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VACCINI E VACCINAZIONI

NAPOLI
11 giugno 2016

Martino Barretta

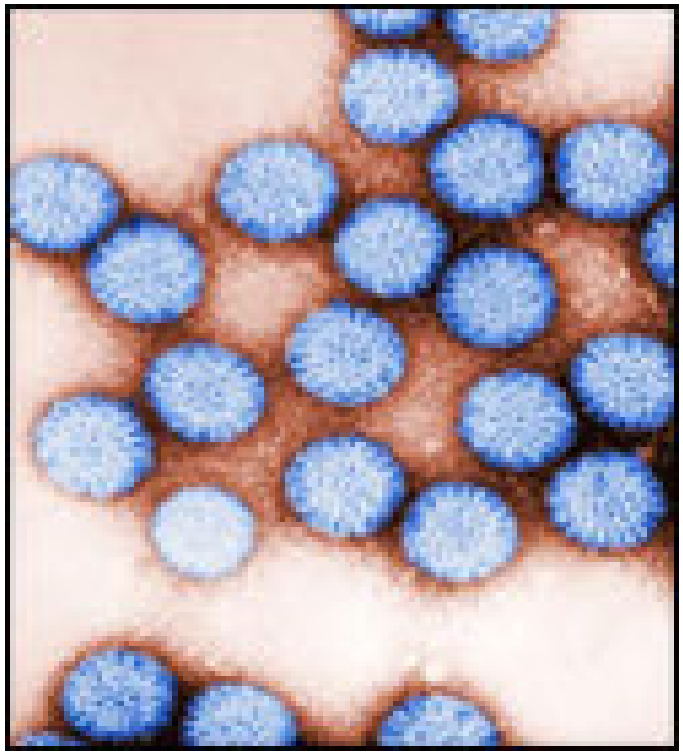
Rotavirus: ci convinciamo, dati alla mano, a vaccinare?

Vaccinando su e giù per lo stivale

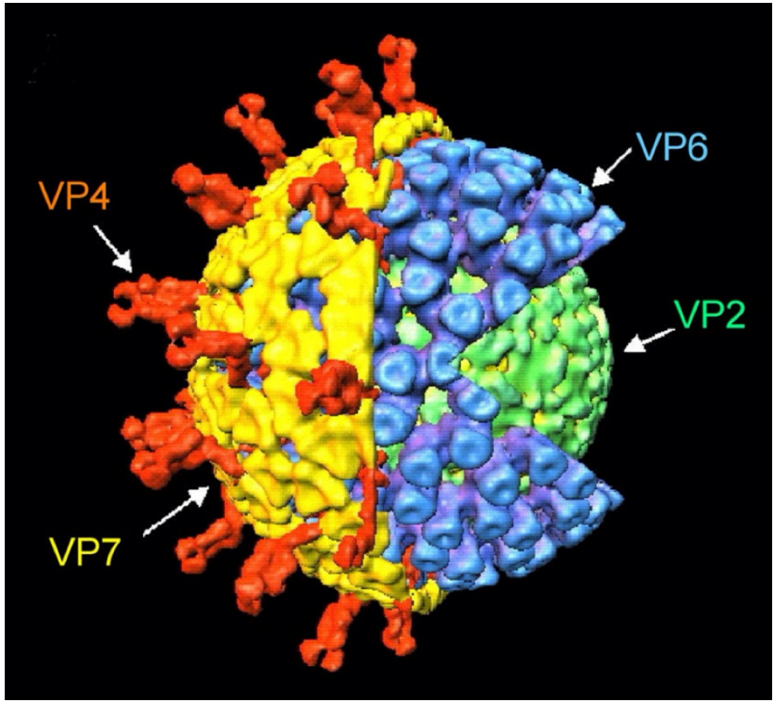
2ª edizione

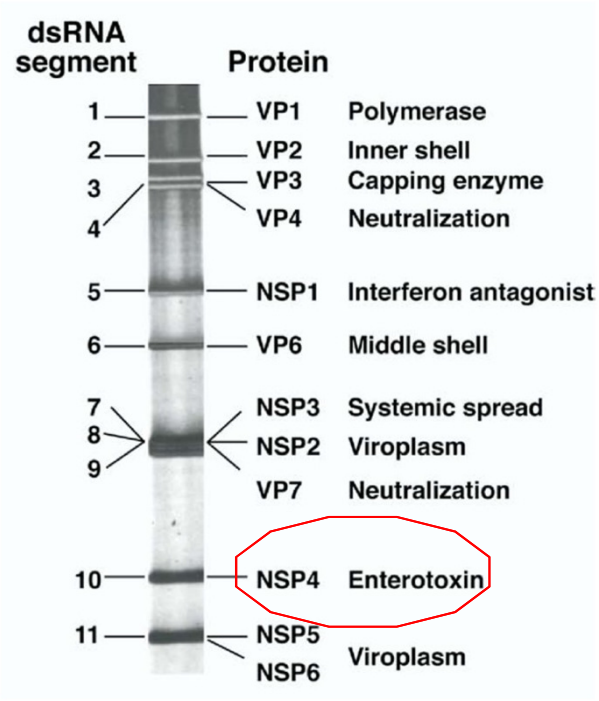
Rotavirus

Sono stati identificati nel 1973, da Bishop, nella mucosa duodenale di un bambino affetto da diarrea, virioni morfologicamente simili a quelli già isolati in altre specie animali



Rotavirus umani

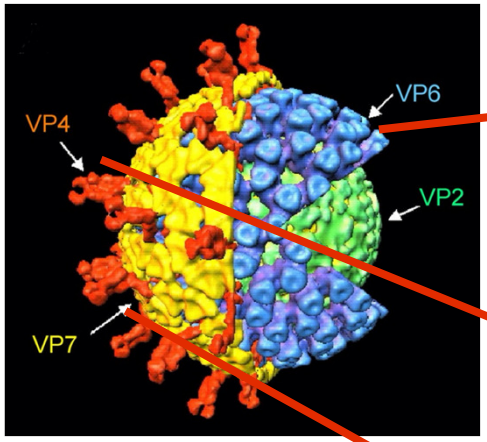




Virus costituito da 3 strati proteici che avvolgono il genoma

Genoma: 11 segmenti ognuno codifica almeno una proteina

Rotavirus umani



VP6 — **Gruppo** — **A** B C

D, E, F, G

VP4 ⬇ **P** (1-15)

VP7 ⬇ **G** (1-12)

Sierotipo

Sierotipi più comuni nell'uomo

G1P[8] **G2P[4]** **G3P[8]** **G4P[8]** **G9P[8]**

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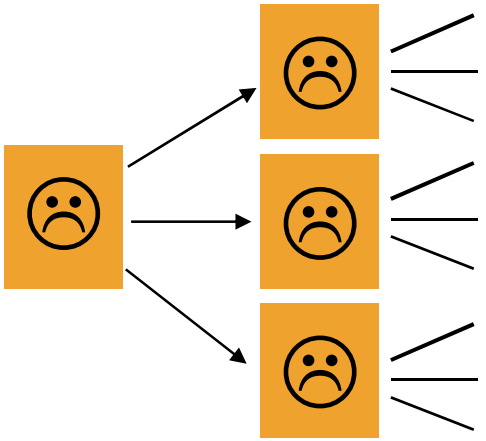
Rotavirus umani

✓ **virus altamente contagioso (***bastano 100 particelle virali, 1 gr di feci ne contiene miliardi)*

Tasso di contagiosità' R0:

- Morbillo 15
- Rotavirus 10
- Poliomielite 5



Penelope H. Dennehy Advance in pediatrics 59(2012) 47-74;

Rotavirus umani

- ✓ **Il virus entra nell'organismo attraverso la via orale**
- ✓ **La replicazione avviene nell'epitelio dell'intestino tenue. La replicazione fuori dall'intestino e la diffusione sistemica (viremia) è ancora sconosciuta**
- ✓ **L'infezione provoca diarrea più o meno grave**

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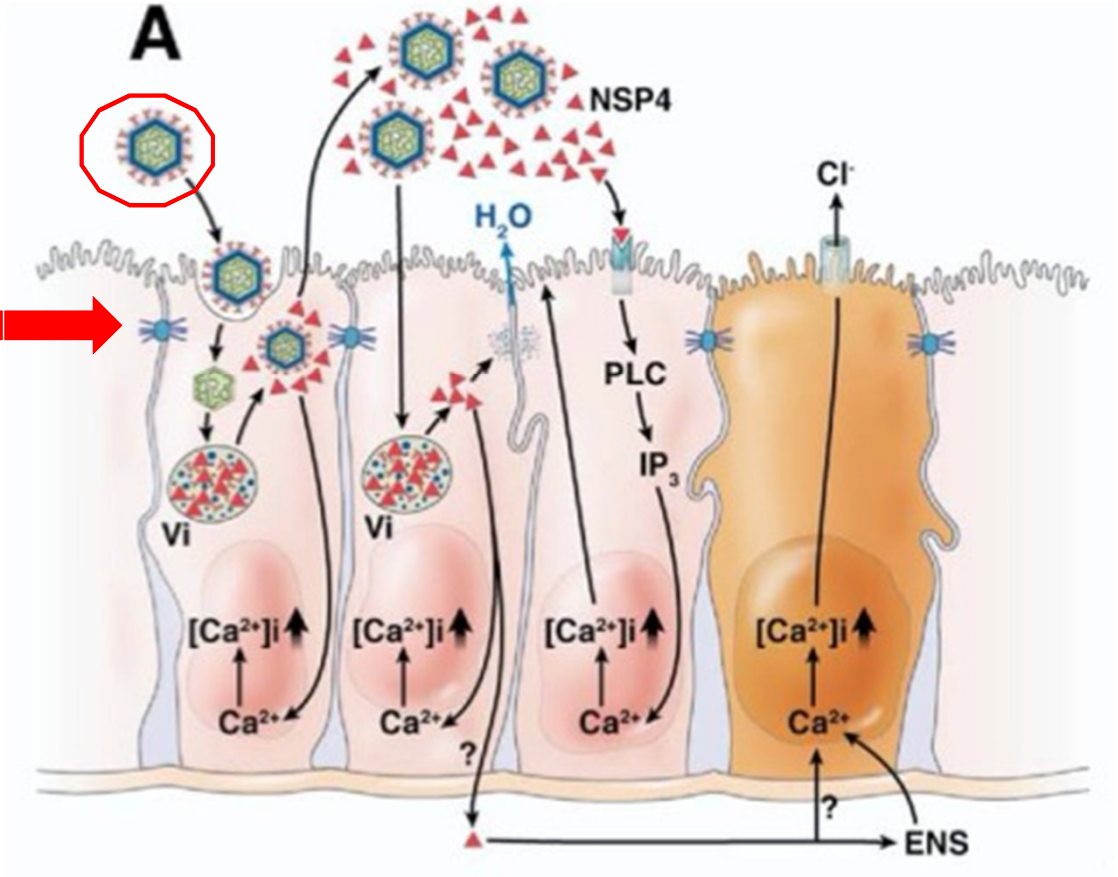
Rotaviruses: From Pathogenesis to Vaccination

