Gestione clinica delle virosi respiratorie e complicanze infettive

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CIRI-IT Centro Interuniversitario Ricerca Influenza e altre Infezioni Trasmissibili

È solo influenza?
Epidemiologia dei patogeni respiratori e nuovi strumenti di prevenzione.

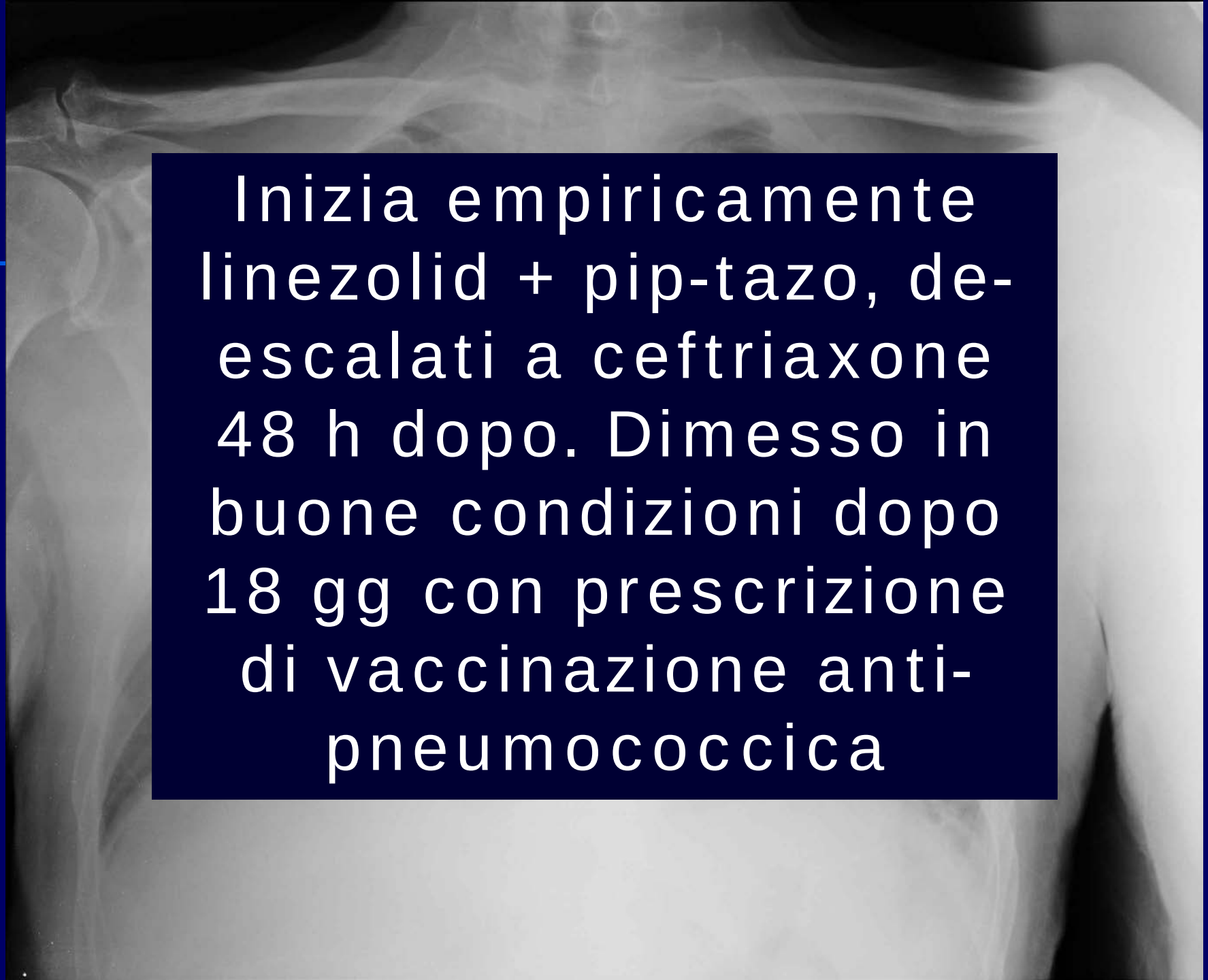
Aula A - Dipartimento di Scienze della Salute
Via A. Pastore, 1

Genova, 20 dicembre 2017

Caso clinico

- Uomo, 76 aa, BPCO
- Cardiomiopatia dilatativa in terapia con carvedilolo e diuretici
- Non vaccinato per pneumo
- Infezione alte vie aeree 7 gg prima (1 Aprile)
- Intubato in PS e trasferito in UTI per insufficienza respiratoria grave in quadro di sepsi severa

- 19.000 GB/µl, PCR 542, procalcitonina 82
- Ag urinari per pneumo positivo
- RT-PCR (tampone faringeo) positivo per metapneumovirus e coronavirus
- Emocolture positive per *Str. pneumoniae*



Inizia empiricamente linezolid + pip-tazo, de-escalati a ceftriaxone 48 h dopo. Dimesso in buone condizioni dopo 18 gg con prescrizione di vaccinazione anti-pneumococcica

NEW YORK POST

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NEW SARS CRISIS

$30B

The cost of deadly plague on economy

The staggering economic toll of SARS has already topped $30 billion — and it's expected to skyrocket even more, as panicked nations desperately fight to stem the spread of the deadly virus.

The Chinese capital of Beijing yesterday abruptly shuttered its theaters, discos and other entertainment centers where large groups of people are likely to gather, as news surfaced of nine more deaths there.

Meanwhile, in New York, Chinatown business leaders today plan to release details of a survey that found that SARS has devastated commerce in the neighborhood.

STORY: PAGES 4-5

A woman yesterday covers her face in Chinatown, where the fear of SARS has walloped business.

SARS

Sindrome respiratoria da coronavirus (SARS-CoV)

2002 Cina -→ Hong Kong 8000 casi → 774 decessi.

Causa: SARS coronavirus (SARS-CoV)

