Quoi de neuf en infectiologie pédiatrique

Julie Toubiana

22 juin 2017

Pédiatrie générale et maladies infectieuses
Hôpital Necker – Enfants malades

Déclaration d'intérêts de 2013 à 2016

- **Intérêts financiers : AUCUN**
- **Liens durables ou permanents : AUCUN**
- **Interventions ponctuelles : AUCUN**
- **Intérêts indirects : AUCUN**

Sélection restreinte autour des…

- Pratiques en infectiologie pédiatrique courante
- Infections néonatales
- Vaccins
- Zika

THE JOURNAL OF PEDIATRICS • www.jpeds.com
ORIGINAL ARTICLES
2017

Nonsteroidal Anti-Inflammatory Drug without Antibiotics for Acute Viral Infection Increases the Empyema Risk in Children: A Matched Case-Control Study

Muriel Le Bourgeois, MD[1], Agnès Ferroni, MD[2], Marianne Leruez-Ville, MD[2], Emmanuelle Varon, MD[3,4], Caroline Thumerelle, MD[5], François Brémont, MD, PhD[6], Michael J. Fayon, MD, PhD[7], Christophe Delacourt, MD, PhD[1,8], Caroline Ligier, MPh[9,10,11], Laurence Watier, PhD[9,10,11], and Didier Guillemot, MD, PhD[9,10,11,12], on behalf of the Children, Antibiotics, Nonsteroidal Anti-inflammatory Drugs and Childhood Empyema (ChANCE) Study Group*

- Etude cas/témoins appariés / source de diagnostic de virose et / âge (± 1 an)
  - Cas: pleuroPNP + infection virale dans les 15 jours précédents
  - Témoins: infection virale dans la même période
- Inclusion: 3 mois-15 ans avec infections virales : respiratoire sup/inf/autre
  - Au moins 24h d'apyrexie entre le virus et l'empyème
  - pas de comorbidité ni immunosuppression


94 Controls
215 Empyemas
6 Controls ineligible: AVI not confirmed
119 Empyemas ineligible: AVI not confirmed
Eligible
88
96
11 Empyemas excluded:
- 5 too short (≤ 72h) intervals between AVI onset and pleural puncture
- 6 absence of apyrexia between lower AVI onset and pleural puncture
(when AVI were LRTVI)
Before matching
88 Controls
85 Empyemas
5 unmatched Controls
2 unmatched Empyemas
Retained
83 Controls
83 Cases

- 86% *S. pneumoniae*
- Sérotypes 1 et 19A, 3

Table I. General characteristics of the 83 cases and 83 matched controls: Univariable analyses

Characteristics	Cases (n = 83)	Controls (n = 83)	*P* value
Male sex, n (%)	44 (53.0)	44 (53.0)	1
Age, y			
Mean ± SD	4.1 ± 2.3	3.8 ± 2.3	.41
Range	0.6-13.1	0.6-12.4	
Number of siblings, n (%)			
1	40 (48.2)	44 (53.0)	.39
2	29 (34.9)	22 (26.5)	
≥3	12 (14.5)	15 (18.1)	
NR	2 (2.4)	2 (2.4)	
Father's profession, n (%)			
Senior executive or self-employed	26 (31.3)	22 (26.5)	.54
Employee	23 (27.7)	33 (39.8)	
Farmer/craftsman, storekeeper, head of company	14 (16.9)	15 (18.1)	
Others†	17 (20.5)	12 (14.5)	
NR	3 (3.6)	2 (2.4)	
Mother's profession, n (%)			
Senior executive or self employed	25 (30.1)	23 (27.7)	.55
Employee	35 (42.2)	31 (37.3)	
Farmer/craftswoman, storekeeper, head of company	3 (3.6)	4 (4.8)	
Others†	17 (20.5)	23 (27.7)	
NR	3 (3.6)	2 (2.4)	
Site of viral infection,‡ n (%)			
Upper respiratory tract	52 (62.7)	48 (57.8)	.21
Lower respiratory tract	19 (22.9)	28 (33.7)	
Others	12 (14.5)	7 (8.4)	
Fever on day 1 of viral infection, n (%)			
No	40 (48.2)	27 (32.5)	.19
Yes	37 (44.6)	42 (50.6)	
NR	6 (7.2)	14 (16.9)	
Vaccinated with PCV-7,‖ n (%)	45 (54.2)	48 (57.8)	.62
Drug used on day 1 of viral infection			
Antibiotic intake, n (%)	7 (8.4)	12 (14.5)	.21
Beta-lactam agent	5	9	
Macrolide	1	1	
Others	1	3	
NSAID intake, n (%)	32 (38.6)	22 (26.5)	.08
Ibuprofen	32	21	
Ketoprofen	0	1	
Other antipyretic intake, n (%)	39 (46.9)	41 (49.4)	.79
Acetaminophen	39	41	

Pleuropneumopathies et AINS

Table III. Conditional logistic-regression analyses: Drug exposure when exposure began within the 72 hours after acute viral infection according its duration

Drug exposure	n*	OR_C	95% CI	*P* value
Antibiotic intake				
≥3 consecutive days	10/17	0.46	0.18-1.21	.12
≥6 consecutive days	6/16	0.33	0.12-0.92	.03
NSAID intake				
≥1 day	49/28	2.75	1.42-5.32	.003
≥2 consecutive days	45/25	2.82	1.42-5.61	.003
≥3 consecutive days	42/22	2.67	1.37-5.18	.004
Acetaminophen intake				
≥1 day	58/49	1.53	0.83-2.82	.17
≥2 consecutive days	56/44	1.75	0.95-3.23	.07
≥3 consecutive days	52/30	2.57	1.39-4.77	.003

Durée du traitement antibiotique

- ✓ Forte « pression » pour réduire les durées de traitement antibiotique dans l'objectif de diminuer la pression de sélection
- ✓ Réduction de la masse d'antibiotiques …Satisfaction des autorités de santé et rapprochement de la France de la norme européenne
- ✓ Réduire la durée plus facile que limiter le nombre de prescriptions
  - ✓ Dans la littérature, aucune étude démontrant qu'un traitement plus court réduit le risque de résistance dans les infections courantes
  - ✓ Néanmoins autres avantages : Coût, compliance, effets indésirables….

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Shortened Antimicrobial Treatment for Acute Otitis Media in Young Children

Alejandro Hoberman, M.D., Jack L. Paradise, M.D., Howard E. Rockette, Ph.D.,

N ENGL J MED 375;25 NEJM.ORG DECEMBER 22, 2016

RESULTS

Children who were treated with amoxicillin–clavulanate for 5 days were more likely than those who were treated for 10 days to have clinical failure (77 of 229 children [34%] vs. 39 of 238 [16%]; difference, 17 percentage points [based on unrounded data]; 95% con-

CONCLUSIONS

Among children 6 to 23 months of age with acute otitis media, reduced-duration antimicrobial treatment resulted in less favorable outcomes than standard-duration treatment; in addition, neither the rate of adverse events nor the rate of emergence of antimicrobial resistance was lower with the shorter regimen. (Funded by the National

10j ou 5j chez les moins de 2 ans?

Table 1. Cumulative Meta-Analysis of Double-Blind, Randomized, Controlled Trials Using the Same Antibiotic Agent in Each Group and Comparing Reduced-Duration with Standard-Duration Treatment in Young Children with Acute Otitis Media.*

Study	Drug	Rate of Clinical Failure		Risk Difference (95% CI)
		5-Day Regimen	10-Day Regimen	
		no./total no. (%)		*percentage points*
Cohen et al. 1998	Amoxicillin–clavulanate	51/192 (27)	28/186 (15)	12 (3–20)
Cohen et al. 2000	Cefpodoxime	46/226 (20)	23/222 (10)	10 (3–17)
Summary estimate	—	—	—	11 (5–16)
Hoberman et al. 2016	Amoxicillin–clavulanate	77/229 (34)	39/238 (16)	17 (9–25)
Updated summary estimate	—	—	—	13 (8–17)

Cohen R, Levy C, Chalumeau M. Shortened Antimicrobial Treatment for Acute Otitis Media. N Engl J Med. 2017 Mar 30;376(13):e24

13 % de taux d'échec supplémentaire seulement : intérêt ATB courte?

- Pas vraiment…
  - Pas de différence d'impact écologique sur l'acquisition de R
    - Pneumocoque
    - H influenzae
    - MAIS flore digestive non étudiée
  - Pas plus d'effet indésirable
  - OMA: problème de diffusion, biofilm…