GASTROENTEROLOGY 2009;136:1939–1951

Giunzioni apicali



Sintomi caratteristici

✓ **Febbre**

- **In metà dei bambini infettati.**

✓ **Vomito**

- **80-90% dei bambini con infezione presenta vomito, di solito di breve durata (meno di 24 ore)**

✓ **Diarrea**

- **In media 10-20 scariche al giorno e persiste dai 3 ai 7 giorni**

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Le manifestazioni cliniche, più o meno gravi dipendono dalla presenza di alcuni fattori di rischio

✓ Prima infezione

- La prima infezione dopo 3 mesi di età determina una diarrea più grave che può provocare disidratazione

✓ Pretermine

- Anticorpi della madre, per pregresse infezioni, attraversano la placenta e proteggono i il neonato che avrà una forma asintomatica o lieve
- Un eccezione è il pretermine, a rischio severa malattia per mancanza di anticorpi materni

✓ Immunodeficit

- Gastroenterite grave è stata riportata in b. immunodeficit cellulare o combinato severo o dopo trapianto di midollo
- L'infezione in bambini con trapianto d'organo è più grave
- Il rotavirus non provova diarrea grave in bambino con HIV

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PERCHE PREOCCUPARSI DI UNA SEMPLICE GASTROENTERITE ?

RETE VACCINI

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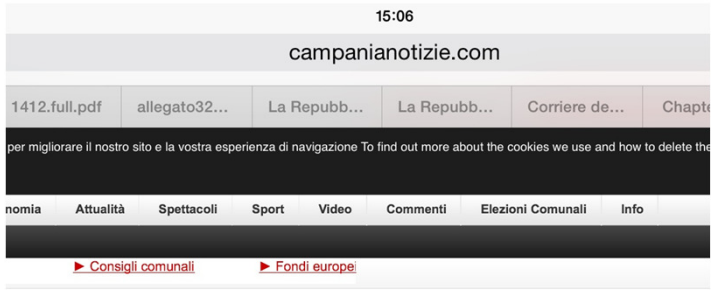
HOME CRONACA ECONOMIA POLITICA SOCIETA' AMBIENTE SPORT ESTERI

NOTE LEGALI CONTATTI REDAZIONE

Epidemia del rotavirus, colpiti soprattutto i bambini: prontosoccorso del Santobono in tilt per le emergenze



Allarme rotavirus: migliaia di casi in Campania, bimbi a rischio. Ecco consigli e rimedi

Non si ferma l'emergenza rotavirus in Campania. Da giorni infatti sono migliaia gli accessi in ospedale in particolare di bambini (per la maggior parte al Santobono di Napoli) che vengono colpiti dalla gastroenterite da rotavirus (leggi articolo). Ma che cos'è il rotavirus e come si può combatterlo? Ecco alcuni consigli. Innanzitutto bisogna dire che colpisce maggiormente i neonati ed i bambini fino ai 5 anni e, benché sia un virus attivo tutto l'anno, ha il suo picco stagionale nel periodo tra novembre e marzo. Quest'anno però si è registrato un picco anche in piena estate La gastroenterite da rotavirus non è una malattia di per sé letale ma la sue complicanze possono essere molto gravi nei soggetti affetti da altre patologie. Negli adulti sani, questa malattia ha un decorso positivo nella quasi totalità dei casi mentre nei bambini provoca una grave disidratazione che deve essere tenuta sotto stretto controllo.

Virosi intestinale al Santobono più ricoveri

IL CASO

SANTOBONO preso d'assalto, file di mamme negli studi medici. Pediatri di famiglia che corrono da una casa all'altra. Sorpresa di fine maggio, siamo in piena epidemia. Contro ogni previsione, una violenta virosi gastrointestinale sta colpendo neonati e bambini. Con la conseguenza di un sovraffollamento delle corsie, degli ambulatori pediatrici e dei pronti soccorso (ormai sono rimasti attivi solo quelli di Santobono e Annunziata). Tra i virus responsabili delle manifestazioni patologiche, il rotavirus, un agente infettivo tra i più frequenti. Ieri mattina, nella Pediatria d'urgenza diretta da Antonio Campa, c'erano letti aggiunti e barelle una affianco all'altra. E nelle sale di degenza destinate ad accogliere al massimo trenta piccoli pazienti, si è sfiorata quota 45 e più. Un numero spropositato rispetto al personale disponibile.

- ✓ **Il rotavirus è la principale causa di diarrea grave nei bambini dai 3 mesi ai 2 anni di età e tra le principali cause tra i 2 ed i 5 anni.**

Penelope H. Dennehy : infect Dis Clin N Am 29(2015) 617-635

Complicanze da infezione RV

- **DISIDRATAZIONE**
- **SQUILIBRIO ELETTROLITICO**
- **ACIDOSI METABOLICA**

RISK OF HOSPITALISATION FOR CHILDREN WITH ROTAVIRUS GASTROENTERITIS AND NON-ROTAVIRUS ACUTE GASTROENTERITIS: THE REVEAL* STUDY

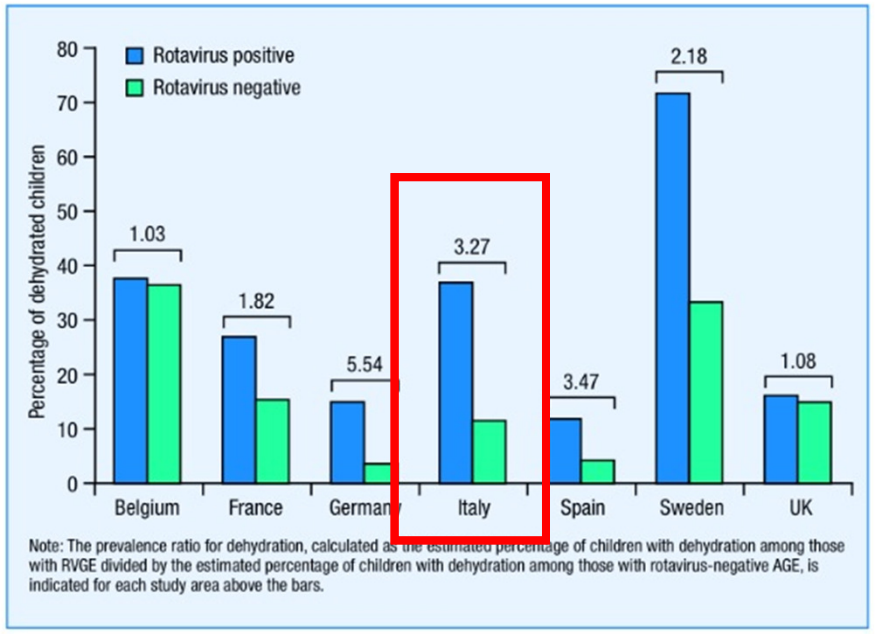
*Rotavirus Gastroenteritis Epidemiology and Viral Types in Europe Accounting for Losses in Public Health and Society

Carlo Giaquinto[1], Pierre Van Damme[2], Frédéric Huet[3], Leif Gothefors[4], Melanie Maxwell[5], Peter Todd[5], Liviana da Dalt[1] for the REVEAL Study Group

[1]University of Padua, Italy; [2]University of Antwerp, Belgium; [3]Hôpital d'Enfants, Dijon, France; [4]Umeå University, Sweden; [5]Wirral Hospital NHS Trust, Merseyside, UK

% bambini disidratati con GE rotavirus positivi e rotavirus negativi

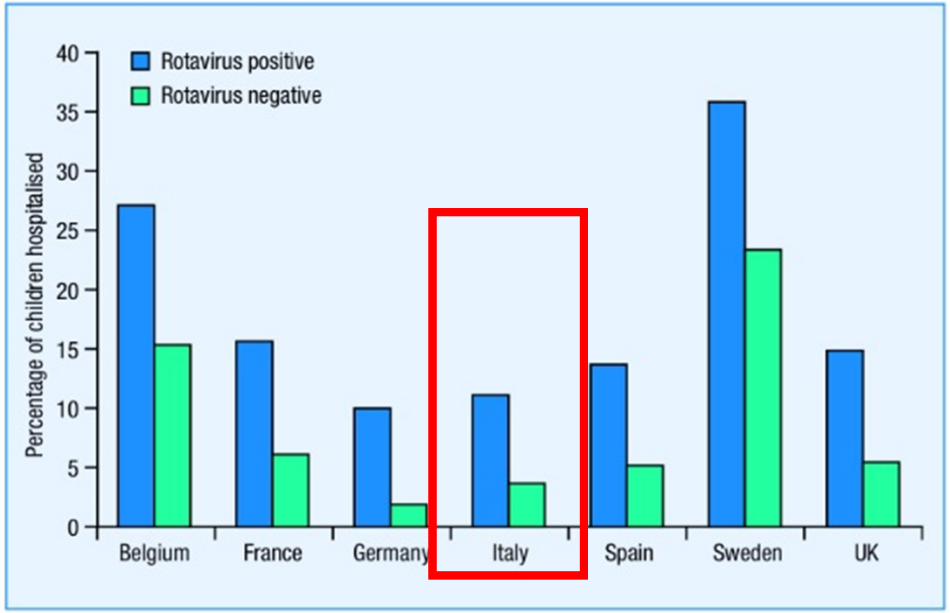
Figure 3. Estimated percentages of children with dehydration among those with rotavirus-positive AGE or rotavirus-negative AGE, by study area.