ACE2 identificato come recettore

Zoonosi: pipistrello, zibetto dell'Himalaya, trasmissione interumana

Epidemia rapidamente controllata

MERS

2012: Arabia Saudita 60enne obeso muore di insufficienza respiratoria acuta

Causa coronavirus (MERS-CoV) Medio Oriente

Recettore CD26

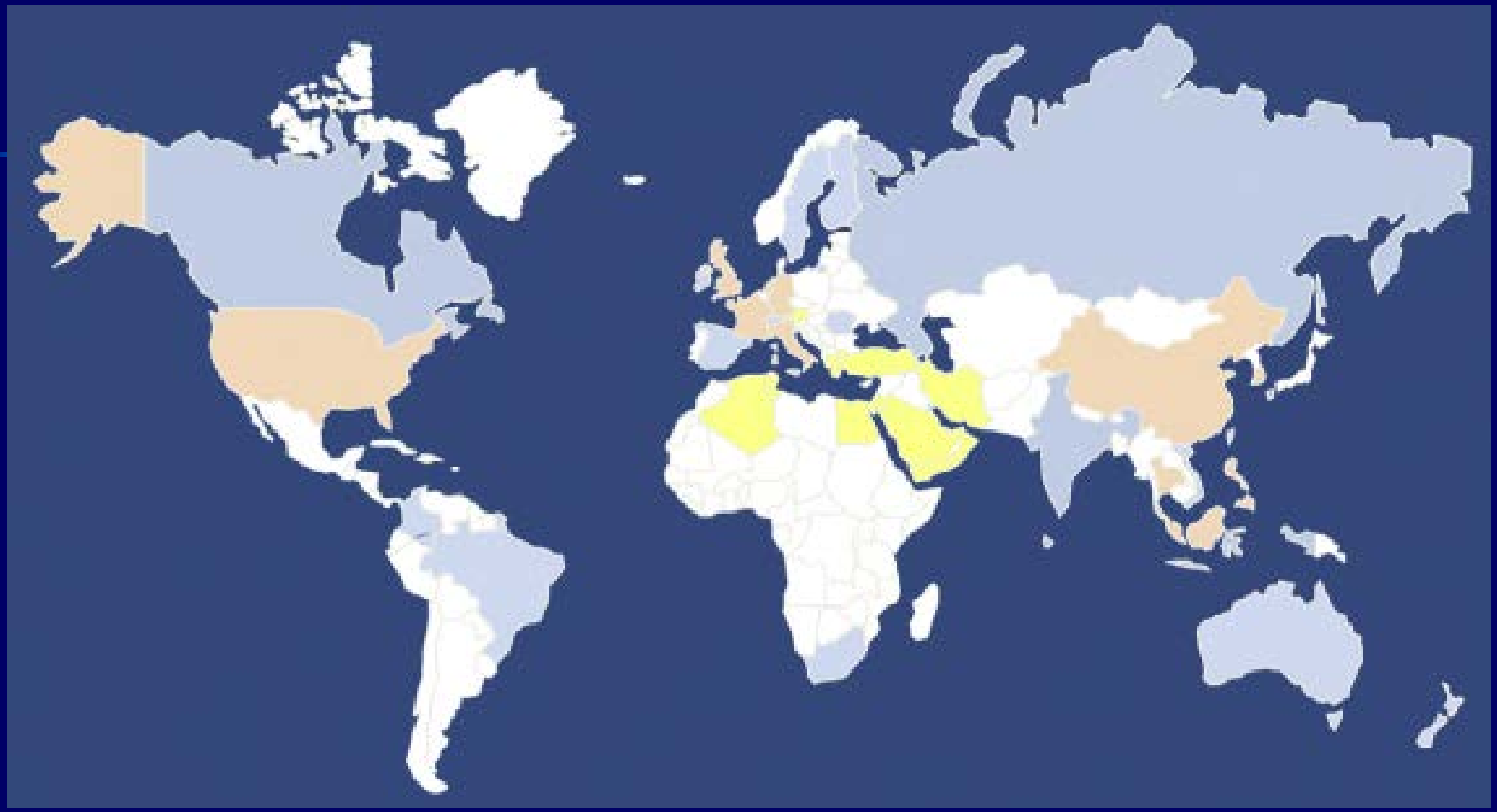
Zoonosi: pipistrello → dromedario →uomo

2000 casi mortalità 35% (FR >BMI, diabete, IRC) Trasmissione interumana in South Korea

Vaccino (MVA-CoV) efficace in dromedari

Epidemia sotto controllo

Diffusione globale di SARS e MERS



Lessons from 1918 influenza pandemic

- *Str.pneumoniae* was the most common (>50%) isolated bacterium in 16 of the 24 studies
- 274/371 (73.9%) blood cultures taken from pts with pneumonia were positive for *Str.pneumoniae*
- *Str.pneumoniae* was found in 173 (53.4%) of the 324 positive post-mortem cultures of heart blood and was the predominant organism in five of the eight autopsy studies

Klugman et al. Vaccine, 2009; 27: C9-C14

Impact of preceding respiratory viral infections on the clinical severity of patients with pneumococcal pneumonia

Young Kyung Yoon,[a,b] Kyung Sook Yang,[c] Jang Wook Sohn,[a,b] Chang Kyu Lee,[d] Min Ja Kim[a,b]

DOI: 10.1111/irv.12265
www.influenzajournal.com

Table 5. Multivariable logistic regression analysis of risk factors associated with severe pneumococcal pneumonia in 191 patients with pneumococcal pneumonia*

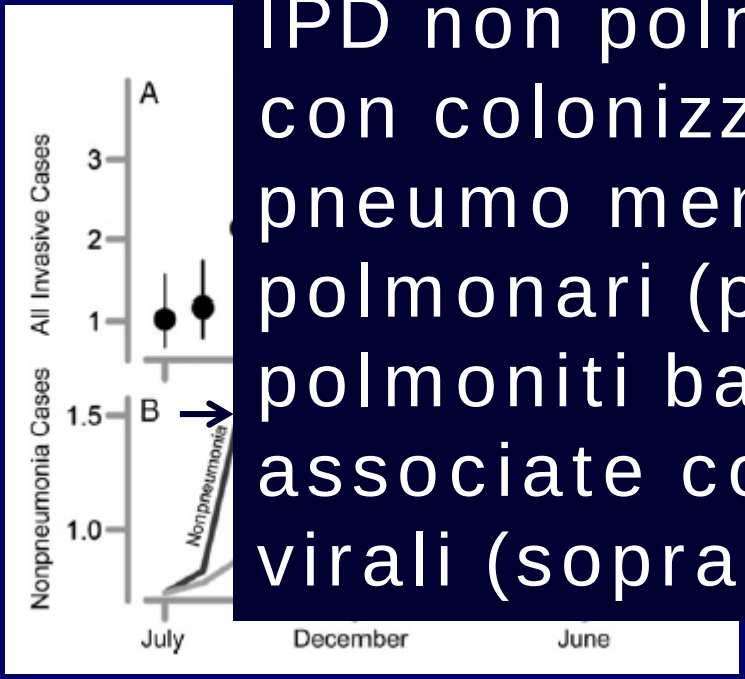
Variables	Odds ratio	95% confidence interval	*P*-value
Preceding respiratory viral infection	2·49	1·10–5·60	0·028
Male sex	2·58	1·24–5·38	0·012
Age ≥65 years	2·92	1·37–6·24	0·006
Albumin < 3·0 mg/dl	3·26	1·56–6·84	0·002
Blood urea nitrogen ≥19 mg/dl	2·24	1·08–4·67	0·031
Underlying diabetes mellitus	2·12	0·87–5·17	0·098
Underlying malignancy	2·36	0·91–6·12	0·079

