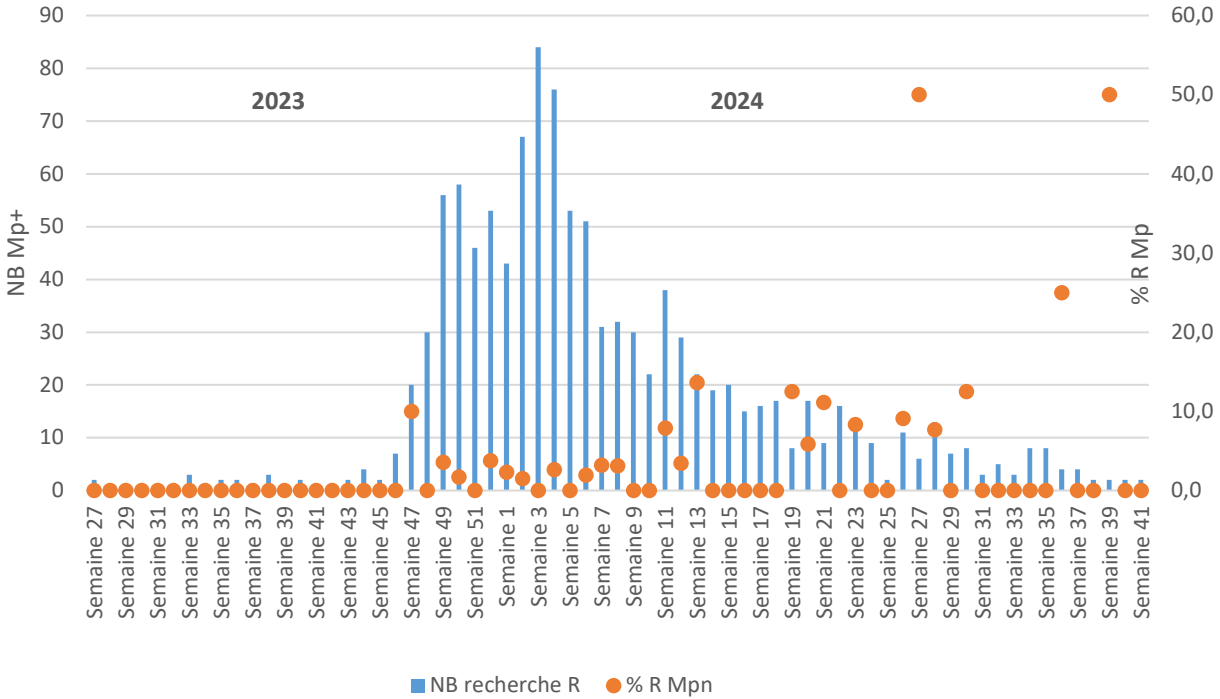
Résistance aux macrolides *M. pneumoniae* 2023-2024

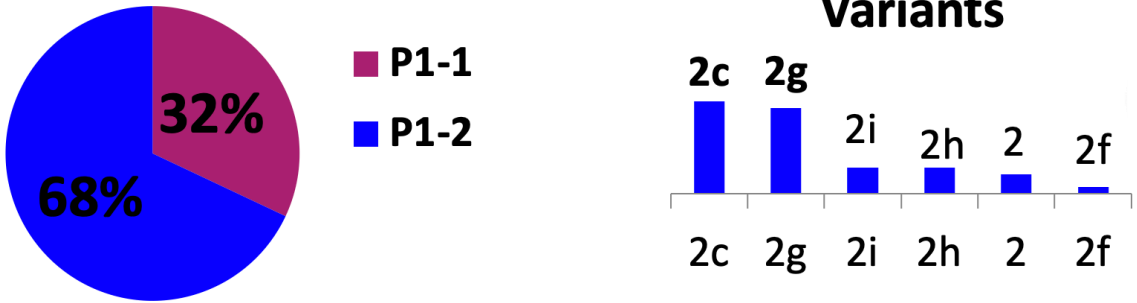


33 souches résistantes sur 1123 prélèvements amplifiés entre les semaines 27/2023 et 41/2024 (2,93%)

476 prélèvements patients < 15 ans (42,4%); 647 patients de plus de 15 ans (57,6%)

Typing and antimicrobial resistance

- **P1 subtype 2 was the predominant subtype (68%, n=55), different clones from the Asian ones**