Note: The prevalence ratio for dehydration, calculated as the estimated percentage of children with dehydration among those with RVGE divided by the estimated percentage of children with dehydration among those with rotavirus-negative AGE, is indicated for each study area above the bars.

% bambini ospedalizzati con GE rotavirus positivi e rotavirus negativi

Figure 2. Estimated percentages of children with rotavirus-positive AGE or rotavirus-negative AGE who were hospitalised, by study area.



Burden of Rotavirus Disease in Norway

Using National Registries for Public Health Research

Tone Bruun, MD, Beatriz Valcarcel Salamanca, MSc, PhD,† Terese Bekkevold, MPhil,* Kirsti Vainio, PhD,‡ Moustafa Gibory, MSc,‡ Kirsti Egge Haugstad, RN,§ Astrid Rojahn, MD,§ Kirsti Jakobsen, MSc,¶ Gunnar Størvold, MD,¶ Anette Lunde, RN,‖ Ketil Størdal, MD, PhD,‖ Anita Kanestrøm, MD,** Magnhild Owesen Eidem, RN,†† Henrik Døllner, MD, PhD,†††‡ Lars Høsøien Skanke, MD,†† Svein Arne Nordbø, MD,‡‡§§ Heidi Christin Sivertsen, RN, ¶¶ Ann Marit Gilje, MD,¶¶ Elisebet Haarr, MD,‖‖ and Elmira Flem, MD, PhD,† for the Norwegian Enhanced Pediatric Immunisation Surveillance (NorEPIS) Network*

The Pediatric Infectious Disease Journal • Volume 35, Number 4, April 2016

TABLE 1. Incidence of Gastroenteritis-related Primary Care Consultations and Hospital Contacts in Children <5 Years Old, Norway 2009–2013

	Primary care, No. per 1000 (95% CI)			Hospital care, No. per 1000 (95% CI)		
	Total (N = 175,702)	GP (N = 123,500)	EPC (N = 52,202)	Total (N = 18,037)	Inpatients (N = 9638)	Outpatients (N = 8399)
Total <5 yr	114.5 (114.0–115.0)	80.5 (80.0–80.9)	34.0 (33.7–34.3)	11.8 (11.6–11.9)	6.3 (6.2–6.4)	5.5 (5.4–5.6)

Sentinel Rotavirus Surveillance

During hospital rotavirus surveillance, we enrolled 400 children younger than 5 years old or approximately 50% of those eligible for enrollment at 4 hospitals during February 2014–January 2015. Stool samples were available for 318 (80%) enrolled patients, and rotavirus was detected in 65% [95% confidence interval (CI):

65% dei bambini <5 anni, ricoverati per GE, rotavirus positivi

Rotavirus-related Hospitalizations Are Responsible for High Seasonal Peaks in All-cause Pediatric Hospitalizations

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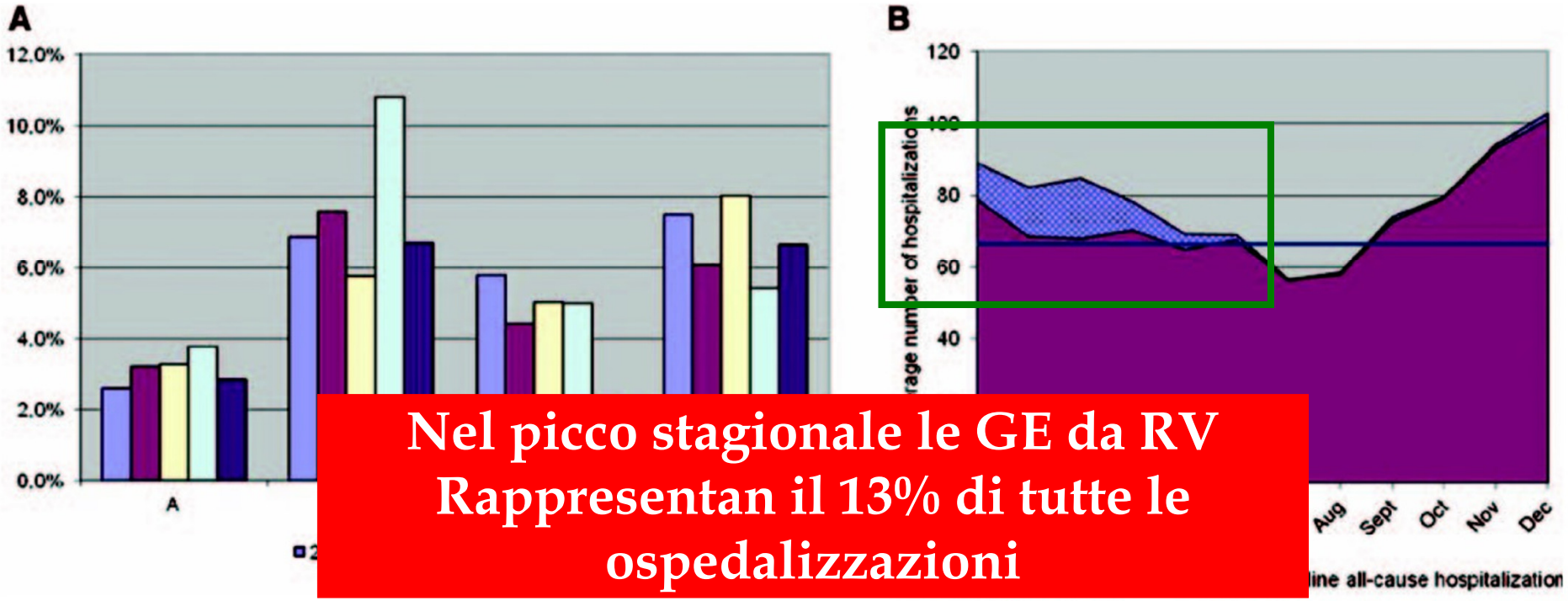
Charlie van den Born, MD,‡ Esther Bleeker, MD,§ Steven Thijsen, MD, PhD,¶ Ed P. F. Ijzerman, MD, PhD,||
*Vincent H. J. van der Velden, MD, PhD,** and Marc J. M. Bonten, MD, PhD**



Nel picco stagionale le GE da RV Rappresentan il 13% di tutte le ospedalizzazioni

FIGURE 1. Proportion of all-cause pediatric hospitalizations related to rotavirus (community-acquired and nosocomial) per hospital and year after adjustment for RV underreporting (A) and rotavirus contribution to seasonal excess in all-cause pediatric hospitalizations among general hospitals (B).

Altre Complicanze

Convulsioni in corso di gastroenterite lieve

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Medico e Bambino 3/2010

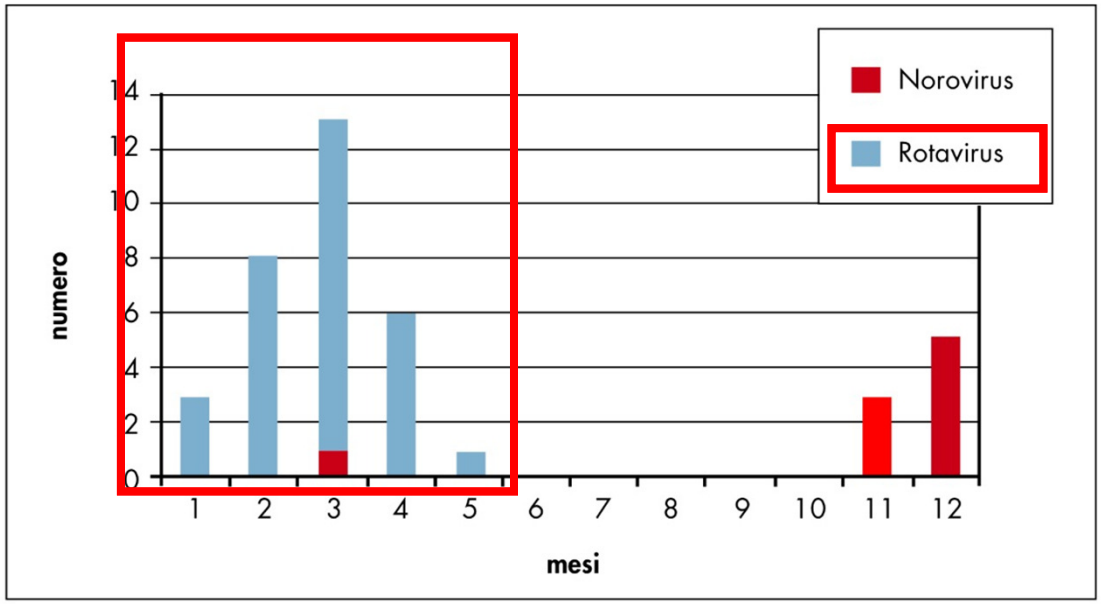

Figura 1. *Distribuzione per mese ed eziologia virale in bambini con CWG (da voce bibliografica 9).*