Seasonal Drivers of Pneumococcal Disease Incidence: Impact of Bacterial Carriage and Viral Activity

Daniel M. Weinberger,[1,2] Lindsay R. Grant,[3] Claudia A. Steiner,[5] Robert Weatherholtz,[3] Mathuram Santosham,[3] Cécile Viboud,[2] and Katherine L. O'Brien[3,4]

Clinical Infectious Diseases 2014;58(2):188–94

IPD non polmonari associate con colonizzazione da pneumo mentre IPD polmonari (particolarmente polmoniti batteriemiche) associate con co-infezioni virali (soprattutto RSV)



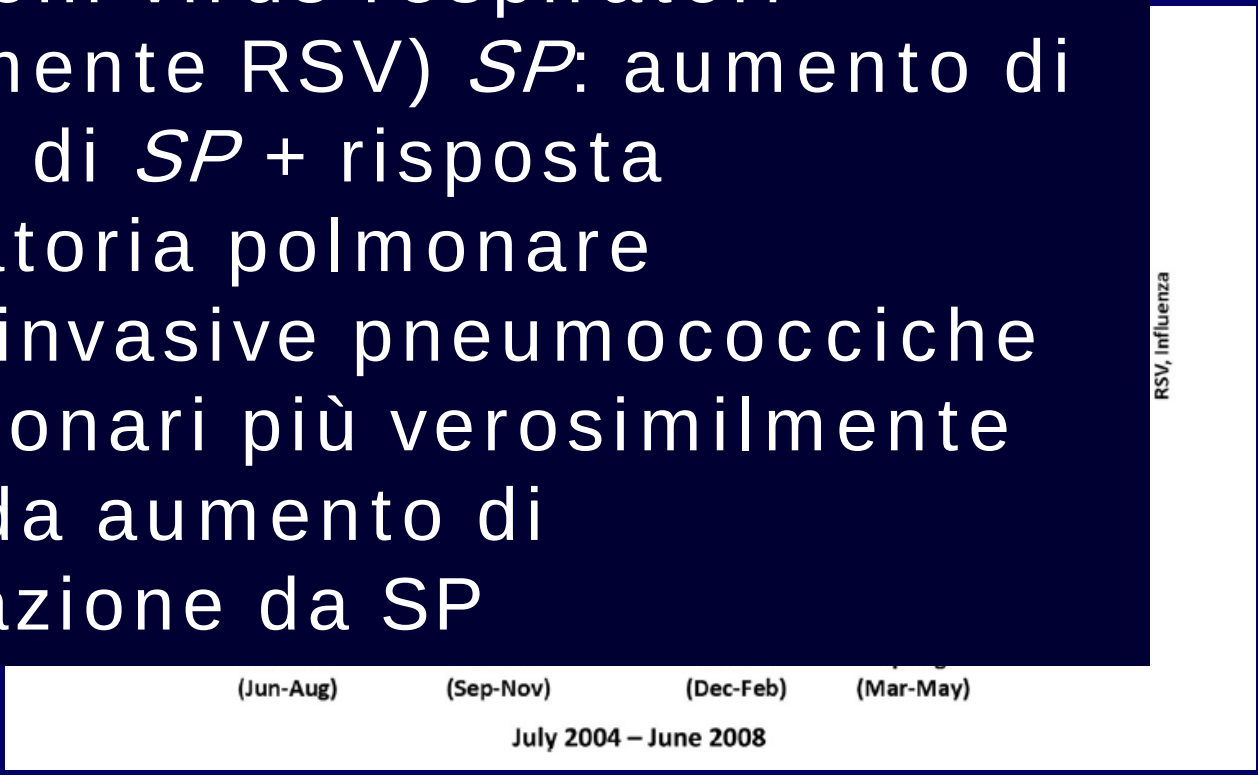
Seasonality of Both Bacteremic and Nonbacteremic Pneumonia Coincides With Viral Lower Respiratory Tract Infections in Early Childhood, in Contrast to Nonpneumonia Invasive Pneumococcal Disease, in the Pre-Pneumococcal Conjugate Vaccine Era

Shalom Ben-Shimol,[1,2] David Greenberg,[1,2] Guy Hazan,[1,2] Yonat Shemer-A

Clinical In

Co-infezioni virus respiratori (specialmente RSV) *SP*: aumento di virulenza di *SP* + risposta infiammatoria polmonare

Malattie invasive pneumococciche non polmonari più verosimilmente favorite da aumento di colonizzazione da SP



Risk factors for a poor outcome among children admitted with clinically severe pneumonia to a university hospital in Rabat, Morocco

Imane Jroundi [a,b], Chafiq Mahraoui [c,d], Rachid Benmessaoud [a], Cinta Moraleda [a], Houssain Tligui [c,d], Myriam Seffar [c], Salma Ech-Cherif El Kettani [c,d], Badr Sououd Benjelloun [c,d], Saad Chaacho [a,e], Carmen Muñoz-Almagro [f], Joaquim Ruiz [a], Pedro L. Alonso [a], Quique Bassat [a,*]

International Journal of Infectious Diseases 28 (2014) 164–170

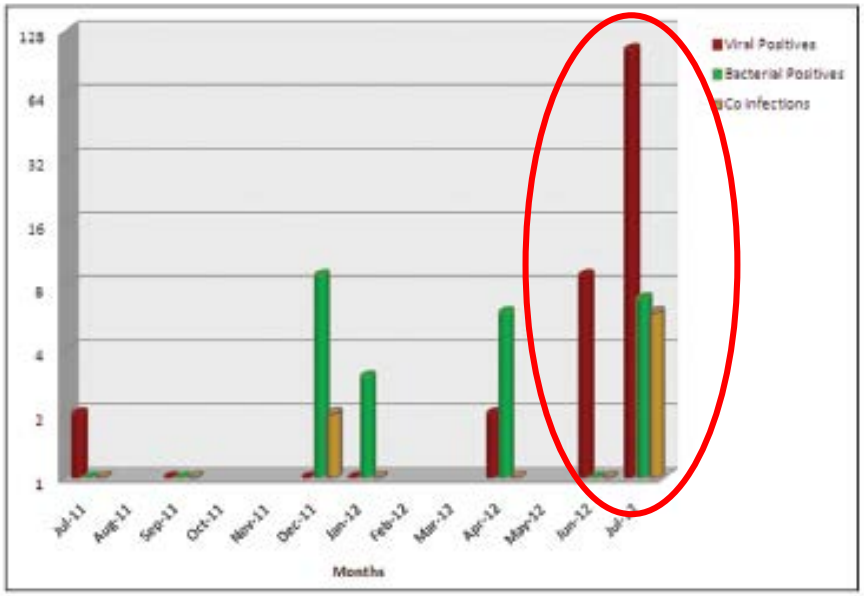
Table 4
Independent risk factors for a poor prognosis among admitted Moroccan children with WHO-defined severe pneumonia, according to multivariate analysis[a]