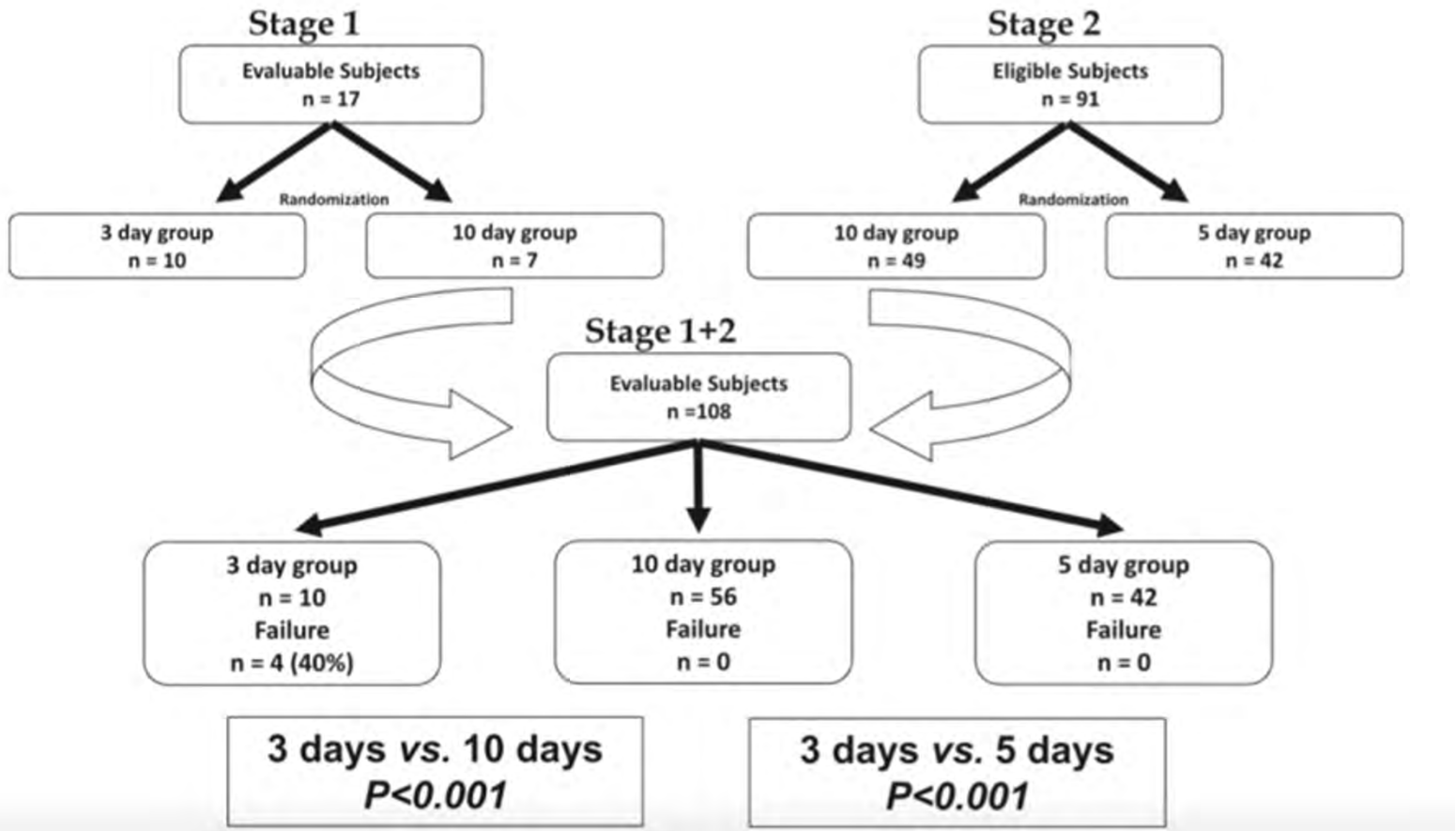
ORIGINAL STUDIES

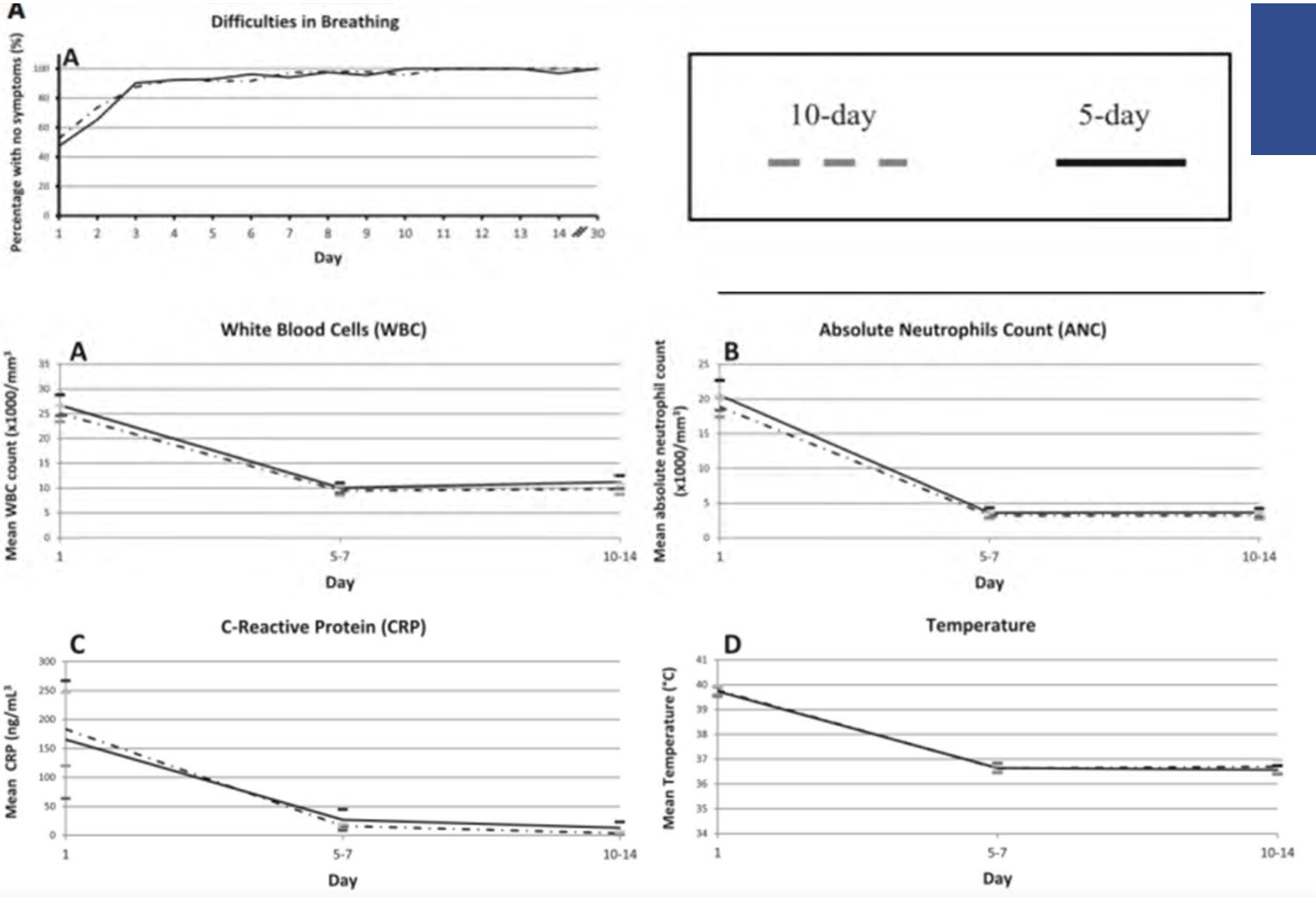
Short-course Antibiotic Treatment for Community-acquired Alveolar Pneumonia in Ambulatory Children

A Double-blind, Randomized, Placebo-controlled Trial

David Greenberg, MD,† Noga Givon-Lavi, PhD,*† Yair Sadaka, MD,*† Shalom Ben-Shimol, MD,*† Jacob Bar-Ziv, MD,‡ and Ron Dagan, MD*†*

Greenberg et al The Pediatric Infectious Disease Journal • Volume 33, Number 2, February 2014




A
Difficulties in Breathing
A
Percentage with no symptoms (%)
Day
10-day
5-day
White Blood Cells (WBC)
A
Mean WBC count (x1000/mm³)
Day
Absolute Neutrophils Count (ANC)
B
Mean absolute neutrophil count (x1000/mm³)
Day
C-Reactive Protein (CRP)
C
Mean CRP (ng/mL³)
Day
Temperature
D
Mean Temperature (°C)
Day

Durée de traitement ATB

- ✓ La durée du traitement n'est pas fonction de la gravité de la maladie, mais du risque de récidive précoce après traitement
- ✓ Pour les otites et les sinusites, ce risque est élevé, du fait
  - Du dysfonctionnement des trompes d'Eustache ou des ostium
  - De l'importance du biofilm dans ces pathologies et dans la flore
- ✓ Pour les pneumonies, ce risque de récidive est faible
  - Diffusion
  - Pneumocoque plus invasif moins résistant?
  - Moins de biofilm ?

ELSEVIER

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www.em-consulte.com

Médecine et maladies infectieuses

Médecine et maladies infectieuses 47 (2017) 92–141

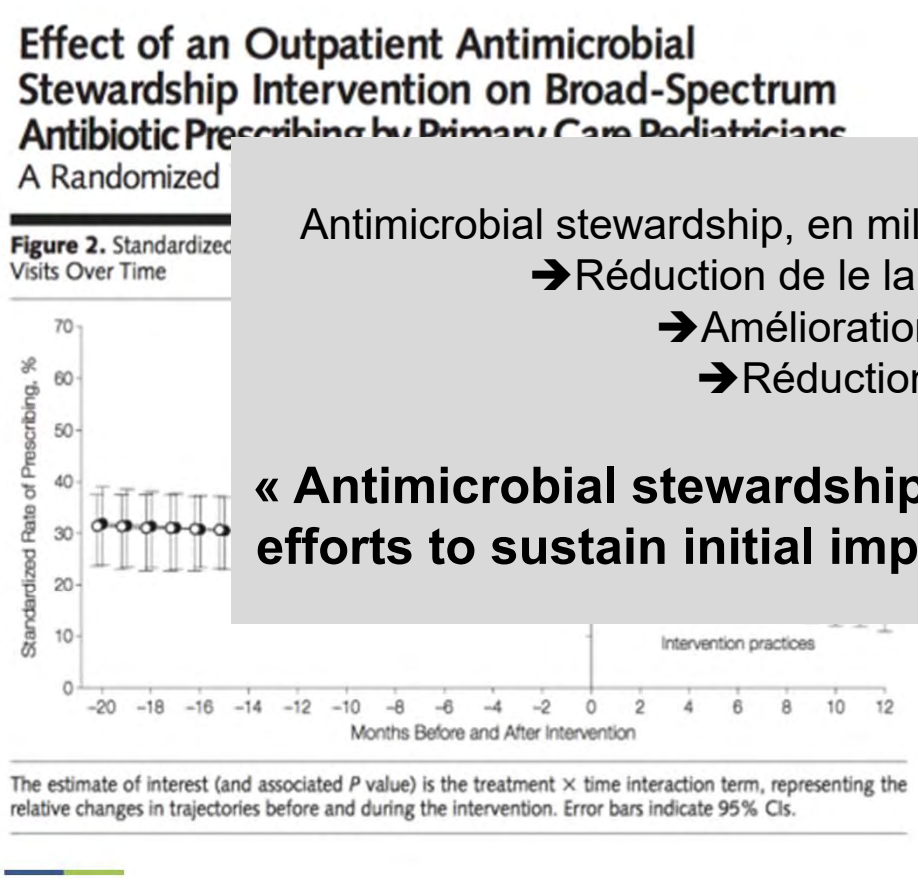
Original article

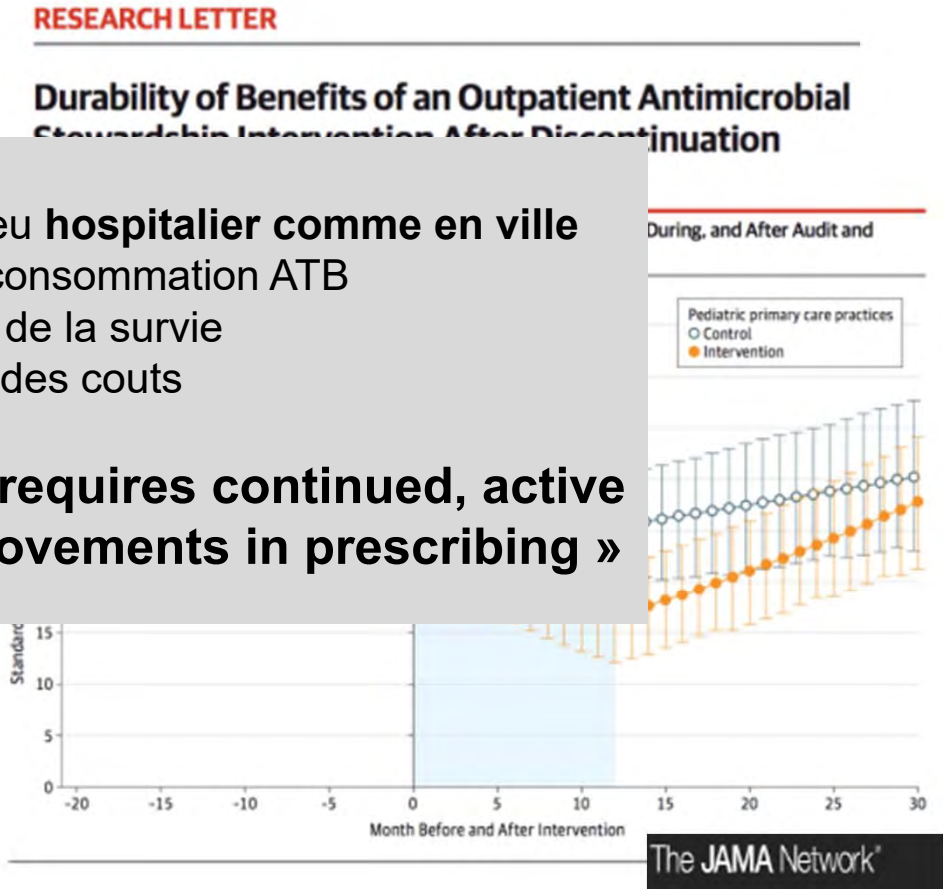
Proposal for shorter antibiotic therapies

Propositions pour des antibiothérapies plus courtes

C. Wintenberger[a], B. Guery[b], E. Bonnet[c], B. Castan[d], R. Cohen[e], S. Diamantis[f], P. Lesprit[g], L. Maulin[h], Y. Péan[i], E. Peju[j], L. Piroth[j], J.P. Stahl[k], C. Strady[l], E. Varon[m], F. Vuotto[b], R. Gauzit[n,*], Recommendation Group of the SPILF

« Antibiotic stewardship » en pédiatrie





Antimicrobial stewardship, en milieu **hospitalier comme en ville**

➔Réduction de le la consommation ATB

➔Amélioration de la survie

➔Réduction des couts

« Antimicrobial stewardship requires continued, active efforts to sustain initial improvements in prescribing »

Effet des antibiotiques sur le microbiote du nourrisson?

Original Investigation

Antibiotic Exposure During the First 6 Months of Life and Weight Gain During Childhood

Jeffrey S. Gerber, MD, PhD; Matthew Bryan, PhD; Rachael K. Ross, MPH; Carrie Daymont, MD, MSCE; Elizabeth P. Parks, MD, MSCE; A. Russell Localio, PhD; Robert W. Grundmeier, MD; Virginia A. Stallings, MD; Theoklis E. Zaoutis, MD, MSCE

IMPORTANCE Early-life antibiotic exposure has been associated with increased adiposity in animal models, mediated through the gut microbiome. Infant antibiotic exposure is common and often inappropriate. Studies of the association between infant antibiotics and childhood weight gain have reported inconsistent results.

DESIGN AND SETTING Retrospective, longitudinal study of singleton births and matched longitudinal study of twin pairs conducted in a network of 30 pediatric primary care practices serving more than 200 000 children of diverse racial and socioeconomic backgrounds across Pennsylvania, New Jersey, and Delaware.

Exposition ATB dans les 6 premiers mois: Pas d'effet (-> 7 ans)

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Early Life Antibiotic Exposure and Weight Development in Children

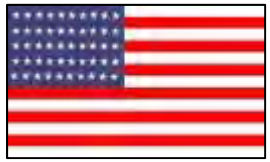
Catherine A. Mbakwa, MSc[1,2,*], Lotte Scheres, BSc[2,*], John Penders, PhD[2,3], Monique Mommers, PhD[2], Carel Thijs, MD, PhD[2], and Ilja C. W. Arts, PhD[2,4]

Study design Within the Child, Parents and Health: Lifestyle and Genetic Constitution Birth Cohort Study, antibiotic exposure record was obtained from general practitioners. Anthropometric outcomes (age- and sex-standardized body mass index, weight and height z-scores, and overweight) were measured repeatedly at 7 time points during the first 10 years of life. Generalized estimating equations method was used for statistical analysis.