CARATTERISTICHE DELLE CONVULSIONI IN CORSO DI GASTROENTERITE

- Bambini precedentemente sani in età per lo più dai 6 mesi ai 3 anni che presentano convulsioni in apiressia, con manifestazioni prevalentemente generalizzate
- In corso di episodio diarroico (talora lo precedono), per lo più di lieve entità, spesso in periodo invernale
- Convulsioni per lo più brevi, ma ripetute, talora in veri e propri cluster pluriquotidiani
- Esami ematici e liquorali normali, così come il tracciato EEG intercritico
- Ricerca fecale del rotavirus, spesso (ma non necessariamente) positiva
- Prognosi eccellente, con normale sviluppo psicomotorio
- Possibilità di recidive in caso di altro episodio diarroico

Tabella II

Risposta immunitaria all'infezione ed alla malattia

Rispetto ad altre infezioni virali, come il morbillo, l'infezione da rotavirus, normalmente fornisce una protezione breve ed immunità che protegge dalla malattia grave

✓ **Dopo la prima infezione naturale (risposta omotipica)**

- **38% dei bambini sono protetti da una successiva infezione**
- **77% sono protetti dalla diarrea**
- **87% sono protetti dalla diarrea grave**

✓ **Successive infezioni (risposta eterotipica)**

- **Conferiscono una sempre maggiore protezione**
- **Sono meno gravi della prima**

✓ **Correlati di protezione**

- **Non ancora definiti**
- **Anticorpi sierici e mucosali rivolti contro le proteine virali, VP7 e VP4, sono importanti per la protezione dalla malattia. Utilizzato il livello sierico di IgA anti-totavirus per valutare l'immunogenicità dei vaccini.**

Penelope H. Dennehy : infect Dis Clin N Am 29(2015) 617-635

PREVENZIONE

Ne consegue, che la strategia preventiva in grado di minimizzare l'impatto dell'infezione da rotavirus debba prevedere che il primo contatto sia con gli antigeni vaccinali anzichè con il virus selvaggio, per evitare l'infezione severa.

VACCINI

NOME	ORIGINE
Rotarix	Ceppo umano attenuato Genotipo **G1P(8)**
RotaTeq	Riassortante **pentavalente** Ceppo bovino(WC-3) riassortito geneticamente con segmenti di RNA di rotavirus umani. Ciascuno dei 5 virus vaccinali contiene I geni del ceppo WC-3 ed un singolo gene del rotavirus umano che codifica per una delle proteine VP4 o VP7 appartenenti ai sierotipi più diffusi: **G1**,**G2**,**G3**,**G4** (VP7) e **P[8]** (VP4)

*Basato su schedule approvate dall'EMEA

[1]*Rotarix*™ SPC (Europe), Dec 2006. [2]*RotaTeq*™ SPC (Europe), July 2006.

VACCINI

Raccomandazioni	RV5 (RotaTeq)	RV1 (Rotarix)
Numero dosi	3	2
Età per dose	2,4 e 6 mesi	2 e 4 mesi
Minimo età prima dose	6 settimane	6 settimane
Massimo età prima dose	12 settimane	12 settimane
Minimo intervallo tra dosi	4 settimane	4 settimane
Massimo età ultima dose	26 settimane (pref. entro 20-22 sett.)	24 settimane (pref. 16a sett.)

*Basato su schedule approvate dall'EMEA

[1]*Rotarix*™ SPC (Europe), Dec 2006. [2]*RotaTeq*™ SPC (Europe), July 2006.

Co-somministrazione

I due vaccini possono essere somministrati in concomitanza con tutti i vaccini dell'infanzia monovalenti o combinati

E’ UN VACCINO SICURO ?

RETE VACCINI

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INVAGINAZIONE

Alcuni studi postmarketing hanno rilevato un lieve incremento di invaginazione intestinale entro sette giorni dalla somministrazione della prima dose.

Postmarketing Surveillance of Intussusception Following Mass Introduction of the Attenuated Human Rotavirus Vaccine in Mexico

F. Raúl Velázquez, MD, MSc, Romulo E. Colindres, MD, MPH,† Concepción Grajales, MD, MPH,‡ M. Teresa Hernández, MD,* María Guadalupe Mercadillo, MD, MSc,§ F. Javier Torres, PhD,* MariaYolanda Cervantes-Apolinar, MD,¶|| Rodrigo DeAntonio-Suarez, MD, MSc,† Eduardo Ortega-Barria, MD,|| Maxim Blum, MSc,† Thomas Breuer, MD,† and Thomas Verstraeten, MD†*

TABLE 3. Relative Incidence of Intussusception During the Three Predefined Risk Periods After Vaccination With the Attenuated Human Rotavirus Vaccine*

Dose	Risk Period (days after vaccination)	Episodes of Definite Intussusception During Risk Period	Episodes of Definite Intussusception During Control Period	Follow-up Time in Risk Period (child-months)	Follow-up Time in Control Period (child-months)	Relative Incidence†	95.5% CI	*P*
1	0–30	102	599	698	6045	1.75	1.24–2.48	0.001
2	0–30	131	328	456	3009	1.06	0.75–1.48	0.75
1	0–15	72	599	360.3	6045	3.24	2.15–4.87	<0.001
2	0–15	69	328	235.4	3009	1.06	0.69–1.61	0.79
1	0–6	56	599	157.6	6045	6.49	4.17–10.09	<0.001
2	0–6	36	328	103.0	3009	1.29	0.80–2.11	0.29

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Attributable Risk

The number of additional cases of intussusception attributable to vaccination with the attenuated human rotavirus vaccine in Mexico was estimated to be 3.7 (95.5% CI: 1.2–7.3) cases per 100,000 person-years (assuming a baseline incidence of intussusception of 87 cases per 100,000 person-years).

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 6, 2014 VOL. 370 NO. 6

Intussusception Risk after Rotavirus Vaccination in U.S. Infants

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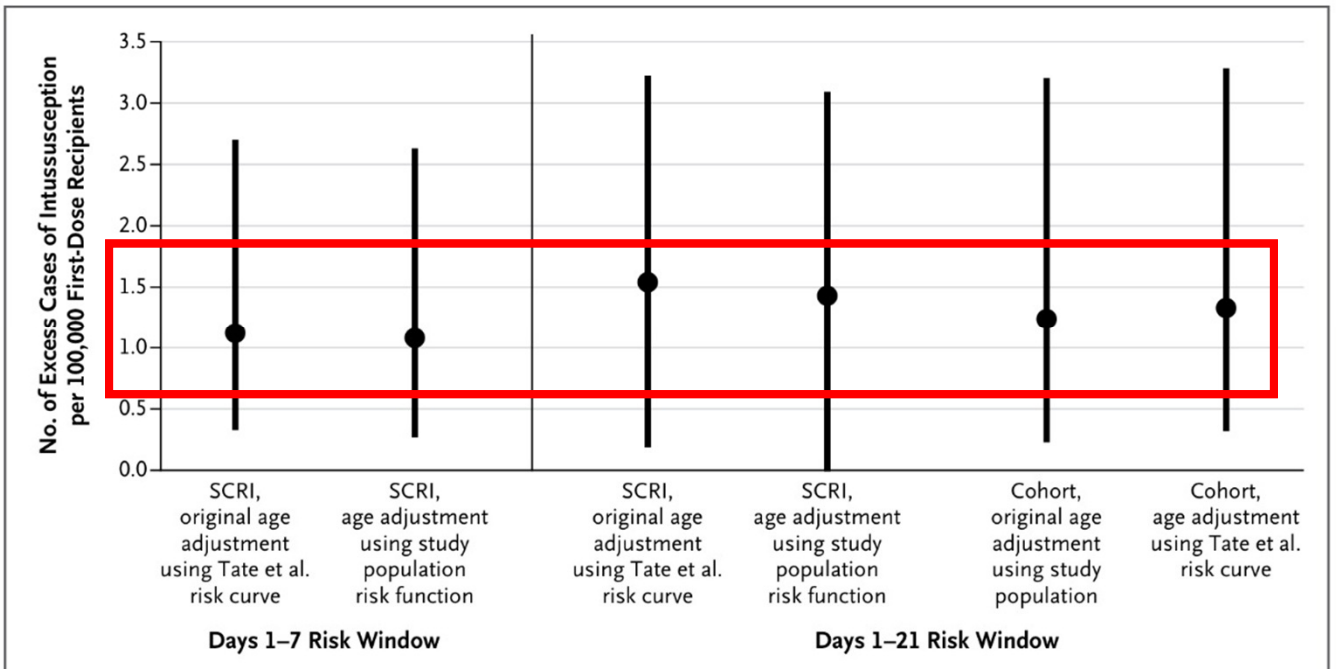

Review

Value of post-licensure data on benefits and risks of vaccination to inform vaccine policy: The example of rotavirus vaccines

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ARTICLE INFO

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Table 1
Risk of intussusception and benefits of rotavirus vaccination in Mexico, Brazil, Australia, and the United States.

Country	Diarrhea hospitalizations (deaths) prevented by vaccination	Intussusception cases (deaths) potentially caused by vaccination
Mexico	11,600 (663)	41 (2)
Brazil	69,600 (640)	55 (3)
Australia	7000 (0)	6 (0)
United States	53,444 (14)	35–166 (0.1–0.5)

has emerged. Based on consideration of the substantial benefits of vaccination in the face of low intussusception risk (Table 1), policy makers in the United States, Mexico, Brazil, and Australia, as well as global health authorities such as the World Health Organization (WHO), continue to strongly support routine rotavirus vaccination of infants [55].