- **Low-level of macrolide resistance in France and Europe (<3%), A2063G +++**

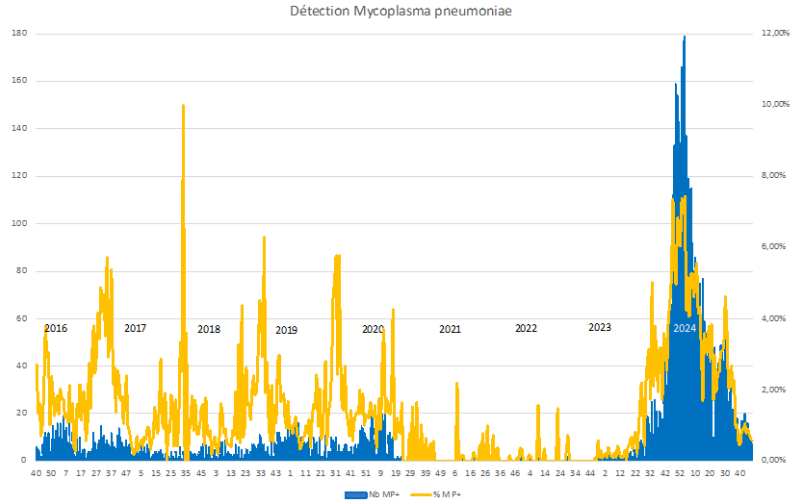
  In contrast to Asia (71,2% China, Taiwan, Rep. Korea, Meyer Sauteur et al. Lancet Microbe 2025**)**

- **No resistance-associated mutation found for tetracyclines or fluoroquinolones**

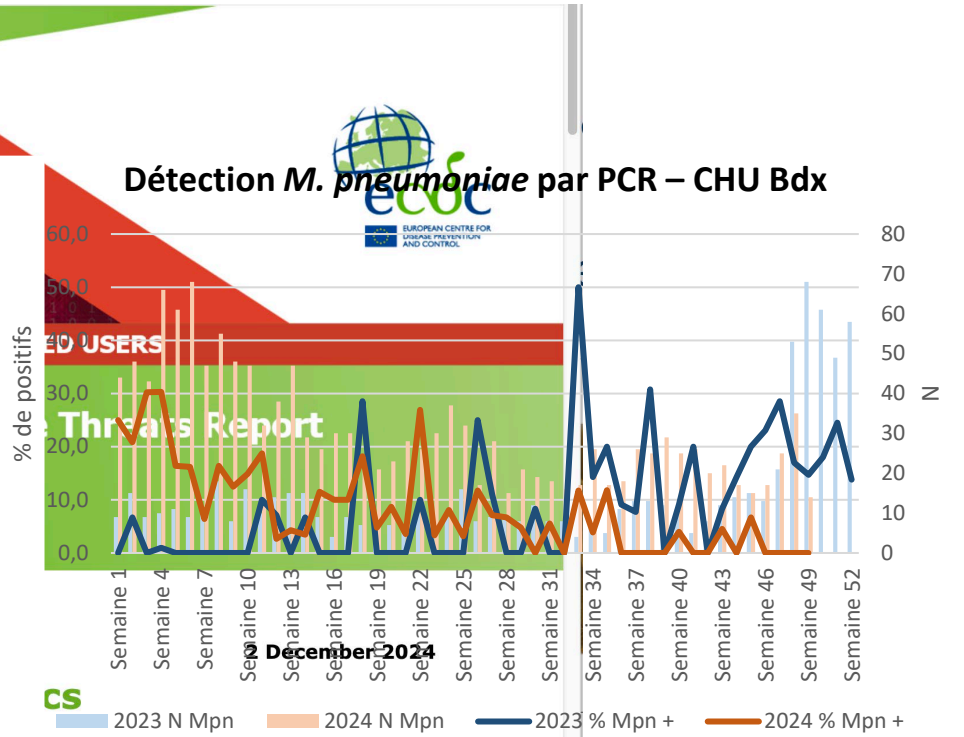
Conclusion : *Mycoplasma pneumoniae*

- **Epidémie mondiale 2023-2024, post-COVID-19** de très grande ampleur
- **Nombre de décès** en relation avec *M. pneumoniae* relativement bas
- **Ré-émergence plus tardive** en post-covid liée au temps de génération long et faible taux de transmission de *M. pneumoniae*
- **Clinique**
  - Formes essentiellement respiratoires et bénignes
  - Pneumonies plus rares 5-15 ans +++
  - ¼ de formes extra-respiratoires
- **Diagnostic:** Contexte épidémiologique, microbiologique (PCR + recherche R macrolides).
- **Thérapeutique : macrolides (résistance rare en France)**, alternatives : doxycycline, voire lévofloxacine

Mycoplasma pneumoniae : et maintenant ?



Réseau RENAL : de S40_2015 à S248_2024



1. Overview of respiratory virus epidemiology in the EU/EEA
2. SARS-CoV-2 variant classification
3. Increase in respiratory infections due to Mycoplasma pnemoniae in the EU/EEA during the season 2024/2025
4. Middle East respiratory syndrome coronavirus (MERS-CoV) – Multi-country – Monthly update

Acknowledgments

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Léo Gillet
Nadège Henin
Carla Balcon
Amandine Dolzy
Laurie Madras

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