Risk factors for a poor prognosis	Adjusted OR	95% CI		p-Value[b]
		Lower	Upper	
History of prematurity	2.50	1.24	5.04	0.010
History of asthma	0.46	0.25	0.84	0.012
History of fever	2.25	1.32	3.83	0.003
Smoker at home	1.79	1.18	2.72	0.006
Pallor	2.27	1.34	3.84	0.002
Cyanosis	2.09	1.05	4.15	0.035
Rhonchi	2.45	1.58	3.79	<0.001
Impaired consciousness	10.96	2.88	41.73	<0.001
Human metapneumovirus infection	2.13	1.13	4.02	0.019

Surveillance of Acute Respiratory Infections in Mumbai during 2011-12

*RD Chavan, ST Kothari, K Zunjarrao, AS Chowdhary

Indian Journal of Medical Microbiology, (2015) 33(1): 43-50



Increased Risk for and Mortality From Invasive Pneumococcal Disease in HIV-Exposed but Uninfected Infants Aged <1 Year in South Africa, 2009–2013

Claire von Mollendorf,[1,2] Anne von Gottberg,[1,3] Stefano Tempia,[1,4,5] Susan Meiring,[6] Linda de Gouveia,[1] Vanessa Quan,[6] Sarona Lengana,[1] Theunis Avenant,[7] Nicolette du Plessis,[7] Brian Eley,[8] Heather Finlayson,[9] Gary Reubenson,[10] Mamokgethi Moshe,[11] Katherine L. O'Brien,[12] Keith P. Klugman,[13,14] Cynthia G. Whitney,[15] and Cheryl Cohen[1,2]; for the Group for Enteric, Respiratory and Meningeal Disease Surveillance in South Africa (GERMS-SA)

Clinical Infectious Diseases Advance Access published February 23, 2015

Table 1. Invasive Pneumococcal Disease Incidence Rates and Incident Rate Ratios Between Infants Aged <12 Months, <6 Months, and 6 to <12 Months, South Africa, 2009 and 2013

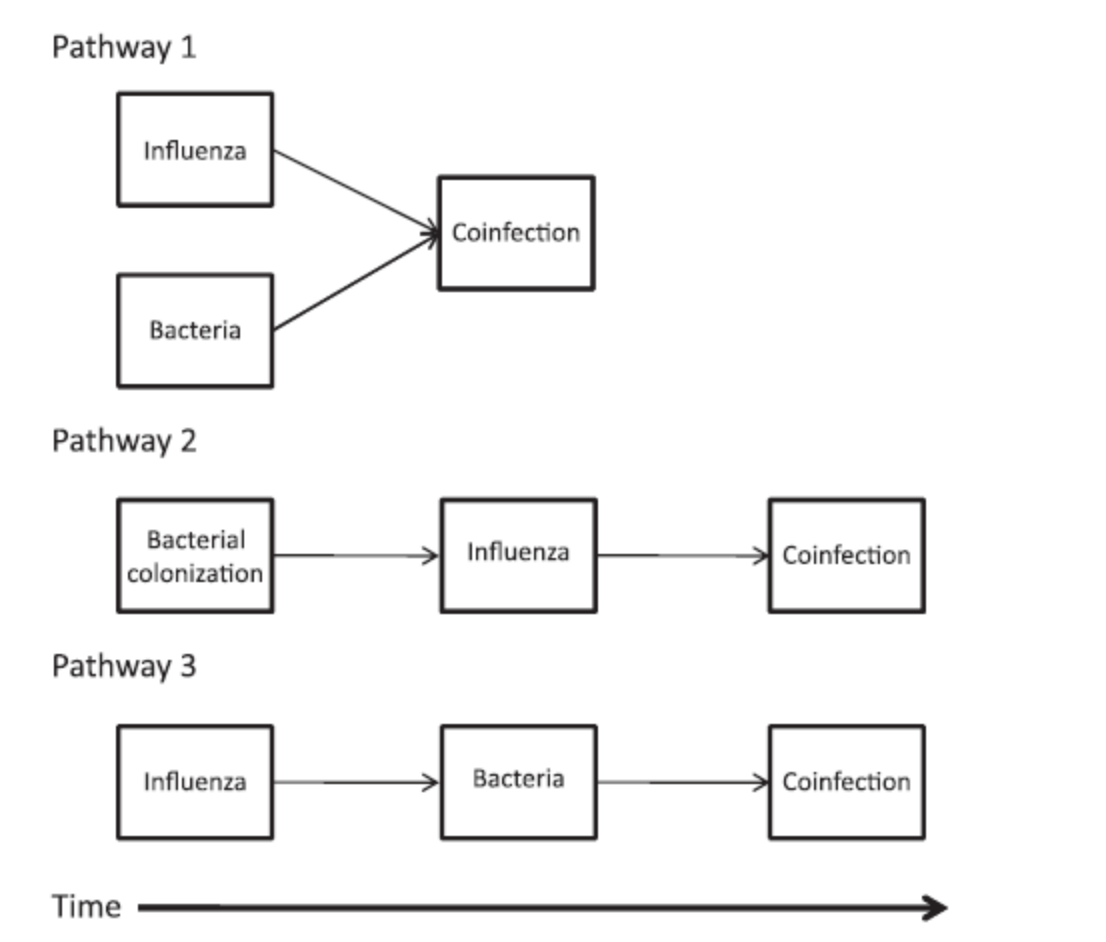
	Incidence Rates per 100 000 Population (95% CI)			Incidence Rate Ratio (95% CI)		
Age Group	HI	HEU	HUU	HI/HEU	HI/HUU	HEU/HUU
2009 (prevaccine)						
<6 mo	1156 (972–1364)	112 (94–132)	31 (26–37)	10.3 (8.1–13.1)	37.0 (29.0–47.2)	3.6 (2.8–4.6)
6 to <12 mo	467 (394–551)	59 (46–75)	26 (21–31)	7.9 (5.9–10.8)	18.0 (14.0–23.3)	2.3 (1.7–3.1)
<12 mo	654 (579–736)	88 (76–100)	28 (25–32)	7.5 (6.2–9.0)	23.1 (19.4–27.6)	3.1 (2.6–3.7)
2013 (postvaccine)						
<6 mo	581 (389–835)	57 (46–71)	21 (17–26)	10.1 (6.4–15.7)	27.2 (17.2–41.7)	2.7 (2.0–3.7)
6 to <12 mo	149 (92–227)	11 (6–18)	14 (11–18)	13.9 (6.7–29.5)	10.4 (6.0–17.4)	0.8 (.4–1.4)
<12 mo	272 (203–357)	33 (26–40)	18 (15–21)	8.4 (5.9–12.0)	15.0 (10.7–20.6)	1.8 (1.4–2.3)