Exposition ATB dans les 6 premiers mois ou multiples expositions dans les 2 premières années: Augmentation de du poids et de la taille (-> 10 ans) β-lactamines

Les infections néonatales bactériennes précoces (INBP)

- Anciennement infection « materno-foetale » (< 3-7 jours)
- SGB reste le plus fréquent chez le NN à terme, pas d'augmentation des INBP à *E. coli* depuis la prophylaxie maternelle
- En France
  - Enviro… naissance
  - Parmi …
  - Plus d… icion d'INBP
  - Plus d… giques (liquide gastric…

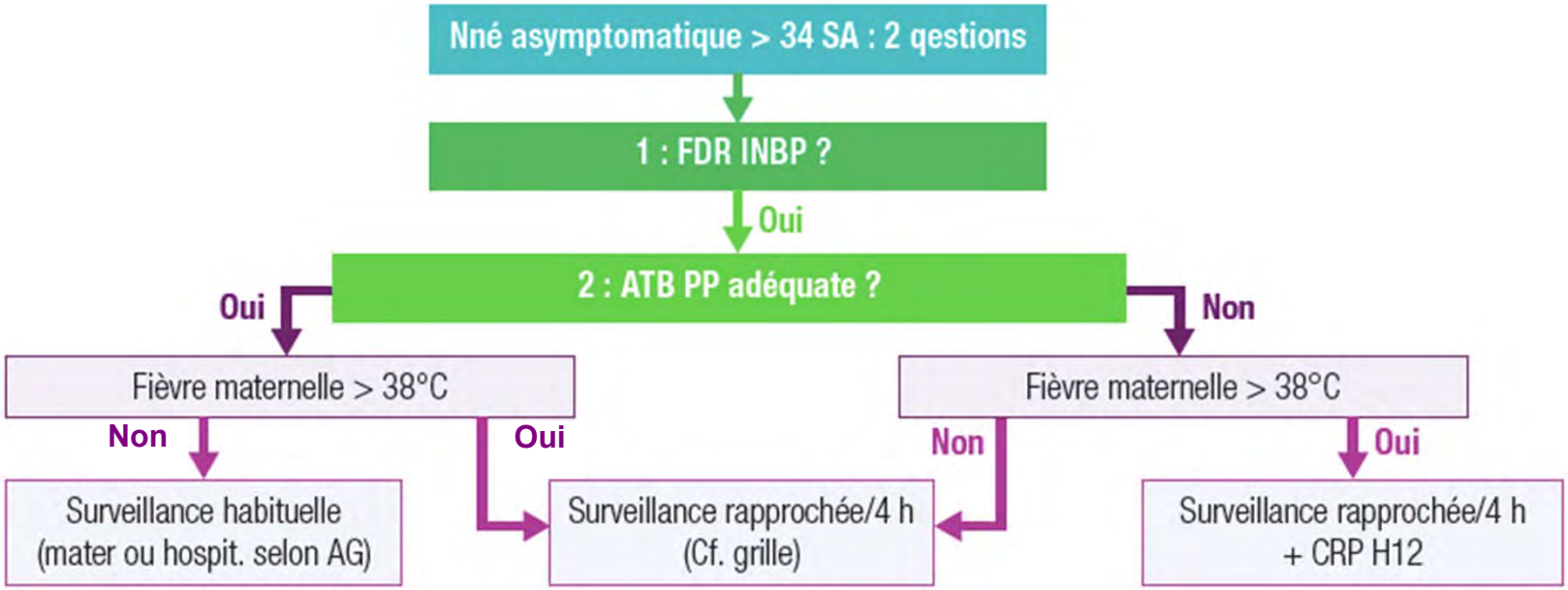




Recommandations plus récentes (2012-2013) et …
- Pas de prélèvement périphérique
- Notion de FDR, notion de surveillance
- USA: notion ATBprophylaxie adéquate
- Amoxicilline + gentamicine

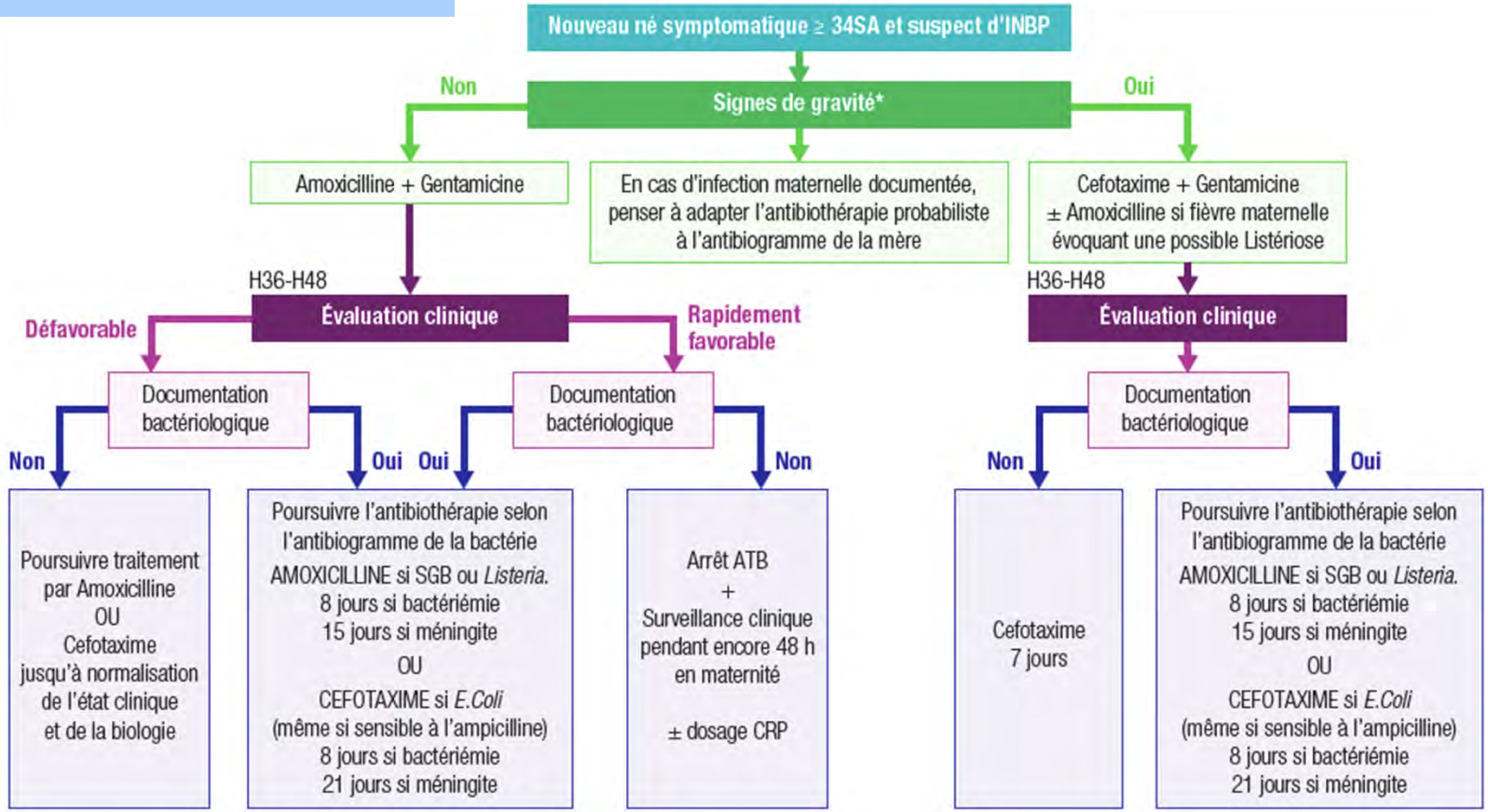
➔Ces prélèvements identifient des **colonisations chez 20% de ces nouveau-nés**

Schrag S, Pediatrics 2016; Sikias P, Arch Ped 2015

Les nouvelles recos HAS prévues fin 2017…



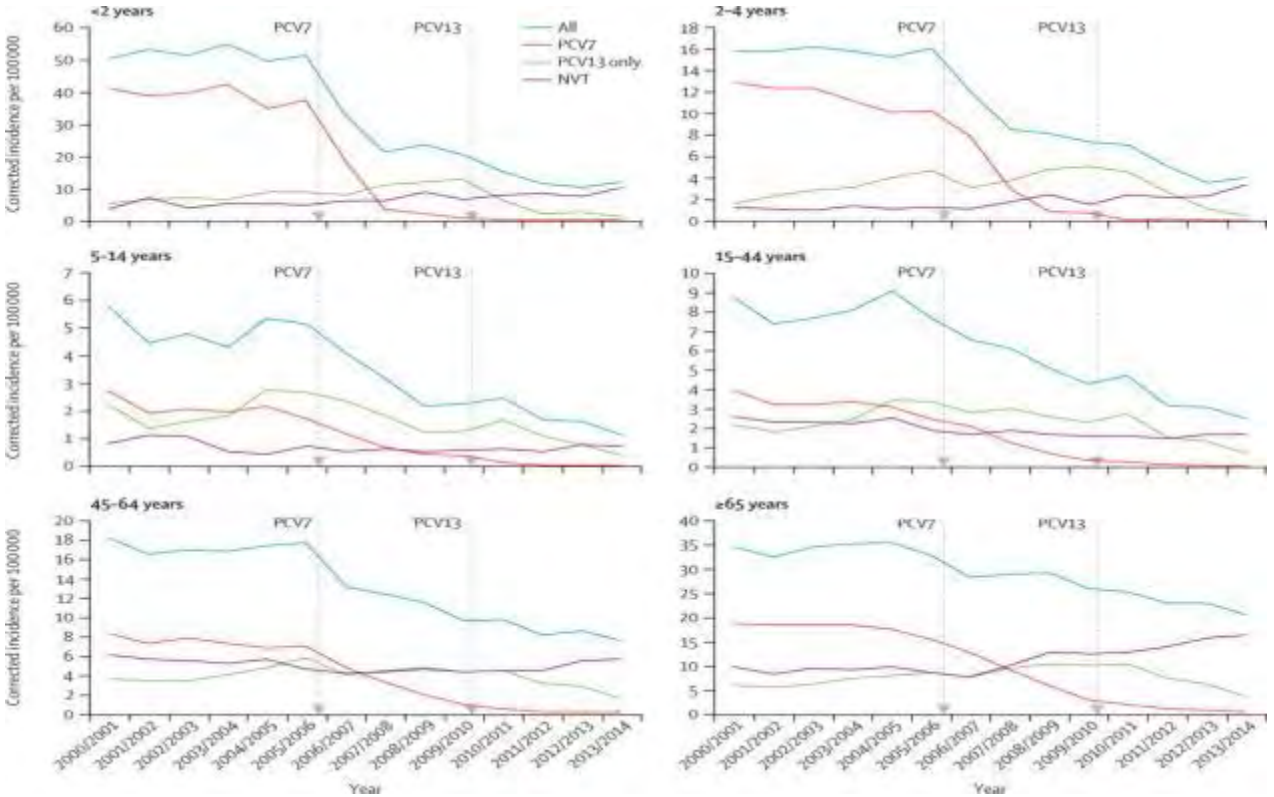
Infections néonatales



Signes de gravité

- Détresse respiratoire avec assistance respiratoire et $FiO_2 > 30$ %
- Troubles hemodynamiques nécessitant un remplissage vasculaire ou des amines
- Signes neurologiques comportant un trouble de la conscience ou des convulsions

Vaccin conjugué anti-pneumocoque
Angleterre et Pays de Galle : Incidence des IIP 2000 - 2014