Intussusception After Human Rotavirus Vaccine

To the Editors:

Velásquez and colleagues[1] show in a large Mexican cohort study that there is a small but finite risk of intussusception (IS) associated with the first dose of human rotavirus vaccine (Rotarix; GlaxoSmith-Kline Biologicals, Rixensart, Belgium). The number of additional cases of IS attributable to Rotarix vaccination was estimated at approximately 2 per 100,000 infants vaccinated, which is somewhat less than what was estimated for RotaShield (Wyeth, New York, NY) vaccine before its withdrawal. A study from Australia also identified a risk of similar magnitude after the first dose of both Rotarix and RotaTeq (Merck, Whitehouse Station, NJ) vaccines.[2] While, unlike Mexico, the risk of IS after Rotarix could not be detected in Brazil,[1] and a recent report from

E' POSSIBILE
RIDURRE I CASI DI IS?
L'esperienza con rotaShield:

Vaccino somministrato a
30-59 gg : 0 casi
60-89 giorni: 9 casi
90-150 giorni: 3-4 volte in più

dose after 14 weeks of age as compared with those at 14 weeks or less. They also mention that only 18.2% of IS cases were among infants who received the first dose after the recommended limit of 16 weeks of age,[4] but do not report what percentage of all children received the first dose of Rotarix after the age of 16 weeks.

A further question is where this "recommended" upper age limit of 16 weeks comes from. In the prelicensure trials of Rotarix (and RotaTeq), the first dose of vaccine was administered strictly between ages 6 and 12 weeks. This age range is also the still existing recommendation in the ESPID/

Il vaccino somministrato precocemente è meno reattogeno, per la presenza di anticorpi materni, e ridurre il rischio di invaginazione

and view the risk of IS as a potential concern. Rather, the critical question is what can be done to reduce the risk of rotavirus vaccine–associated risk of IS, and an obvious issue is the age at the time of administration of the first dose of vaccine.

The background for the importance of age lies with the RotaShield experience. According to Simonsen and colleagues, there were no cases of IS in infants vaccinated between 30 and 59 days of age (denominator 69.123), 9 cases in infants vaccinated between 60 and 89 days of age (denominator 197.144), but a much higher number and 3–4 times higher rate of cases among infants who participated in the catch-up program and received their first dose of RotaShield vaccine between ages of 90 and 159 days.[4] A plausible assumption is that the lower risk of IS associated with the current live oral rotavirus vaccines would follow a similar pattern for age. In fact, a recent report from Germany has found just that an increased risk of IS was observed in infants who received the first dose of rotavirus vaccine, either RotaTeq or Rotarix, between ages 90–179 days, but not in infants less than 89 days of age at the time of vaccine administration.[5]

Velázquez and colleagues mention the age issue only in passing, and note that an exploratory analysis showed no increased risk of IS in infants who received the first

be sufficient to control rotavirus vaccine–associated IS in Europe.[5] Consequently, all recommendation issuing bodies should unequivocally recommend the administration of the first dose of rotavirus vaccine between ages 6 and 12 weeks, or, even better, as early as possible within this age bracket.

The second step, in the future, for further reduction of the risk of IS should be decreasing the lower age of the first dose to neonatal age. Neonatal dosing might be optimal for safety (for IS) without compromising efficacy, as shown by immunogenicity studies of RotaShield[8] and efficacy studies of bovine rotavirus vaccine in the past.[9] Neonatal studies are urgently needed for the currently licensed live oral rotavirus vaccines.

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2. Buttery JP, Danchin MH, Lee KJ, et al. Intussusception following rotavirus vaccine administration: post-marketing surveillance in the National Immunization Program in Australia. *Vaccine*. 2011:29:3601–3636.

European Society for Paediatric Infectious Diseases Consensus Recommendations for Rotavirus Vaccination in Europe

Timo Vesikari, MD, Pierre Van Damme,† Carlo Giaquinto,‡ Ron Dagan,§ Alfredo Guarino,¶ Hania Szajewska,‖ and Vytautas Usonis***

Invaginazione

a recent postmarketing study in Germany detected a correlation between the ages at the time of the administration of the first dose of RV vaccine. Neither vaccine showed increased risk of IS when administered before the age of 89 days, whereas the risk of IS was increased for both vaccines when the first dose was administrated between 90 and 179 days (Rotarix 4.6 [1.5–10.7] and RotaTeq 5.8

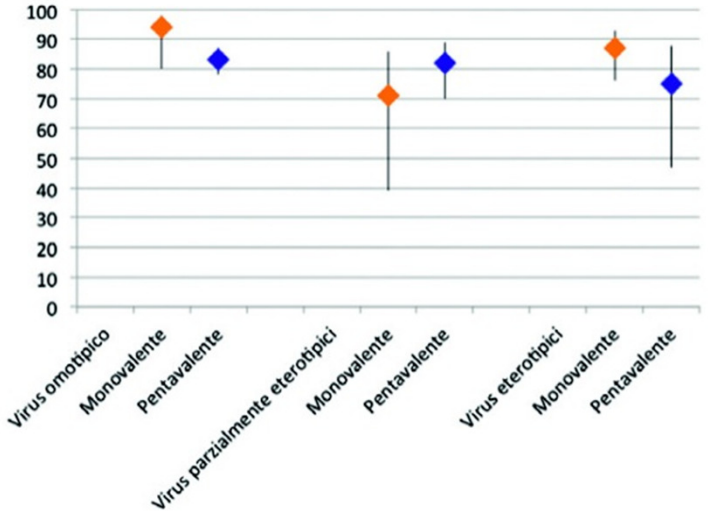
E’ UN VACCINO EFFICACE ?

RETE VACCINI
fimp Federazione Italiana Medici Pediatri

Vaccinazione anti-Rotavirus: razionale, efficacia, impatto

RIAP
Rivista di Immunologia e Allergologia Pediatrica
quattro 2015 • 24-31

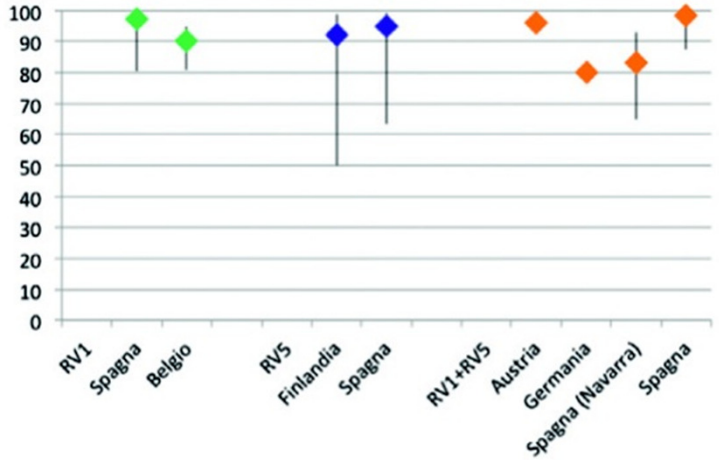
Filippo Ansaldi
Cecilia Trucchi
Dipartimento di Scienze della Salute (DiSSal), Università di Genova



RV1 e RV5, entrambi hanno dimostrato livelli di efficacia alta nei paesi dove viene riscontrata diversità dei ceppi circolanti (risposta eterotipica)

. Efficacia sul campo dei vaccini RV1 e RV5 nei confronti di virus omo- e eterotipici nei Paesi industrializzati.

Per entrambi i vaccini efficacia dall'80 ad oltre il 90% nel prevenire le forme severe di GE nei Paesi europei dove è stato introdotto il vaccino



Efficacia sul campo dei vaccini RV1 e RV5 nei confronti dei ricoveri per gastroenterite da Rotavirus in Europa.

Review

Effectiveness and impact of rotavirus vaccines in Europe, 2006–2014

Emilie Karafillakis [a,*], Sondus Hassounah [a], Christina Atchison [b]

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Table 5
Impact of vaccination on RVGE hospitalisations, nosocomial infections and outpatient visits, and laboratory-confirmed rotavirus infections, Europe.

Country	Vaccine	Outcome measured	Pre-vaccination		Post-vaccination		Vaccination impact % Change (95% CI)	Ref.
			Year	Result	Year	Result		
RVGE hospitalisatio								
Austria	[a]R							[17]
Austria	[a]R							[18]
Austria	[a]R							[8]
						<1 yr: 397	−81	
						1 yr: 332	−81	
						2–3.4 yrs: 216	−65	
						3.5–4 yrs: 201	−3	
						5–9 yrs: 78	+48	
						10–14 yrs: 14	+6	
Austria	[a]RV1 + RV5	Annual number of RVGE hospitalisations	2002–2005	<1 yr: 90 0–18 yrs: 257	2008–2009	<1 yr: 11 0–18 yrs: 67	−88 −74	[19]
Belgium	[a]RV1 + RV5	Annual RVGE hospitalisations as a percentage of annual total AGE hospitalisations	1986–2006	<5 yrs:19%	2007 2008 2009	<5 yrs: 12% <5 yrs: 10% <5 yrs: 6%	−35 −49 −66	[20]
Belgium	[a]RV1 + RV5	Annual number of RVGE hospitalisations	2004–2006	<2 mo: 44 2–24 mo: 716 >24 mo: 121	2008 2009	<2 mo: 22 2–24 mo: 249 >24 mo: 97 <2 mo: 16 2–24 mo: 140 >24 mo: 43	−50 (−64 to −36) −65 (−69 to −62) −20 (−28 to −14) −64 (−76 to −49) −80 (−83 to −77) −64 (−72 to −56)	[22]
Finland	RV5	Annual RVGE hospitalisation rates/1000 person years Annual AGE hospitalisation rates/1000 person years	1999–2005 1999–2005	<1 yr: 4.9 1 yr: 5.7 2 yrs: 2.7 3 yrs: 1.3 4 yrs: 0.7 <1 yr: 20 1 yr: 21 2 yrs: 10 3 yrs: 6 4 yrs: 4	2010 2010	<1 yr: 1.0 1 yr: 1.5 2 yrs: 0.8 3 yrs: 0.4 4 yrs: 0.3 <1 yr: 9 1 yr: 9 2 yrs: 5 3 yrs: 3 4 yrs: 3	−80 (−85 to −75) −74 (−79 to −68) −70 (−77 to −60) −69 (−80 to −54) −53 (−70 to −26) −54 (−58 to −50) −55 (−59 to −51) −51 (−56 to −45) −47 (−54 to −39) −27 (−37 to −15)	[24]
Finland	RV5	Annual number of RVGE hospitalisations Annual number of AGE hospitalisations	2006–2008 2006–2008	<16 yrs: 219 <16 yrs: 434	2009–2011 2009–2011	<16 yrs: 52 <16 yrs: 186	−76 −57	[25]
Finland	RV5	Annual RVGE hospitalisation rates/1000 children Annual AGE hospitalisation rates/1000 children	2001–2006 2001–2006	<16 yrs: 0.66 <16 yrs: NR [b]	2009–2012 2009–2012	<16 yrs: 0.14 <16 yrs: NR	−78 −57	[10]
France	RV5	Annual number of RVGE hospitalisations	2002–2007	<2 yrs: 61	2008–2009	<2 yrs: 30	−51	[26]
Germany	[a]RV1 + RV5	Annual RVGE hospitalisation rates/100,000 population	2004–2006	WFS <2 yrs: NR EFS <2 yrs: NR	2008–2011	WFS <2 yrs: NR EFS <2 yrs: NR	−25 −36	[27]