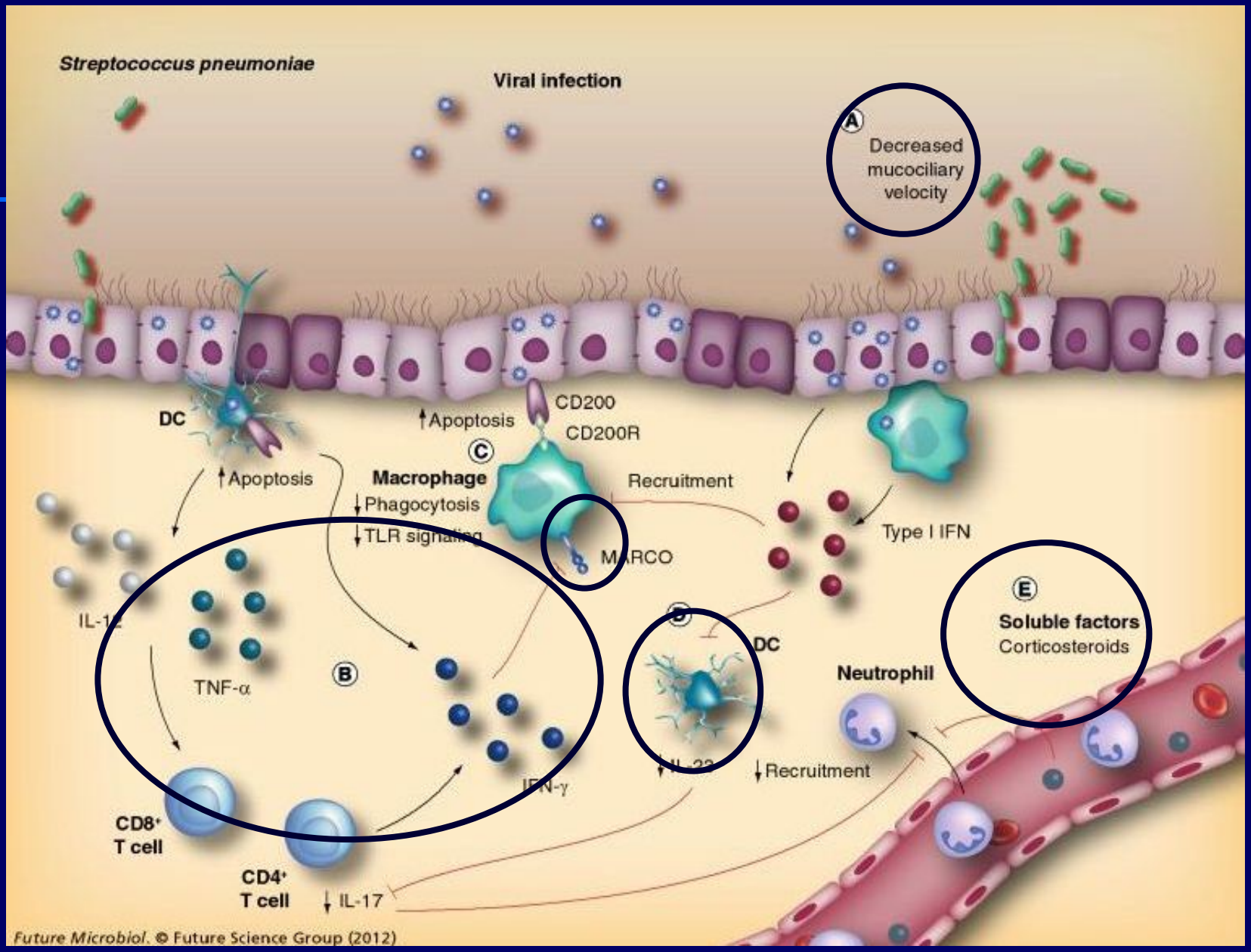
Abbreviations: CI, confidence interval; HEU, HIV exposed but uninfected; HI, HIV infected; HIV, human immunodeficiency virus; HUU, HIV unexposed and uninfected.

Influenza and Community-acquired Pneumonia Interactions: The Impact of Order and Time of Infection on Population Patterns

Brian M. Davis, Allison E. Aiello, Suzanne Dawid, Pejman Rohani, Sourya Shrestha, and Betsy Foxman*

Am J Epidemiol. 2012;175(5):363–367




Streptococcus pneumoniae
Viral infection
A
Decreased mucociliary velocity
DC
Apoptosis
CD200
CD200R
Apoptosis
C
Macrophage
Phagocytosis
TLR signaling
Recruitment
MARCO
Type I IFN
IL-1β
TNF-α
B
IFN-γ
D
DC
IL-23
Recruitment
E
Soluble factors
Corticosteroids
Neutrophil
CD8+ T cell
CD4+ T cell
IL-17
Future Microbiol. © Future Science Group (2012)

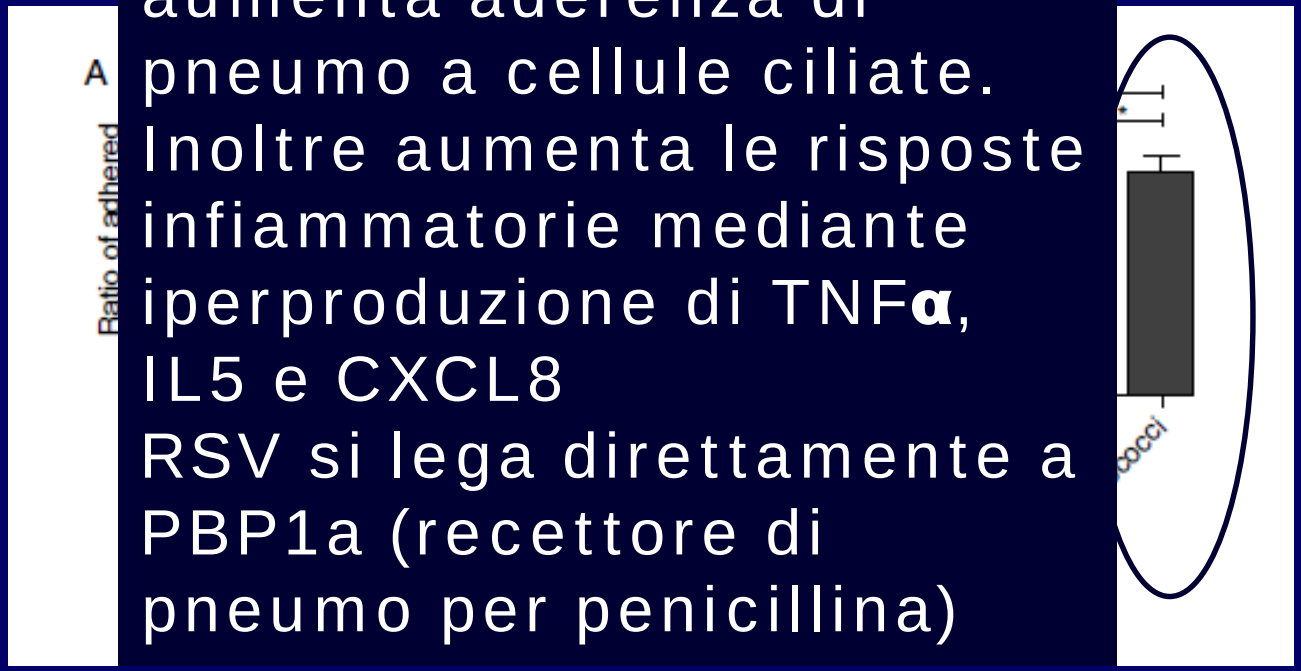
Respiratory Syncytial Virus Increases the Virulence of *Streptococcus pneumoniae* by Binding to Penicillin Binding Protein 1a