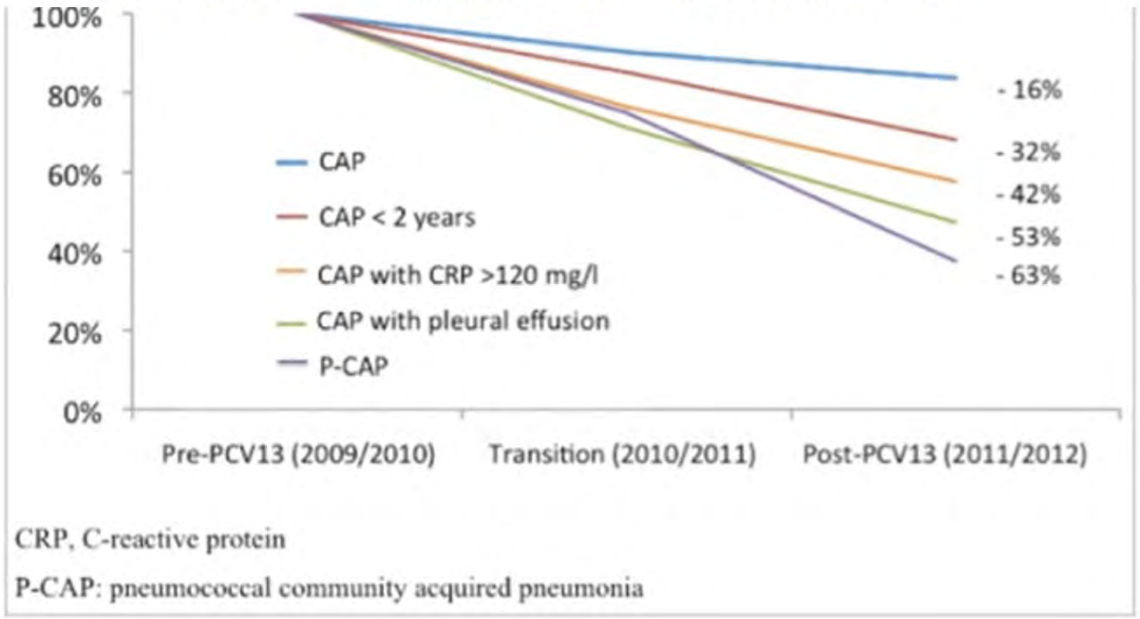
Waight PA, Andrews NJ, Ladhani SN, et al. Lancet Infect Dis 2015

REVIEW

Human Vaccines & Immunotherapeutics 12:2, 277–284; February 2016; © 2016 Taylor & Francis Group, LLC

The multifaceted impact of pneumococcal conjugate vaccine implementation in children in France between 2001 to 2014

Robert Cohen[1,2,3,4,5,*], Sandra Biscardi[1,3,5,6], and Corinne Levy[1,2,3,5]



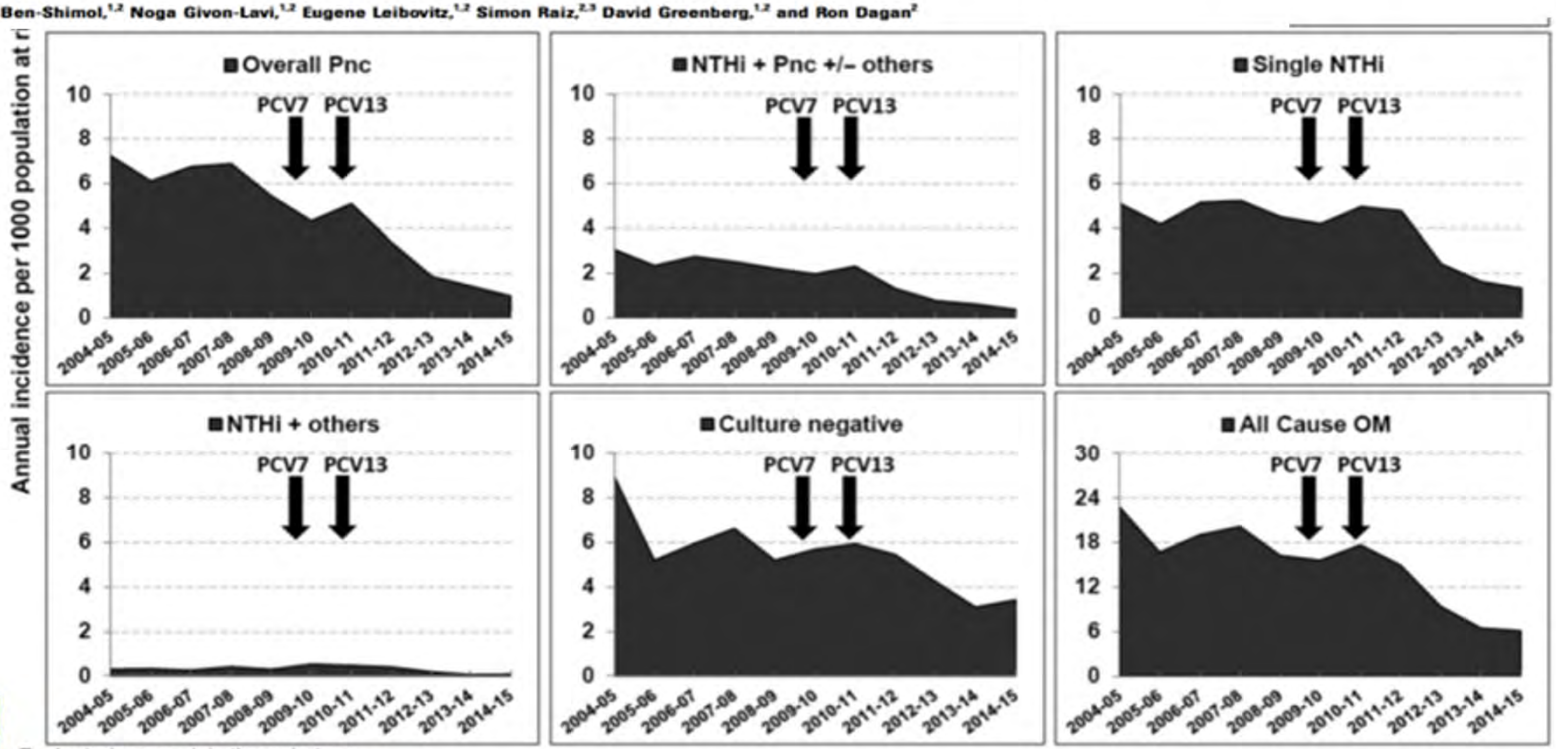
CRP, C-reactive protein

P-CAP: pneumococcal community acquired pneumonia

Clinical Infectious Diseases
MAJOR ARTICLE

Impact of Widespread Introduction of Pneumococcal Conjugate Vaccines on Pneumococcal and Nonpneumococcal Otitis Media

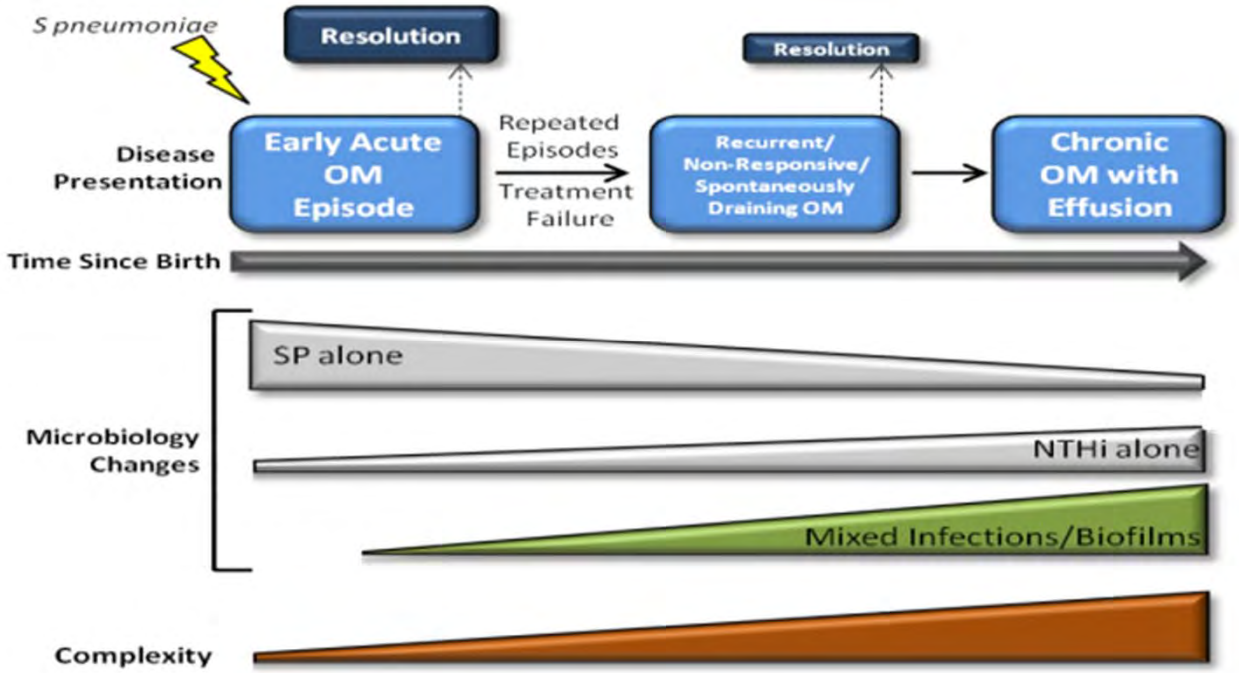
Shalom Ben-Shimol,[1,2] Noga Givon-Lavi,[1,2] Eugene Leibovitz,[1,2] Simon Raiz,[2,3] David Greenberg,[1,2] and Ron Dagan[2]



Each study year: July through June

Prevention of early episodes of otitis media by pneumococcal vaccines might reduce progression to complex disease

Ron Dagan, Stephen Pelton, Lauren Bakaletz, Robert Cohen

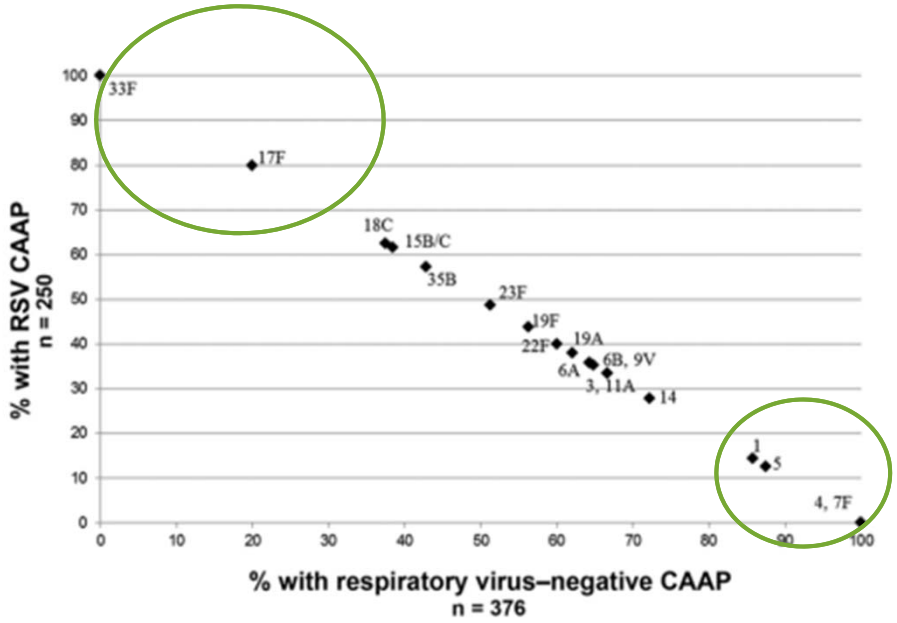


The Journal of Infectious Diseases
MAJOR ARTICLE
2017

Nasopharyngeal Pneumococcal Carriage During Childhood Community-Acquired Alveolar Pneumonia: Relationship Between Specific Serotypes and Coinfecting Viruses

David Greenberg,[1,3] Noga Givon-Lavi,[1,3] Yaniv Faingelernt,[1,3] Shalom Ben-Shimol,[1,3] Yonat Shemer Avni,[2,3] Jacob Bar-Ziv,[4] and Ron Dagan[3]

[1]Pediatric Infectious Disease Unit, and [2]Clinical Virology Laboratory, Soroka University Medical Center, Beer-Sheva; [3]Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva; and [4]Department of Radiology, Hadassah University Medical Center, Jerusalem, Israel



Hypothèse:

- **Sérotypes invasifs**

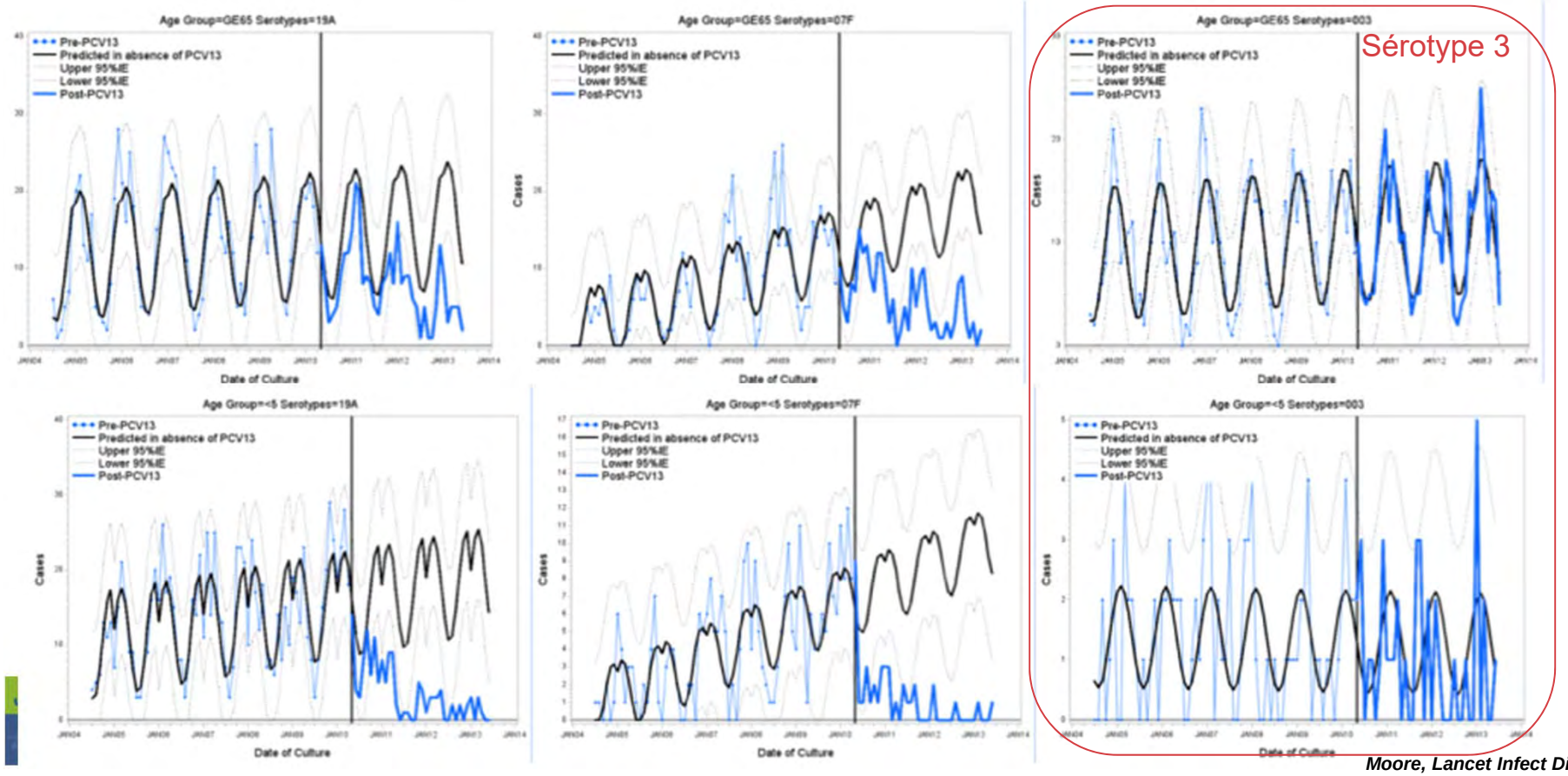
➔ PnP indépendamment d'un virus ss-jacent

- **Sérotypes moins invasifs (non vaccinaux)** :

➔ PnP : nécessite l'infection virale ss jacente (VRS)

Vaccinations

Diminution des sérotypes vaccinaux… et le ST 3?



Moore, Lancet Infect Dis. 2015

AMERICAN SOCIETY FOR MICROBIOLOGY | Clinical and Vaccine Immunology

Capsular Polysaccharide (CPS) Release by Serotype 3 Pneumococcal Strains Reduces the Protective Effect of Anti-Type 3 CPS Antibodies

Eun Hwa Choi,[a,b] Fan Zhang,[a] Ying-Jie Lu,[a] Richard Malley[a]

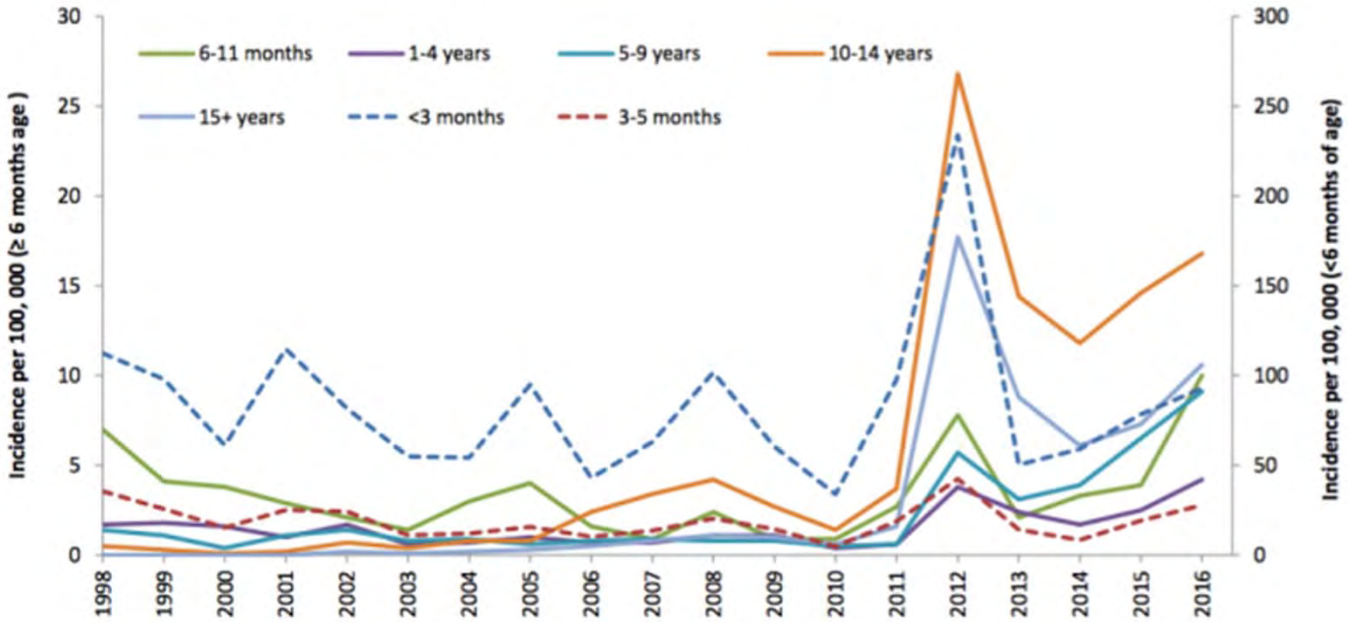
Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts, USA[a]; Department of Pediatrics, Seoul National University College of Medicine, Seoul, South Korea[b]

The efficacy of the serotype 3 (ST3) pneumococcal conjugate vaccine (PCV) remains unclear. While the synthesis of capsular polysaccharide (CPS) of most serotypes is *wzy* dependent, the strains of two serotypes, 3 and 37, synthesize CPS by the synthase-dependent pathway, resulting in a polysaccharide that is not covalently linked to peptidoglycan and can be released during growth. We hypothesized that the release of CPS during growth reduces anti-type 3 CPS antibody-mediated protection and may explain the lower efficacy of the type 3 component of PCV than that of other PCVs. The *in vitro*-released CPS concentrations per 10^7 CFU of ST3 and ST37 strains were significantly higher than those for the ST1, ST4, ST6B, and ST14 strains. Following intraperitoneal (i.p.) injection in mice, blood concentrations of CPS were significantly higher for the ST3 than for the ST4/5 strains. The opsonophagocytic killing assay (OPKA) titer of anti-type 3 CPS antibody was significantly reduced by type 3 CPS, culture supernatant, or serum from *Streptococcus pneumoniae* ST3 strain WU2-infected mice. Mice were injected with capsule-specific antibodies and challenged i.p. with or without the addition of sterile culture supernatant containing type-specific CPS. The addition of 0.2 μl of culture supernatant from WU2 inhibited passive protection, whereas 100-fold-more culture supernatant from *S. pneumoniae* ST4 strain TIGR4 was required for the inhibition of protection. We conclude that released type 3 CPS interferes with antibody-mediated killing and protection by anti-CPS antibodies. The relative failure of ST3 PCV may be due to CPS release, suggesting that alternative immunization approaches for ST3 may be necessary.

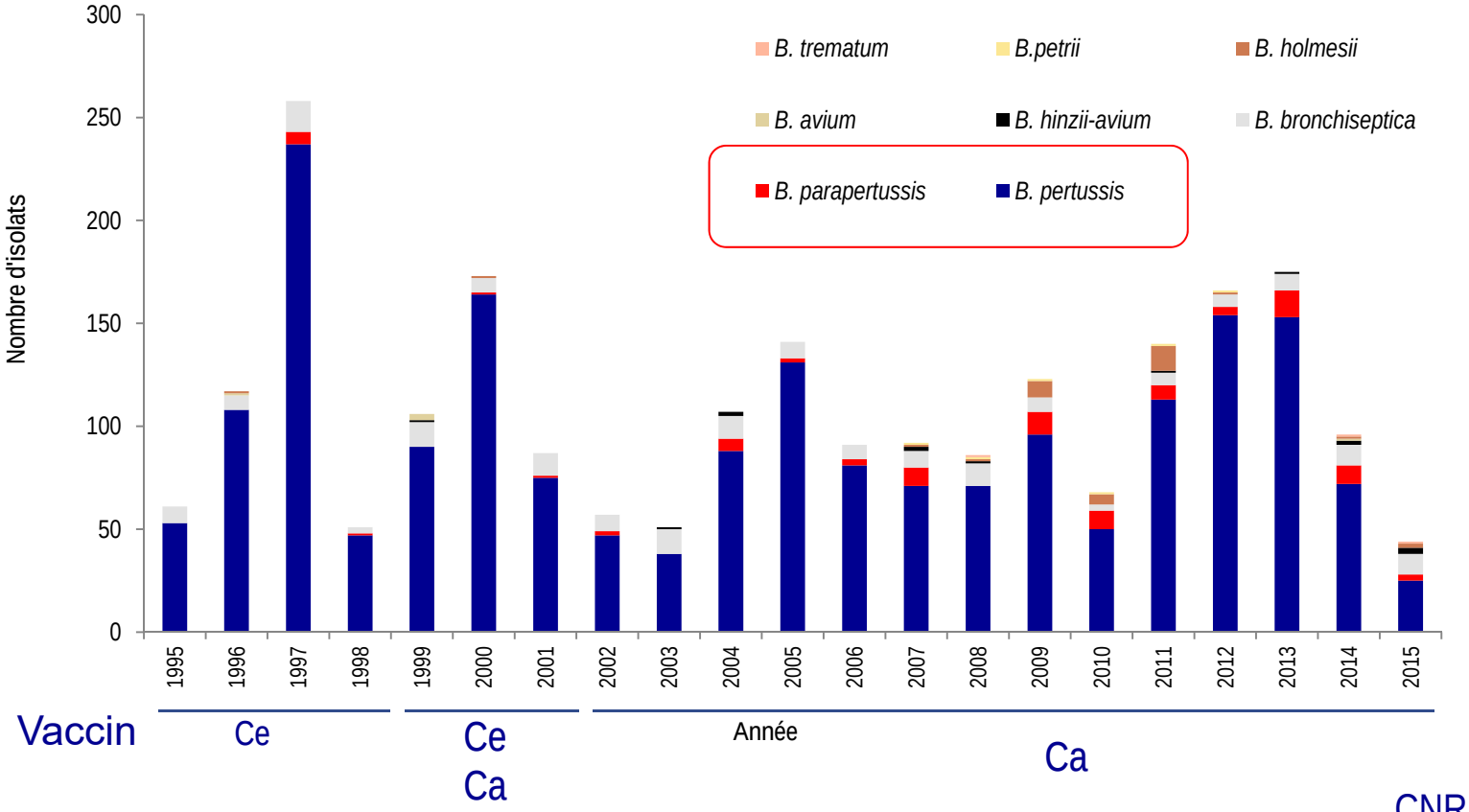
Coqueluche : augmentation de l'incidence..

Public Health England
Health Protection Report
weekly report
Infection report

Figure 2. Incidence of laboratory-confirmed pertussis cases by age group in England: 1998-2016



Surveillance CNR : données microbiologiques 1996-2015



CNR Coqueluche

Pourquoi cette augmentation d'incidence ?