Impatto della vaccinazione su ospedalizzazione da RVGE, infezioni nosocomiali e visite

Review

Effectiveness and impact of rotavirus vaccines in Europe, 2006–2014

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3.2. Vaccine impact

Fifteen studies that assessed the impact of rotavirus vaccination were included (Table 4). From countries where universal

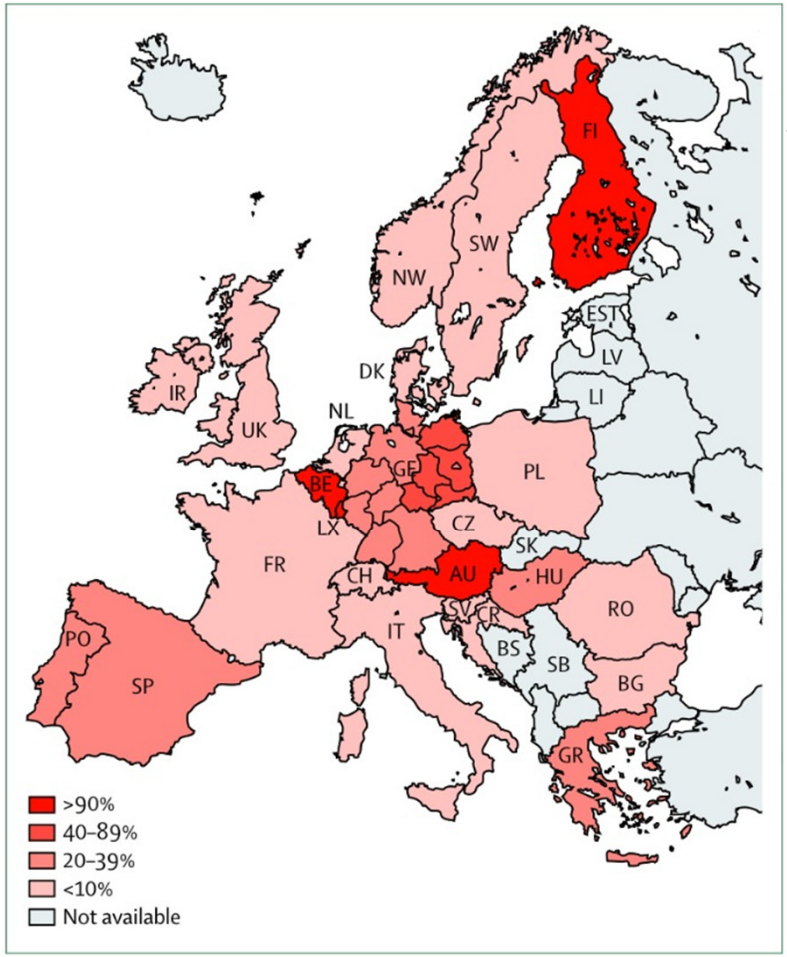

Figure: Estimates of rotavirus vaccination coverage in European countries in 2010 on the basis of the number of vaccines sold
(IMS Health, MIDAS database; SP-MSD). AU=Austria (vaccination coverage

- **15 studi da paesi dove la vaccinazione è universale (4 Austria, 4 Belgio, 3 Finlandia), dove è locale o regionale(2 Spagna, 1 Germania, 1 Francia)**

➢ **AUSTRIA: introdotto vaccino nel 2007-2009(RV5), 2008 e 2010-2012(RV1)**

- **Copertura vaccinale 72% 2008 ,84% 2011.**
- **Riduzione ospedalizzazione < 1 anno, 70% 2008 e 84% 2010, rispetto a 2001-2006**
- **Ospedalizzazione ridotta nei bambini tra i 2 e 3.5 anni nel 2011, che prova l'allungamento della protezione.**
- **Ospedalizzazione ridotta in bambini non vaccinati che suggerisce herd immunity**

➢ **BELGIO: vaccino (RV1) nel 2006-2008, copertura 90% ,coinvolti 12 ospedali, riduzione dal 65% all'80% ospedalizzazione.**

Review

Effectiveness and impact of rotavirus vaccines in Europe, 2006–2014

Emilie Karafillakis[a,*], Sondus Hassounah[a], Christina Atchison[b]

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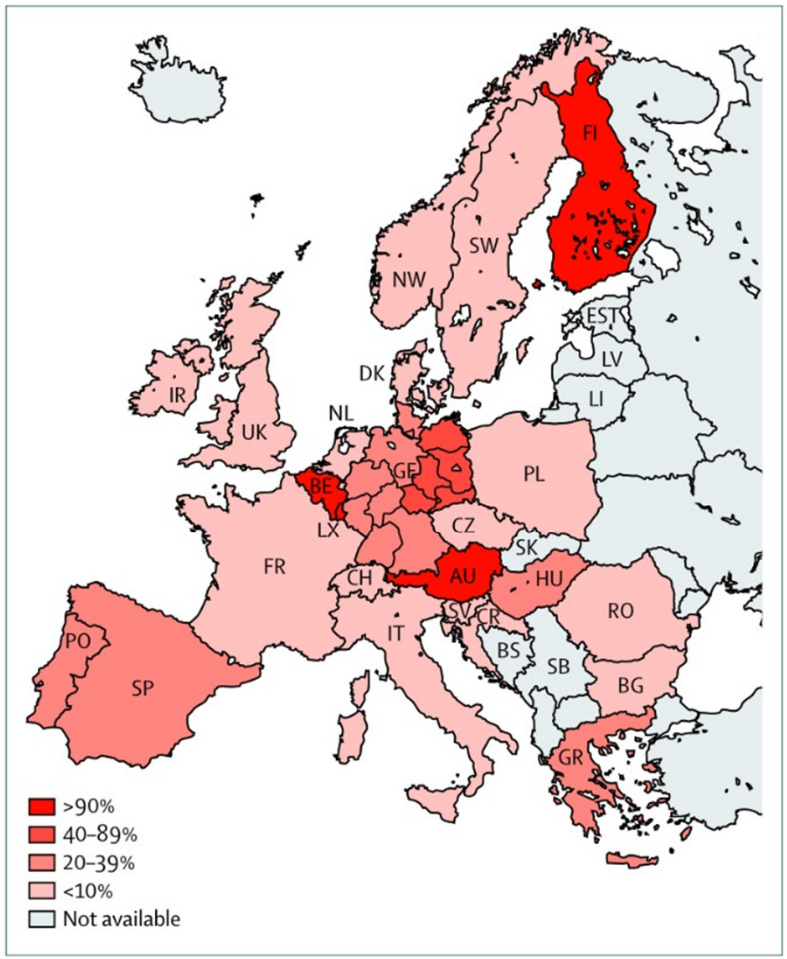

Figure: **Estimates of rotavirus vaccination coverage in European countries in 2010 on the basis of the number of vaccines sold**
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3.2. Vaccine impact

Fifteen studies that assessed the impact of rotavirus vaccination were included (Table 4). From countries where universal

- **GERMANIA: vaccinazione in alcune regioni, moderata(58%)e bassa(22%) copertura , riduzione ospedalizzazione 36 e 25%.**
- **(idem SPAGNA)**

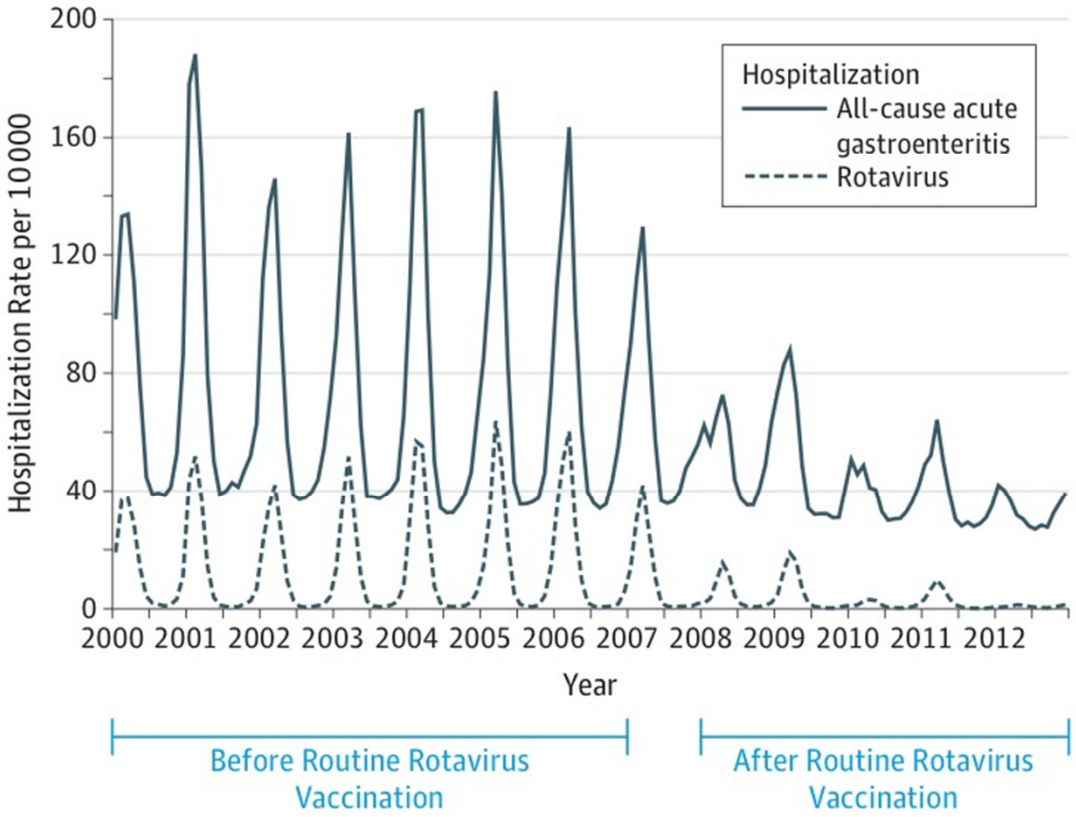
- **FINLANDIA: riduzione del 79% visite per RVGE dopo introduzione vaccino, riduzione del 13% visite per GE.**