A New Paradigm in Respiratory Infection

Claire M. Smith[1,2], Sara Sandrini[2], Sumit Datta[2], Primrose Freestone[2], Sulman Shafeeq[3], Priya Radhakrishnan[1], Gwyneth Williams[2], Sarah M. Glenn[2], Oscar P. Kuipers[3], Robert A. Hirst[2], Andrew J. Easton[4], Peter W. Andrew[2], and Christopher O'Callaghan[1]

Am J Respir Crit Care Med Vol 190, Iss 2, pp 196–207, Jul 15, 2014

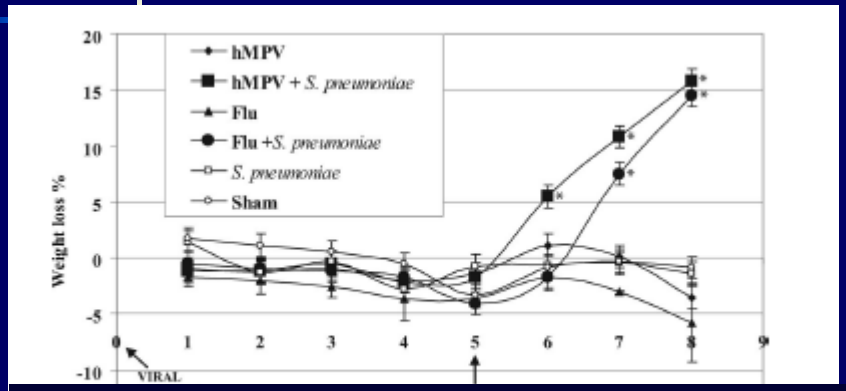
Interazione RSV-pneumo aumenta aderenza di pneumo a cellule ciliate.
Inoltre aumenta le risposte infiammatorie mediante iperproduzione di TNF**α**, IL5 e CXCL8
RSV si lega direttamente a PBP1a (recettore di pneumo per penicillina)

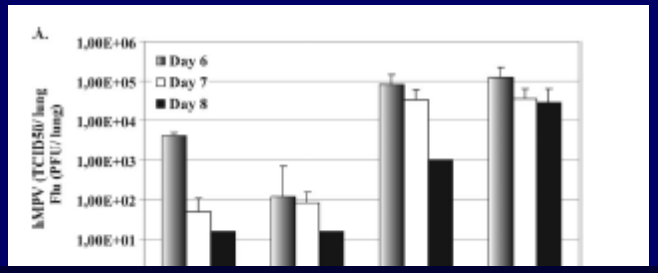


Infection with Human Metapneumovirus Predisposes Mice to Severe Pneumococcal Pneumonia[▽]

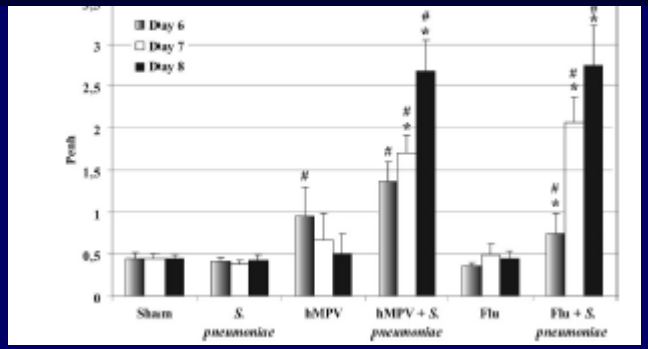
Irena Kukavica-Ibrulj,[1] Marie-Ève Hamelin,[1] Gregory A. Prince,[2] Constance Gagnon,[1] Yves Bergeron,[1] Michel G. Bergeron,[1] and Guy Boivin[1]*

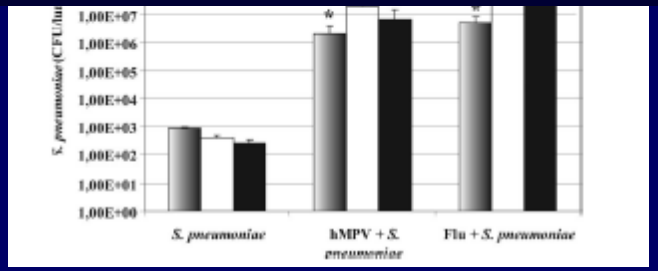
JOURNAL OF VIROLOGY, Feb. 2009, p. 1341–1349