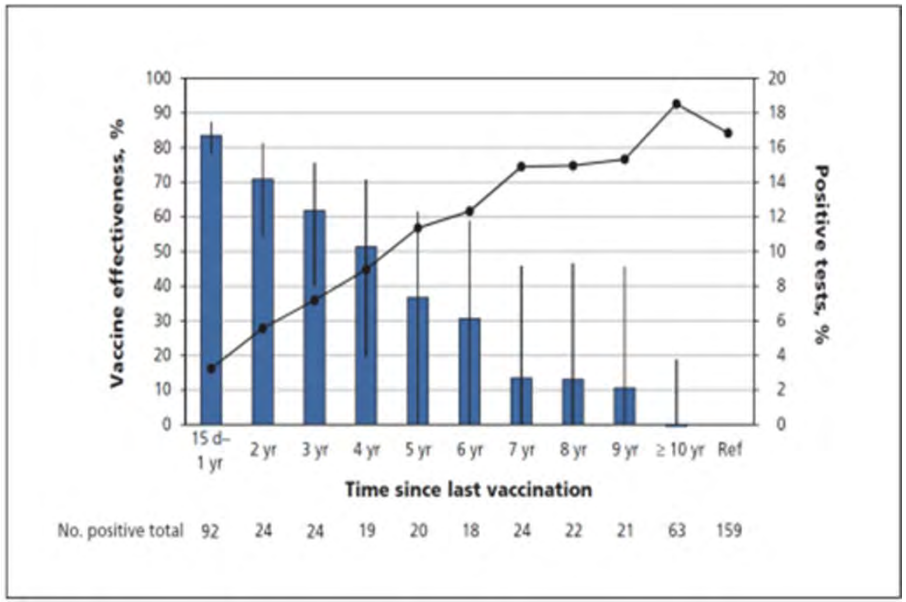
- Amélioration des techniques diagnostiques, PCR « actuelles »
  - + Spécifiques que les sérologies
  - +Sensibles que la culture
  - Mais détecte aussi *B. holmesii* et *B. parapertussis*
- Variations antigéniques des souches (sous la pression des vaccins ?)
  - Souches produisant plus de PTX et ou légèrement modifiés (PTX-P3 allèle)
  - Souches déficientes en Pertactine, meilleur fitness sous pression vaccinale
- Limites des vaccins acellulaires ?

CMAJ Nov 2016

RESEARCH

Effectiveness of pertussis vaccination and duration of immunity

Kevin L. Schwartz MD, Jeffrey C. Kwong MD, Shelley L. Deeks MD, Michael A. Campitelli MPH, Frances B. Jamieson MD, Alex Marchand-Austin MSc, Therese A. Stukel PhD, Laura Rosella PhD, Nick Daneman MD, Shelly Bolotin PhD, Steven J. Drews PhD, Heather Rilkoff MPH, Natasha S. Crowcroft MD(Cantab)

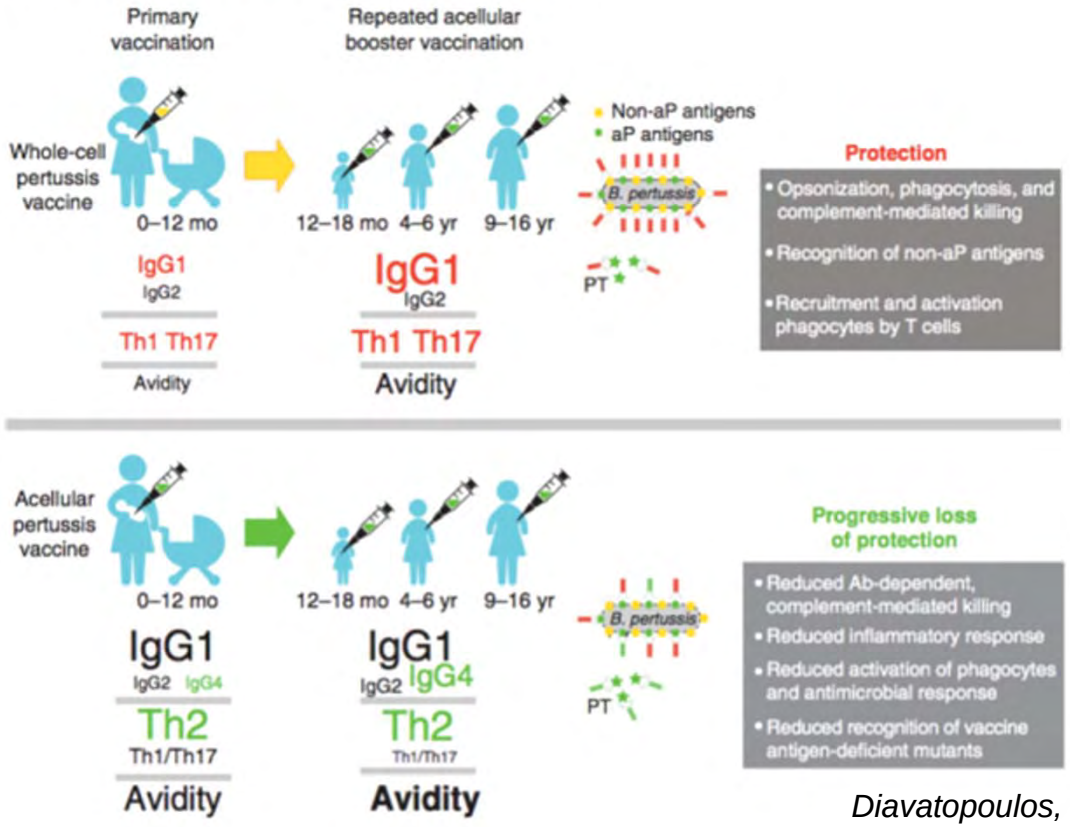


Interpretation: We observed high early effectiveness of the pertussis vaccine that rapidly declined as time since last vaccination surpassed 4 years, particularly with acellular vaccine priming. Considering whole-cell vaccine priming and/or boosters in pregnancy to optimize pertussis control may be prudent.

What Is Wrong with Pertussis Vaccine Immunity?

Why Immunological Memory to Pertussis Is Failing

Dimitri A. Diavatopoulos[1] and Kathryn Margaret Edwards[2,3]



Th17: joue aussi sur le portage et la transmission – immunité de groupe

Diavatopoulos, Cold Spring Harb Perspect Biol 2017

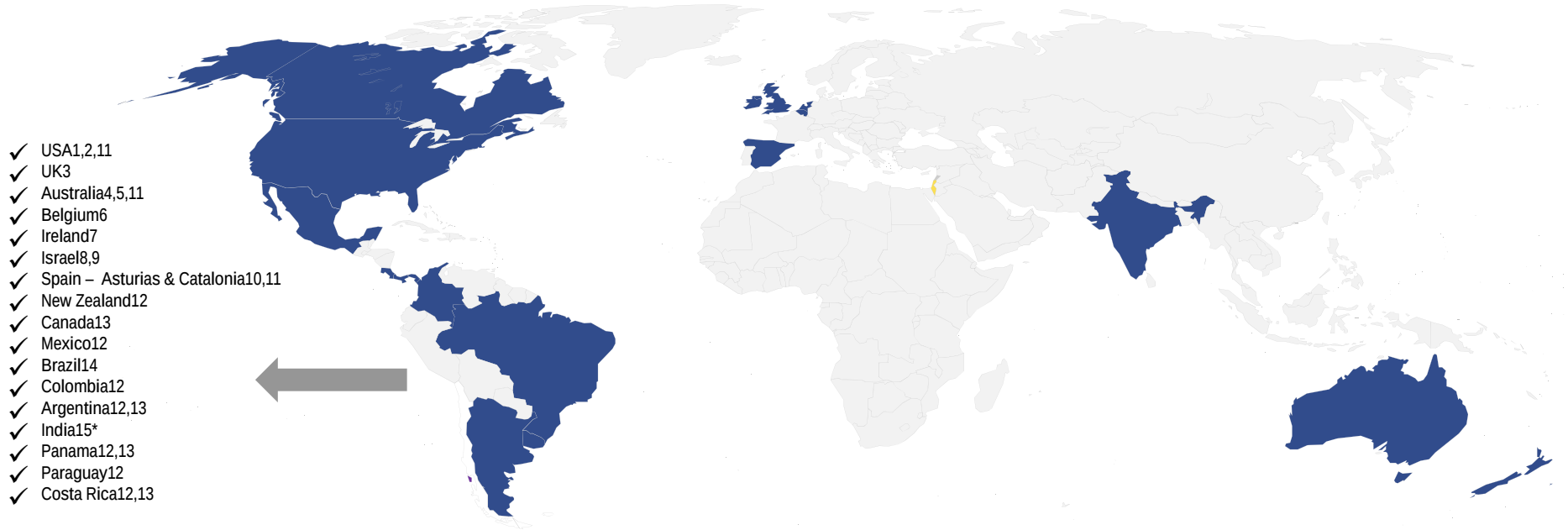
Protéger le jeune nourrisson : Vaccination de la femme enceinte

Concept : protéger la future maman pour protéger le bébé

- Effet barrière (comme le cocooning)
- Anticorps maternels transmis…
- A condition que les taux soient élevés... vaccination récente
- Anticorps anti toxine pertussique ++++

2012

Rappel coquelucheux pendant la grossesse



- * No national funding.

PEDIATRICS Volume 139, number 5, May 2017:

Roger Baxter, MD,[a] Joan Bartlett, MPH, MPP, Bruce Fireman, MA, Edwin Lewis, MPH, Nicola P. Klein, MD, PhD

Effectiveness of Vaccination During Pregnancy to Prevent Infant Pertussis

USA

WHAT THIS STUDY ADDS: Maternal Tdap vaccination during pregnancy is highly effective during the first 2 months of life. There was no evidence of interference between maternal Tdap and infant DTaP vaccines; instead, maternal Tdap vaccination adds to the protection infants receive from DTaP.

TABLE 3 Protection Agains … fant DTaP Vaccination in 148 981 Newborns
Followed From Bir … Pertussis Cases = 103)

	Person-Years)			
	No Maternal Tdap	Maternal Tdap	VE, % (95% CI)	*P*
Maternal Tdap during pregnancy (8+ days before birth)[a]				
0 DTaP doses (birth until day 7 after the first DTaPdose)	31 (177.2)	2 (14.8)	87.9 (41.4 to 97.5)	.009
Protected by 1 DTaP dose[b]	23 (170.3)	5 (43.2)	81.4 (42.5 to 94.0)	.004
Protected by 2 DTaP doses[b]	12 (88.5)	8 (72.8)	6.4 (−165.1 to 66.9)	.901
Protected by 3 DTaP doses[b]	14 (48.7)	7 (32.1)	65.9 (4.5 to 87.8)	.041
Maternal Tdap before pregnancy	89 (89.4)	14 (42.4)	55.6 (20.1 to 75.4)	.007
Maternal Tdap after pregnancy	80 (72.1)	23 (106.2)	24.1 (−28.5 to 55.1)	.305

Clinical Infectious Diseases

MAJOR ARTICLE

Maternal Immunization Earlier in Pregnancy Maximizes Antibody Transfer and Expected Infant Seropositivity Against Pertussis

Christiane S. Eberhardt,[1,2] Geraldine Blanchard-Rohner,[3] Barbara Lemaître,[1] Meriem Boukrid,[4] Christophe Combescure,[5] Véronique Othenin-Girard,[4] Antonina Chilin,[4] Jean Petre,[6] Begoña Martinez de Tejada,[4] and Claire-Anne Siegrist[1,3]

A quel terme vacciner?
3e trimestre? (première hypothèse)

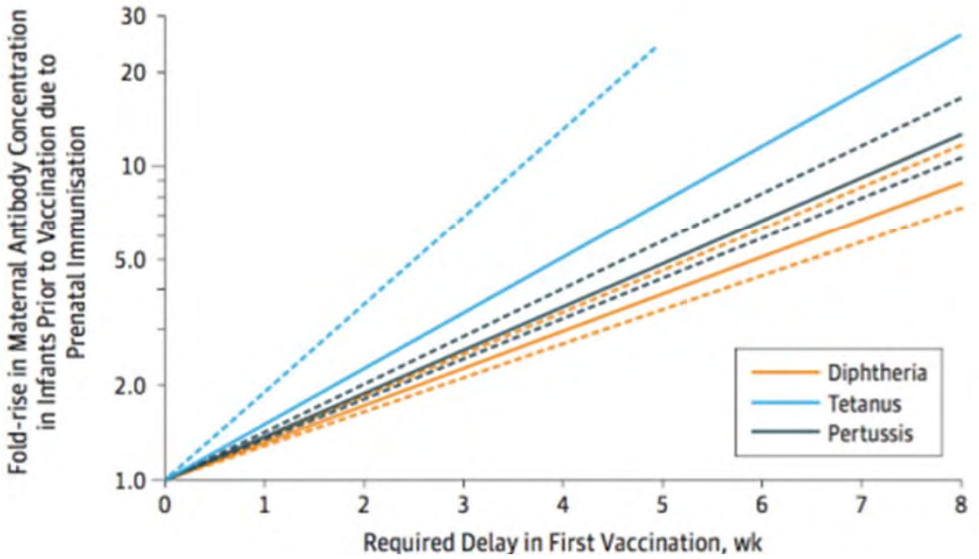
JAMA Pediatrics | Original Investigation