Acute Gastroenteritis Hospitalizations Among US Children Following Implementation of the Rotavirus Vaccine

JAMA

June 9, 2015, Vol 313, No. 22

Figure. Monthly Acute Gastroenteritis and Rotavirus-Coded Hospitalization Rates Among Children Younger Than 5 Years in 24 States During January 2000 Through December 2012



Ospedalizzazione GE (-55% 2012)

...ute gastro-ente..., 73-83 per 10 000) among children younger than 5 years, postvaccine introduction rates declined by 31% (95% CI, 30%-31%) in 2008, 33% (95% CI, 32%-33%) in 2009, 48% (95% CI, 47%-48%) in 2010, 47% (95% CI, 47%-48%) in 2011, and 55% (95% CI, 54%-55%) in 2012 ($P < .001$ for all rate reductions; **Table**). Similar rate declines were noted in males and females, all race/ethnicity groups, and all age groups, with the greatest reductions among children aged 6 months to 23 months.

Ospedalizzazione RVGE (-94% 2012)

Compared with the prevaccine mean annual rotavirus-coded hospitalization rate of 16 per 10 000 (range, 13-19 per 10 000) among children younger than 5 years, rates of rotavirus-coded hospitalizations postvaccine introduction declined by 70% (95% CI 69%-71%) in 2008, 63% (95% CI, 62%-64%) in 2009, 90% (95% CI, 90%-90%) in 2010, 79% (95% CI, 79%-80%) in 2011, and 94% (95% CI, 94%-95%) in 2012 ($P < .001$ for all rate reductions; Table).

- **L'impatto del vaccino nel prevenire le ospedalizzazioni per RVGE è riportat0 negli studi dal 68% al 98%, questo dipende dai gruppi di controllo.**
- **Efficacia riportata nei trial clinici dal 90 al 98% per le RVGE severe e dal 68 al 79% per le RVGE di ogni severità**

Table 4. Efficacy of the HRV Vaccine against Severe Rotavirus Gastroenteritis with a Vesikari Score between 11 and 20 during the Period from Two Weeks after Dose 2 until One Year of Age.*

Vesikari Score	HRV Vaccine (N=9009)		Placebo (N=8858)		Relative Risk†	Vaccine Efficacy (95% CI)
	No. of Infants with ≥1 Episode	1000 Infant-Yr Ratio‡	No. of Infants with ≥1 Episode	1000 Infant-Yr Ratio‡		
≥11	11	1.9	71	12.2	0.152	84.8 (71.1–92.7)
≥15	7	1.2	54	9.3	0.127	87.3 (71.9–95.1)
≥19	0	0	16	2.8	0	100.0 (74.5–100.0)

* Scores on the Vesikari scale range from 0 to 20, with higher scores indicating more severe cases. An episode with a score of 11 or greater was considered severe. CI denotes confidence interval.

e vaccine group with at least one episode to the
pisode.
specified episode per 1000 infants per year.

Table 2*. Vesikari Clinical Severity Scoring System Parameters and Scores.

	Score		
Parameter	**1**	**2**	**3**
Diarrhea			
Maximum Number Stools per Day	1-3	4-5	≥6
Diarrhea Duration (Days)	1-4	5	≥6
Vomiting			
Maximum Number Vomiting Episodes per Day	1	2-4	≥5
Vomiting Duration (Days)	1	2	≥3
Temperature	37.1-38.4	38.5-38.9	≥39.0
Dehydration	N/A	1-5%	≥6%
Treatment	Rehydration	Hospitalization	N/A

N Engl J Med 2006;354:11-22.

Beneficio aggiuntivo

Impact of Rotavirus Vaccination on Childhood Hospitalization for Seizures

Jacobo Pardo-Seco,† Miriam Cebey-López,*† Nazareth Martinón-Torres, MD, PhD,*† Antonio Salas, PhD,*†‡ José Gómez-Rial, MSc,† Carmen Rodriguez-Tenreiro, PhD,*† José María Martinón-Sánchez, MD, PhD,*† and Federico Martinón-Torres, MD, PhD*†*

The Pediatric Infectious Disease Journal • Volume 34, Number 7, July 2015

tively correlated with the admission due to RAGE ($\rho = 0.506$; $P = 0.001$; Table 2). These decrease rates (Table, Supplemental Digital Content 1, http://links.lww.com/INF/C113) ranged from 16.2% [95% confidence interval: 8.3–23.5%] in 2007 to 34.0% (27.3–40.1%) in 2010, as compared with the median rate of the pre-vaccination period (2003–2006). In children 1–2 years of age, there was also a significant decrease in hospitaliza-
tion rate
(38.2–5
vaccinat

Riduzione delle convulsioni dal 16% (2007) al 34% (2010), in linea con l'aumento della copertura vaccinale

Trends in Infectious Disease Hospitalizations in US Children, 2000 to 2012

Tadahiro Goto, MD, Yusuke Tsugawa, MD, MPH,† Jonathan M. Mansbach, MD, MPH,‡ Carlos A. Camargo, Jr., MD, DrPH,* and Kohei Hasegawa, MD, MPH**

The Pediatric Infectious Disease Journal • Volume 35, Number 6, June 2016

TABLE 2. Most Frequently Listed Diagnostic Subgroups in ID Hospitalizations in US Children, 2000 and 2012

2000				2012			
Rank	ID Subgroup	Weighted Sample, n	Proportion of ID Hospitalization, % (95% CI)	Rank	ID Subgroup	Weighted Sample, n	Proportion of ID Hospitalization, % (95% CI)
Overall							
1	Lower respiratory infections*	323,449	44.1% (43.4%–44.9%)	1	Lower respiratory infections	267,809	42.8% (42.2%–43.4%)
2	Abdominal and rectal infections	90,862	12.4% (12.0%–12.9%)	2	Abdominal and rectal infections	86,566	13.8% (13.3%–14.4%)
3	Upper respiratory infections	60,384	8.2% (8.0%–8.5%)	3	Skin infections	68,436	10.9% (10.7%–11.2%)
4	Urinary tract infections	54,930	7.5% (7.3%–7.7%)	4	Upper respiratory infections	48,449	7.8% (7.5%–8.1%)
5	Enteric infections	49,714	6.8% (6.5%–7.1%)	5	Urinary tract infections	46,008	7.4% (7.2%–7.5%)
Age <1 yr							
1	Lower respiratory infections	165,982	60.5% (59.4%–61.6%)	1	Lower respiratory infections	118,632	60.8% (60.0%–61.5%)
2	Urinary tract infections	20,061	7.3% (6.9%–7.7%)	2	Urinary tract infections	16,769	8.6% (8.3%–8.9%)
3	Septicemia	19,545	7.1% (6.6%–7.7%)	3	Septicemia	15,920	8.2% (7.7%–8.6%)
4	Upper respiratory infections	16,466	6.0% (5.8%-6.3%)	4	Upper respiratory infections	12,804	6.6% (6.2%–7.0%)
5	Enteric infections	15,969	5.8% (5.5%–6.1%)	5	Skin infections	9448	4.8% (4.6%–5.1%)
Age 1–4 yr							
1	Lower respiratory infections	104,541	53.6% (52.5%–54.7%)	1	Lower respiratory infections	95,701	54.1% (53.1%–55.1%)
2	Enteric infections	21,319	10.9% (10.4%–11.5%)	2	Skin infections	34,087	14.1% (13.6%–14.6%)
3	Upper respiratory infections	21,023	10.8% (10.4%–11.2%)	3	Upper respiratory infections	18,492	10.5% (10.0%–11.0%)
4	Skin infections	11,735	6.0% (5.6%–6.4%)	4	Enteric infections	9062	5.1% (4.9%–5.4%)
5	Urinary tract infections	10,708	5.5% (5.3%–5.7%)	5	Urinary tract infections	9059	5.1% (4.9%–5.3%)
Age 5–19 yr							
1	Abdominal and rectal infections	86,350	32.8% (31.8%–33.7%)	1	Abdominal and rectal infections	80,986	32.0% (31.1%–32.9%)
2	Lower respiratory infections	52,925	20.1% (19.5%–20.6%)	2	Lower respiratory infections	53,476	21.1% (20.6%–21.6%)
3	Urinary tract infections	24,161	9.2% (8.9%–9.4%)	3	Skin infections	34,087	13.5% (13.1%–13.9%)
4	Skin infections	23,961	9.1% (8.8%–9.4%)	4	Urinary tract infections	20,180	8.0% (7.8%–8.2%)
5	Upper respiratory infections	22,895	8.7% (8.4%–9.0%)	5	Upper respiratory infections	17,153	6.8% (6.5%–7.0%)