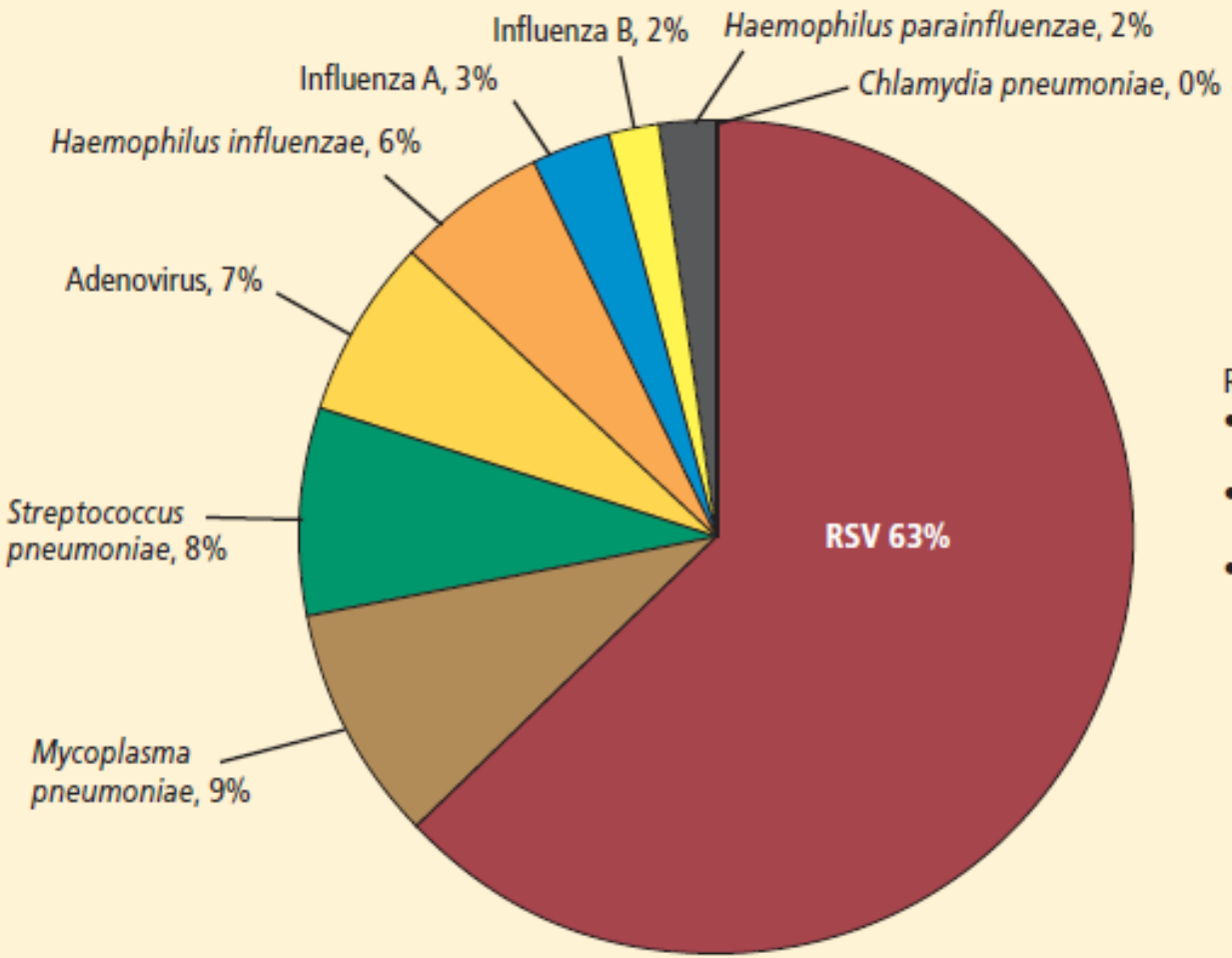
Co-infection virus-pneumo determines increase of: weight loss, airway obstruction, bacterial load





RSV infections: State of the art

Piedimonte G. Cleveland Clinic Journal Of Medicine, 2015



RSV accounts for:

- > 60% of ARIs during entire respiratory season
- 90% of ARIs at peak of respiratory season
- 80% of ARIs in infants < 1 year old during entire respiratory season

Clinical characteristics and outcome of respiratory syncytial virus infection among adults hospitalized with influenza-like illness in France

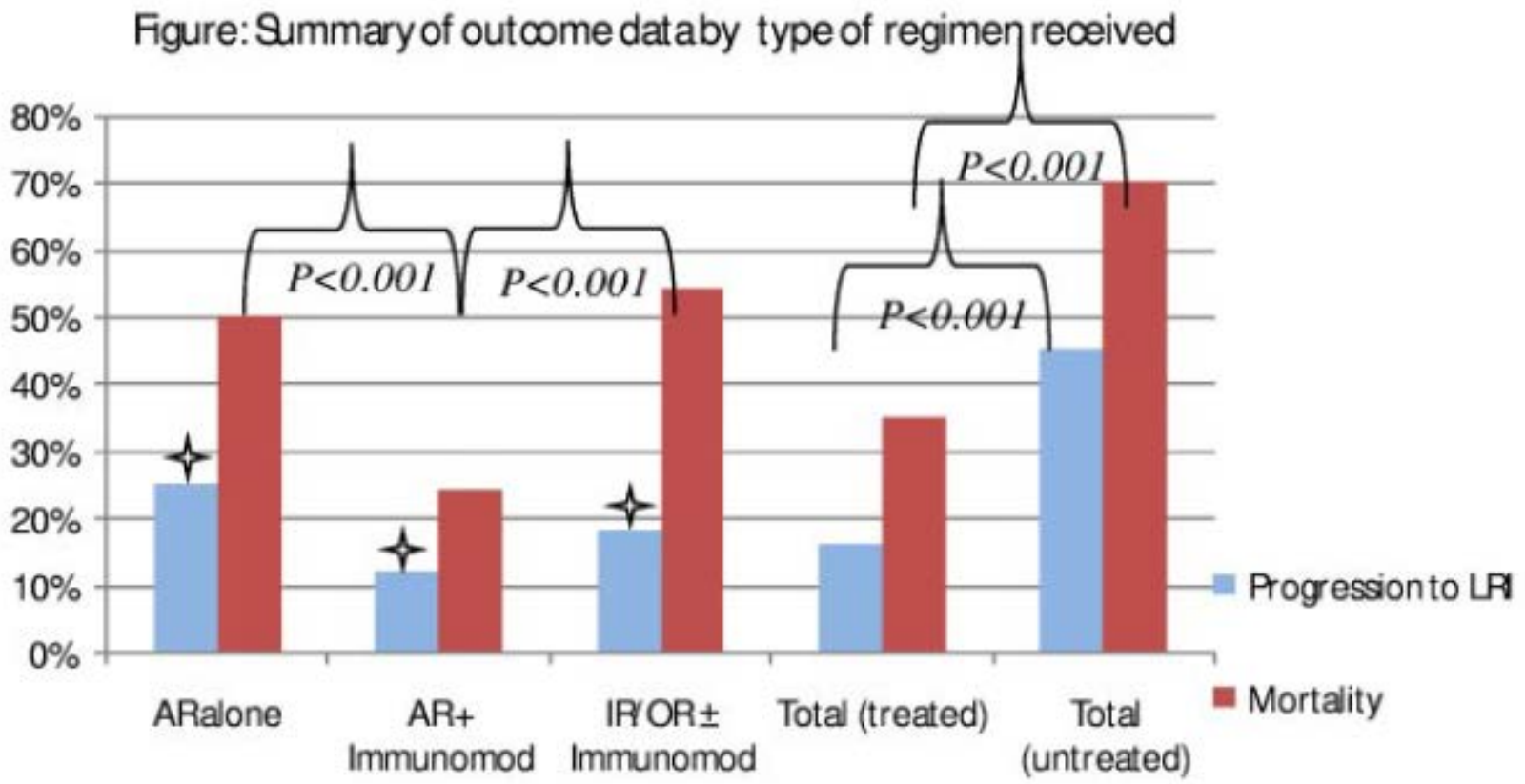
Table 4

Factors associated with pneumonia occurrence (n = 385) among hospitalized patients with influenza-like illness in multivariable logistic regression (excluding patients infected with both respiratory syncytial virus (RSV) and influenza virus)