The Influence of Maternally Derived Antibody and Infant Age at Vaccination on Infant Vaccine Responses

An Individual Participant Meta-analysis

Merryn Voysey, MSc; Dominic F. Kelly, PhD; Thomas R. Fanshawe, PhD; Manish Sadarangani, DPhil; Katherine L. O'Brien, PhD; Rafael Perera, PhD; Andrew J. Pollard, PhD

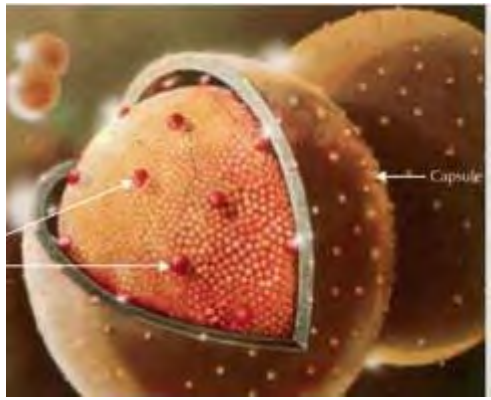
Figure 5. Number of Weeks' Delay Required to Offset the Effect of Increased Infant Concentrations of Maternal Antibody

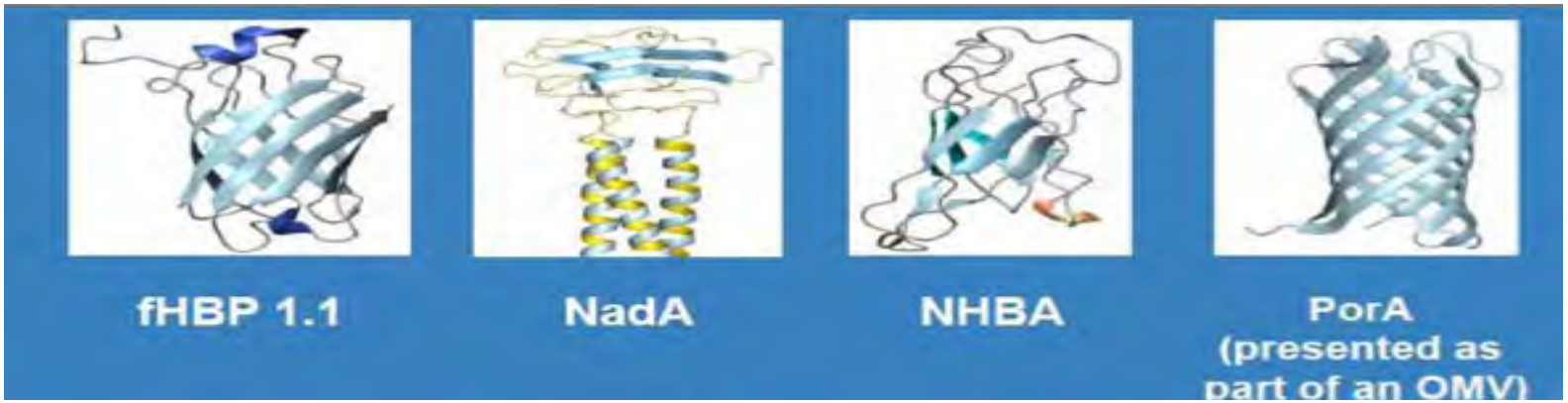


CONCLUSIONS AND RELEVANCE Maternal antibody concentrations and infant age at first vaccination both influence infant vaccine responses. These effects are seen for almost all vaccines contained in global immunization programs and influence immune response for some vaccines even at the age of 24 months. These data highlight the potential for maternal immunization strategies to influence established infant programs.

Vaccination Méningo B (4cMenB)?

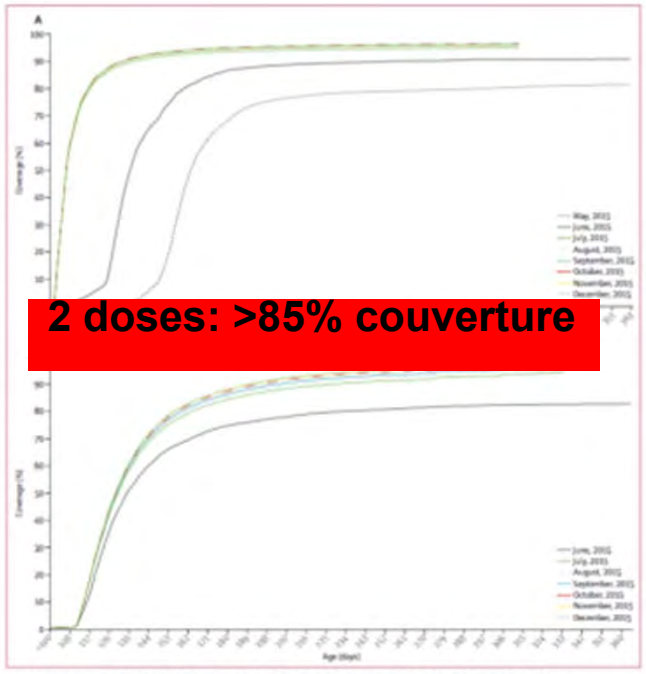
- Génétique inverse
- Vaccin protéique
- Entraîne la production d'Ac bactéricides (hSBA)
- Tolérance acceptable (fièvre)
- Couvrirait 73% des isolats UK (méthode MATS)





Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study

Sydel R Parikh, Nick J Andrews, Kazim Beebeejaun, Helen Campbell, Sonia Ribeiro, Charlotte Ward, Joanne M White, Ray Borrow, Mary E Ramsay, Shamez N Ladhani



2 doses: >85% couverture

Vaccination 2 + 4 mois

Findings Coverage of 4CMenB in infants eligible for routine vaccination was high, achieving 95·5% for one dose and 88·6% for two doses by 6 months of age. Two-dose vaccine effectiveness was 82·9% (95% CI 24·1–95·2) against all MenB cases, equivalent to a vaccine effectiveness of 94·2% against the highest predicted MenB strain coverage of 88%. Compared with the prevaccine period, there was a 50% incidence rate ratio (IRR) reduction in MenB cases in the vaccine-eligible cohort (37 cases *vs* average 74 cases; IRR 0·50 [95% CI 0·36–0·71]; p=0·0001), irrespective of the infants' vaccination status or predicted MenB strain coverage. Similar reductions were observed even after adjustment for disease trends in vaccine-eligible and vaccine-ineligible children.

Effet sur le portage?
Effet sur les autres sérotypes?

Lancet, 2016

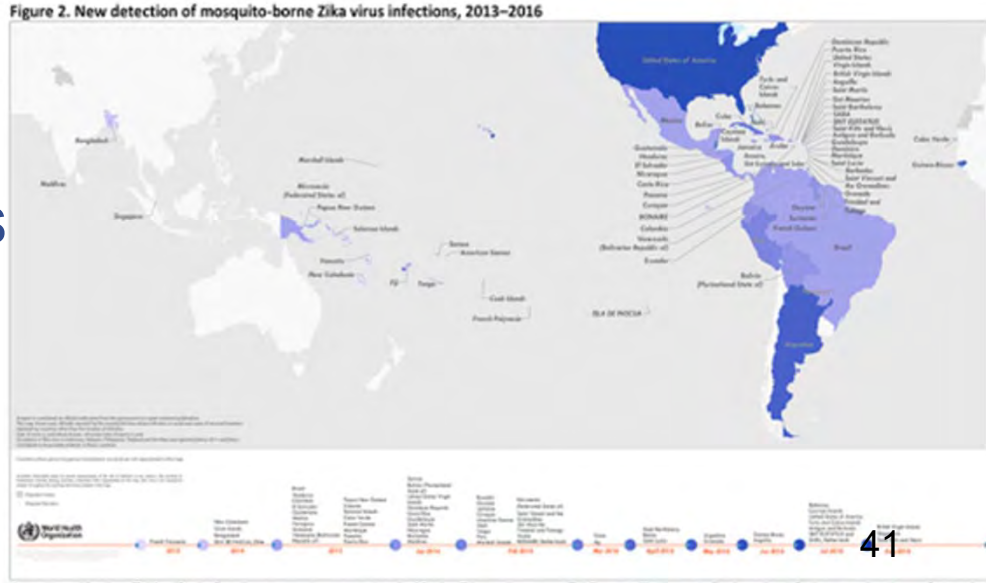
Virus Zika

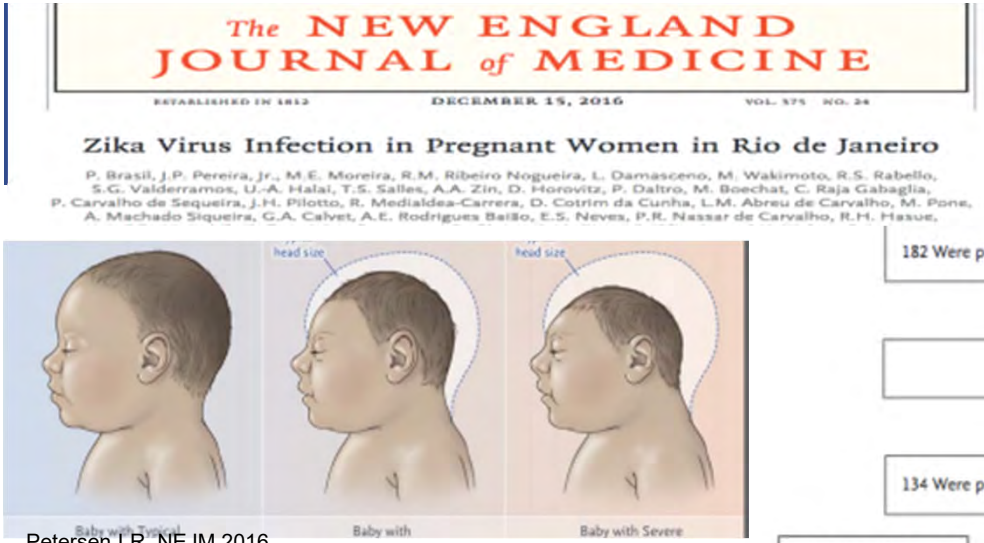
- Arbovirus, flavivirus
- Découverte sur macaque Rh, en Ouganda en 1947
- Transmission moustique *Aedes (aegypti albopictus*++), transmission sexuelle possible
- 25% asymptomatiques
- arthralgies œdème mains et pieds

erythème, conjonctivite, myalgies)

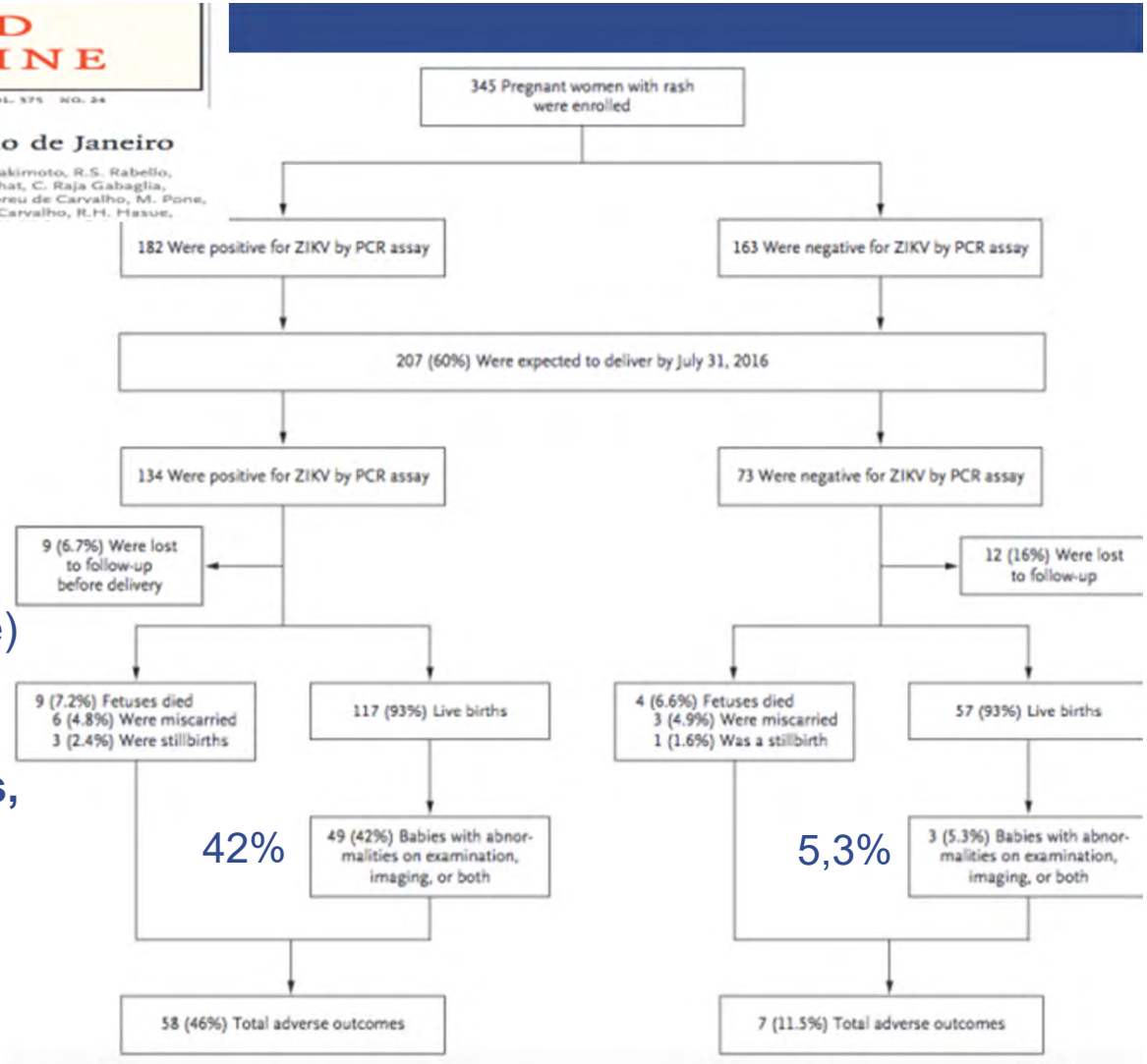
- Guillain Barré sd (incidence x2-17)