Trends in Infectious Disease Hospitalizations in US Children, 2000 to 2012

Tadahiro Goto, MD, Yusuke Tsugawa, MD, MPH,† Jonathan M. Mansbach, MD, MPH,‡ Carlos A. Camargo, Jr., MD, DrPH,* and Kohei Hasegawa, MD, MPH**

Trends in Hospitalization Rates

From 2000 to 2012, the rate of overall ID hospitalizations decreased from 91.0 to 75.8 per 10,000 US children (16.5% decrease; $P_{trend} < 0.001$; Fig. 1). This finding was due largely to the decrease in the rate among children aged <1 year (30.3% decrease; $P_{trend} < 0.001$). A similar downward trend was observed in children aged 1 to 4 years (13.4% decrease, $P_{trend} = 0.002$), whereas the rate was relatively constant in children aged 5 to 19 years (4.7%

These observations were paralleled by the studies that demonstrated a decrease in hospitalization for pneumonia and rotavirus-associated illness in US children after the implementation of pneumococcal conjugate vaccine[6,27] and rotavirus vaccine.[10,11]

Review

Effectiveness and impact of rotavirus vaccines in Europe, 2006–2014

Emilie Karafillakis[a,*], Sondus Hassounah[a], Christina Atchison[b]

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✓ **Il trend di riduzione della ospedalizzazione per VRGE puo essere naturale?**

In 2010, the Spanish Drugs and Health Products Agency did not authorise the release of new batches of the two vaccines onto the Spanish market for five months (June to November 2010) due to t f
F e
i]
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rates decreased by 30% compared to 2010–2011 [31].

Nel 2010 l'Agenzia del farmaco in Spagna ha ritirato i due vaccini per la nota vicenda della contaminazione con il circovirus. L'impatto di questa sospensione è stato valutato in Galizia dove il vaccino era utilizzato, con improvviso calo della copertuta, ed un rimbalzo del 260% di ricoveri per RVGE nei bambini di 12 mesi di età durante gli anni 2010-2011, rispetto alle precedenti stagioni. Nel 2011-2012, ripresa della vaccinazione e diminuizione dei ricoveri del 30%


Grazie dell’attenzione !

Intussusception After Human Rotavirus Vaccine

To the Editors:

Velásquez and colleagues[1] show in a large Mexican cohort study that there is a small but finite risk of intussusception

E' POSSIBILE RIDURRE I CASI DI IS?

L'esperienza con rotaShield:

Vaccino somministrato a

30-59 gg : 0 casi

60-89 giorni: casi

90-150 giorni: 3-4 volte in più

Neonatal Administration of Rhesus Rotavirus Tetravalent Vaccine

Timo Vesikari, MD, Aino Karvonen, MD,* Bruce D. Forrest, MD,† Yasutaka Hoshino, DVM,‡ Robert M. Chanock, MD,‡ and Albert Z. Kapikian, MD‡*

Conclusion: Infants who received the first dose of RRV-TV vaccine during the neonatal period did not develop a febrile reaction. The immune response in a 3-dose schedule initiated in the neonatal period is somewhat dampened but still acceptable. Neonatal immunization might also reduce the very small risk of intussusception, which has been associated with administration of RRV-TV vaccine to older infants.

Il vaccino somministrato precocemente è meno reattogeno, per la presenza di anticorpi materni, e ridurre il rischio di invaginazione

Review

Value of post-licensure data on benefits and risks of vaccination to inform vaccine policy: The example of rotavirus vaccines

Umesh D Parashar*, Margaret M Cortese, Daniel C Payne, Benjamin Lopman, Catherine Yen, Jacqueline E Tate

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3.2. Post-licensure data

Post-marketing surveillance conducted in several countries has shown a low intussusception increased intussusception risk h within 1–7 days after receiving after the second RV1 dose in B 1 excess case per 51,000 vacci 68,000 vaccinated infants in Br were found in a separate post- vaccine manufacturer [16]. In A tion risk has been documented at about 5.6 excess cases of intus infants [17,18]. Finally, US post- fied a small increased risk of int RV5 and RV1, with an estimate ception cases per 100,000 vacci

Furthermore, it is not clear whether the short-term increased risk of intussusception in the first few weeks after vaccination translates into an overall population-level increase in intussusception incidence in the first year of life. In the United States, ecologic analyses of trends in intussusception hospitalization among infants before and after the implementation of rotavirus vaccines have not consistently demonstrated an overall increase in rates post-vaccination [56,57]. This has led some to speculate that rotavirus vaccination might "trigger" intussusception earlier among some infants among whom intussusception would have occurred anyway later in infancy. In addition, intussusception has been associated with three different attenuated live oral rotavirus vaccines, including RV1 that consists of an attenuated single human rotavirus strain of a genotype that is most prevalent globally. Thus, one might hypothesize that wild-type rotavirus infection could be a cause of intussusception. If this is the case, rotavirus vaccination may prevent cases of intussusception caused by wild-type rotavirus infection later in infancy, as was suggested by preliminary data

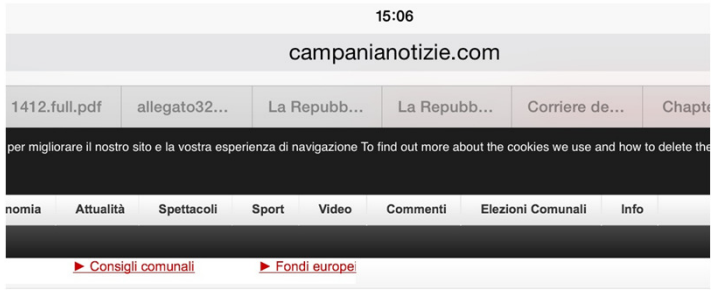
controindicazioni ?

RETE VACCINI
fimp Federazione Italiana Medici Pediatri

HOME CRONACA ECONOMIA POLITICA SOCIETA' AMBIENTE SPORT ESTERI

NOTE LEGALI CONTATTI REDAZIONE

Epidemia del rotavirus, colpiti soprattutto i bambini: prontosoccorso del Santobono in tilt per le emergenze



Allarme rotavirus: migliaia di casi in Campania, bimbi a rischio. Ecco consigli e rimedi

Non si ferma l'emergenza rotavirus in Campania. Da giorni infatti sono migliaia gli accessi in ospedale in particolare di bambini (per la maggior parte al Santobono di Napoli) che vengono colpiti dalla gastroenterite da rotavirus (leggi articolo). Ma che cos'è il rotavirus e come si può combatterlo? Ecco alcuni consigli. Innanzitutto bisogna dire che colpisce maggiormente i neonati ed i bambini fino ai 5 anni e, benché sia un virus attivo tutto l'anno, ha il suo picco stagionale nel periodo tra novembre e marzo. Quest'anno però si è registrato un picco anche in piena estate La gastroenterite da rotavirus non è una malattia di per sé letale ma la sue complicanze possono essere molto gravi nei soggetti affetti da altre patologie. Negli adulti sani, questa malattia ha un decorso positivo nella quasi totalità dei casi mentre nei bambini provoca una grave disidratazione che deve essere tenuta sotto stretto controllo.

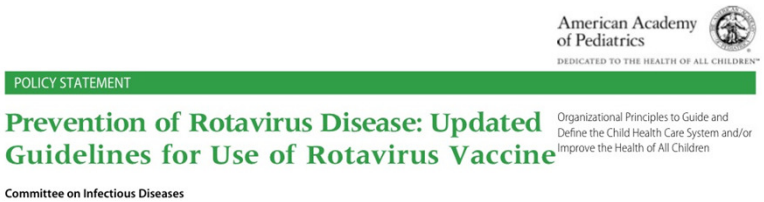
Virosi intestinale al Santobono più ricoveri

IL CASO

SANTOBONO preso d'assalto, file di mamme negli studi medici. Pediatri di famiglia che corrono da una casa all'altra. Sorpresa di fine maggio, siamo in piena epidemia. Contro ogni previsione, una violenta virosi gastrointestinale sta colpendo neonati e bambini. Con la conseguenza di un sovraffollamento delle corsie, degli ambulatori pediatrici e dei pronti soccorso (ormai sono rimasti attivi solo quelli di Santobono e Annunziata). Tra i virus responsabili delle manifestazioni patologiche, il rotavirus, un agente infettivo tra i più frequenti. Ieri mattina, nella Pediatria d'urgenza diretta da Antonio Campa, c'erano letti aggiunti e barelle una affianco all'altra. E nelle sale di degenza destinate ad accogliere al massimo trenta piccoli pazienti, si è sfiorata quota 45 e più. Un numero spropositato rispetto al personale disponibile.

Controindicazioni

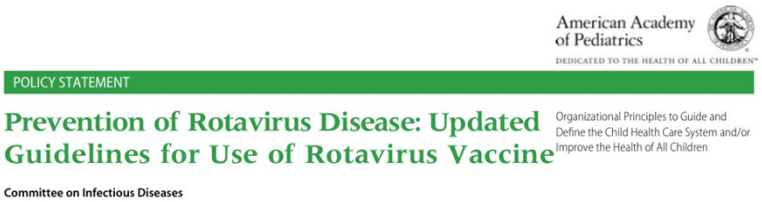
- ✓ **ALLERGIA AL LATEX (latex contenuto nel RV1, RV5 latex-free)**
- ✓ **Allergia grave (anafilassi) ad una precedente dose**
- ✓ **STORIA DI INVAGINAZIONE**
- ✓ **SEVERA IMMUNODEFICIENZA COMBINATA**



Precauzioni

- ✓ **Malattia acuta moderata o severa**
- ✓ **Immunodepressione**

La decisione di vaccinare deve essere presa caso per caso valutando rischi e benefici



NO Precauzioni

- ✓ **Somministrazione emoderivati contenente ab**
  (vaccinazione raccomandata prima, durante e dopo)

- ✓ **Bambini che convivono con donne in gravidanza**
  (in maggioranza con immunità naturale)