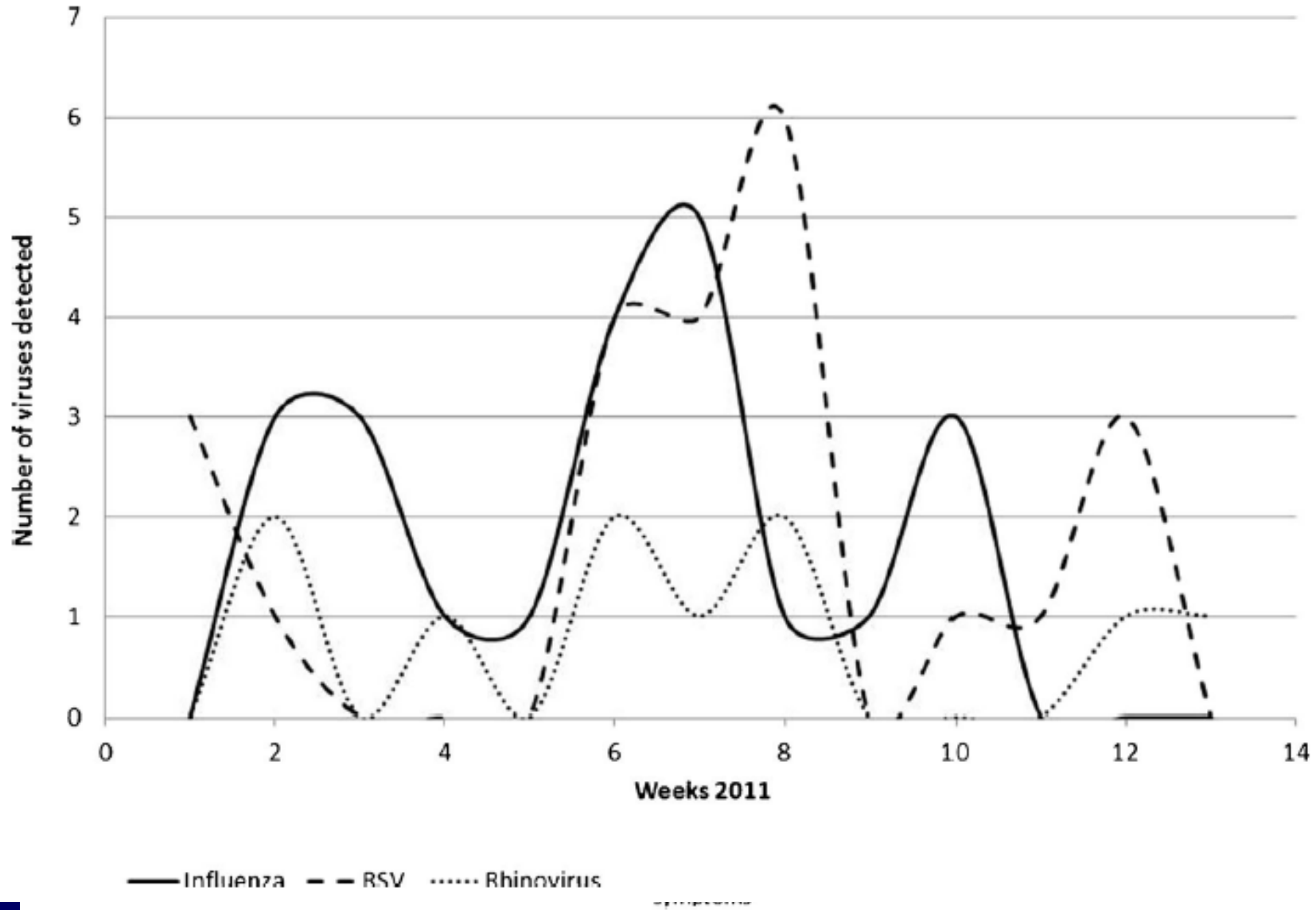
	n/N (%)	Crude OR (95% CI)	p	Adjusted OR (95% CI)	p
Age[a]	—	1.1 (0.9–1.5)	0.20	1.0 (0.9–1.1)	0.20
Chronic respiratory disease			0.7		0.9
No	206/784 (26)	1		1	
Yes	179/657 (27)	1.1 (0.8–1.3)		1.0 (0.8–1.2)	
Chronic cardiac disease			0.03	—	—
No	205/835 (25)	1			
Yes	180/606 (30)	1.3 (1.0–1.6)			
Diabetes			0.9	—	—
No	291/1025 (27)	1			
Yes	94/356 (26)	0.9 (0.7–1.3)			
Chronic renal failure			0.001		0.001
No	313/1249 (25)	1		1	
Yes	72/192 (38)	1.8 (1.3–2.5)		1.8 (1.3–2.5)	
Cancer			0.15	—	—
No	314/1210 (26)	1			
Yes	71/232 (31)	1.3 (0.9–1.7)			
Immunosuppressive treatment			0.6	—	—
No	323/1222 (26)	1			
Yes	62/220 (28)	1.1 (0.8–1.5)			
Influenza vaccination			0.5	—	—
No	205/783 (26)	1			
Yes	177/640 (28)	1.1 (0.9–1.4)			
Active smoking			0.02		0.02
No	170/705 (24)	1		1	
Yes	212/722 (29)	1.3 (1.0–1.7)		1.3 (1.0–1.7)	
RSV infection			0.005		0.008
No	362/1390 (26)	1		1	
Yes	23/52 (44)	2.3 (1.3–3.9)		2.1 (1.2–3.8)	
Influenza virus infection			0.4	—	—
No	228/882 (26)	1			
Yes	157/760 (28)	1.1 (0.9–1.4)	0.4		

Management of RSV infections in adult recipients of hematopoietic stem cell transplantation

Jharna N. Shah[1] and Roy F. Chemaly[1]



Epidemiology of viral respiratory tract infections



Considerazioni conclusive

- Sinergismo virus respiratori (influenza, RSV e hMPV) e *S.pneumoniae* (dati epidemiologici e sperimentali)
- Clinica più severa di IPD nelle coinfezioni
- Attenzione a virosi respiratorie nel paziente fragile

Grazie per l'attenzione!