Figure 2. New detection of mosquito-borne Zika virus infections, 2013–2016





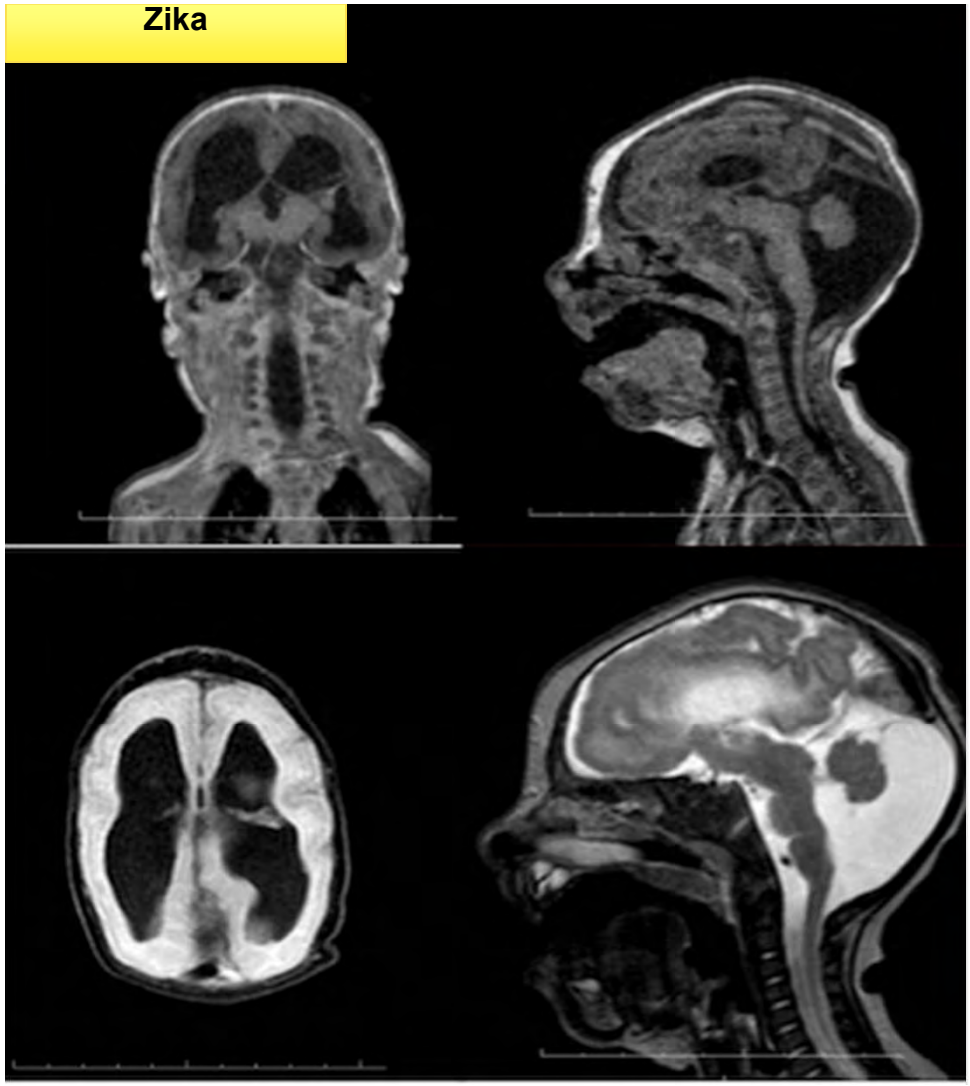
Petersen LR, NEJM 2016

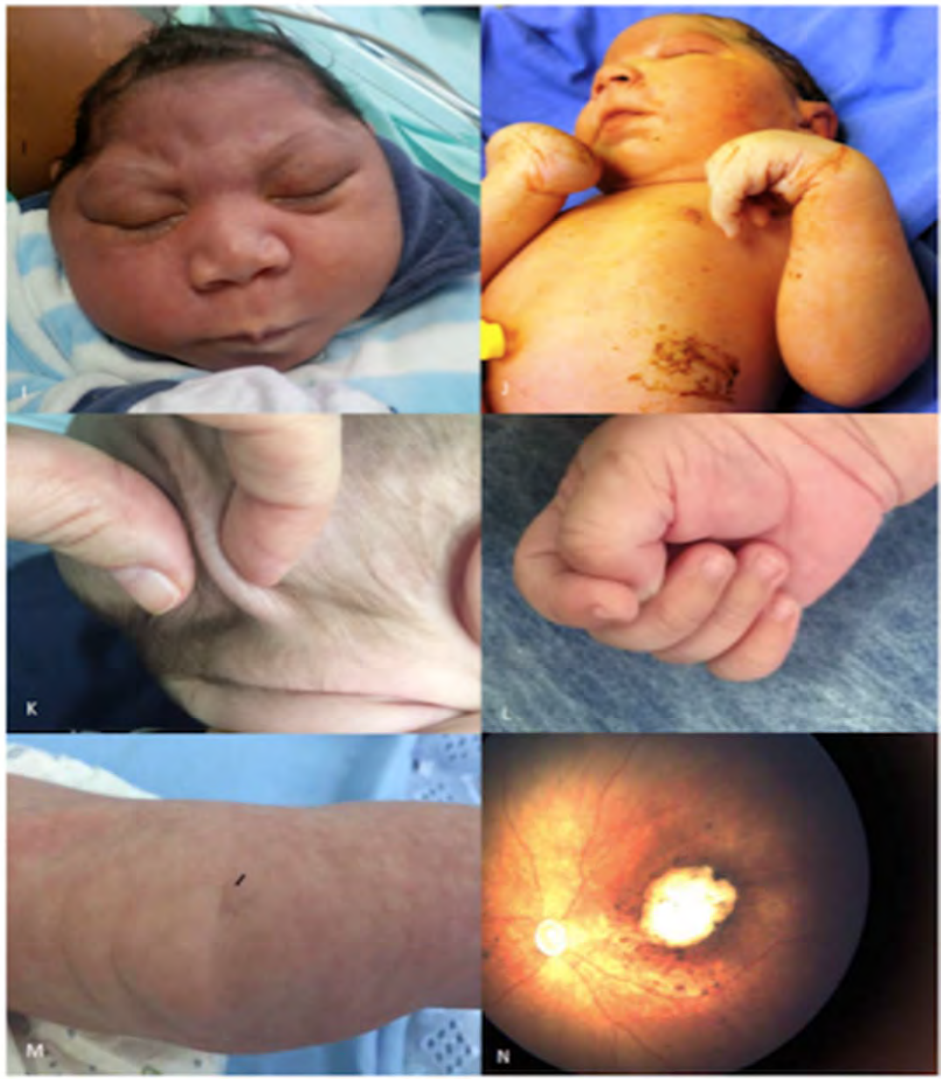


Anomalies : infection 6 – 39 SA

- **Microcephalie** (dysharmonieuse) si infection dans le 1er trimestre
- **Calcifications, hypoplasie/atrophie cérébrales, hémorragie**
- **Hypertonie, spasticité, convulsion, audition**
- **Autre?**

Zika



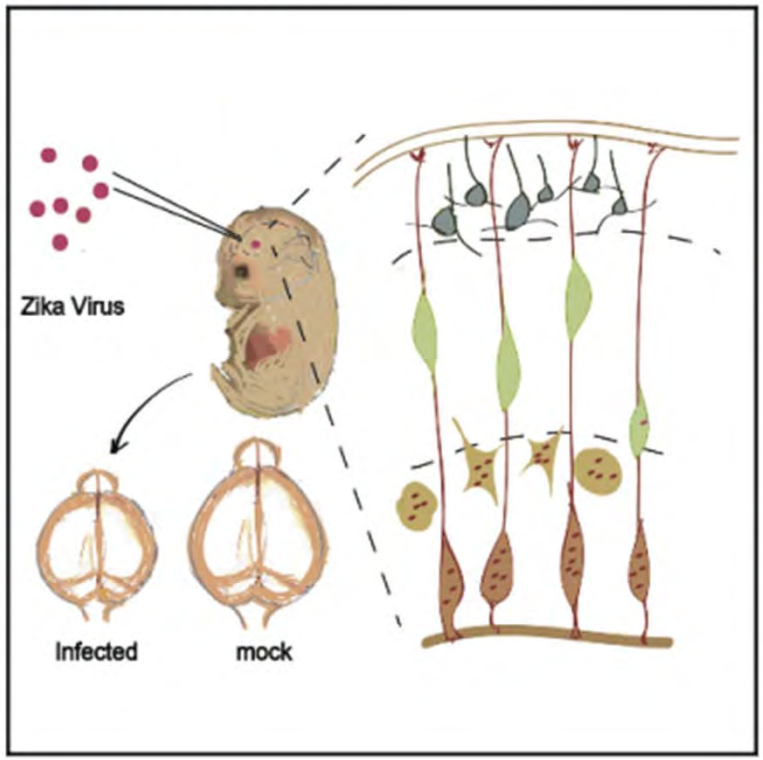


Cell Stem Cell

Short Article
2016

Zika Virus Disrupts Neural Progenitor Development and Leads to Microcephaly in Mice

Graphical Abstract



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In Brief

The suspected link between Zika virus (ZIKV) infection and microcephaly has raised urgent global alarm. However, there is so far no direct evidence for ZIKV infection impacting brain development. In this study, Li, Xu, and colleagues show that ZIKV replicates efficiently in the mouse embryonic brain by mainly targeting neural progenitor cells. They also show that infected brains are smaller with enlarged ventricles and a thinner cortex, consistent with a microcephalic phenotype.

Zika

Science

REPORTS

Cite as: P. L. Chavali *et al.*, *Science* 10.1126/science.aam9243 (2017).

Neurodevelopmental protein Musashi 1 interacts with the Zika genome and promotes viral replication

Pavithra L. Chavali,[1*†] Lovorka Stojic,[1*] Luke W. Meredith,[2] Nimesh Joseph,[1] Michael S. Nahorski,[3] Thomas J. Sanford,[2] Trevor R. Sweeney,[2] Ben A. Krishna,[4] Myra Hosmillo,[2] Andrew E. Firth,[2] Richard Bayliss,[5] Carlo L. Marcelis,[6] Susan Lindsay,[7] Ian Goodfellow,[2] C. Geoffrey Woods,[3] Fanni Gergely[1‡]

A recent outbreak of Zika virus in Brazil has led to a simultaneous increase in reports of neonatal microcephaly. Zika targets cerebral neural precursors, a cell population essential for cortical development, but the cause of this neurotropism remains obscure. Here we report that the neural RNA-binding protein Musashi-1 (MSI1) interacts with the Zika genome and enables viral replication. Zika infection disrupts the binding of MSI1 to its endogenous targets, thereby deregulating expression of factors implicated in neural stem cell function. We further show that MSI1 is highly expressed in neural progenitors of the human embryonic brain, and is mutated in individuals with autosomal recessive primary microcephaly. Selective MSI1 expression in neural precursors could therefore explain the exceptional vulnerability of these cells to Zika infection.

Merci pour votre attention !

Remerciements à R. Cohen, E. Launay, M. Chalumeau