



UNIVERSITÀ
DEGLI STUDI DI BARI
ALDO MORO

CORSO DI IGIENE

**Scuola
di
Medicina**

Rotavirus



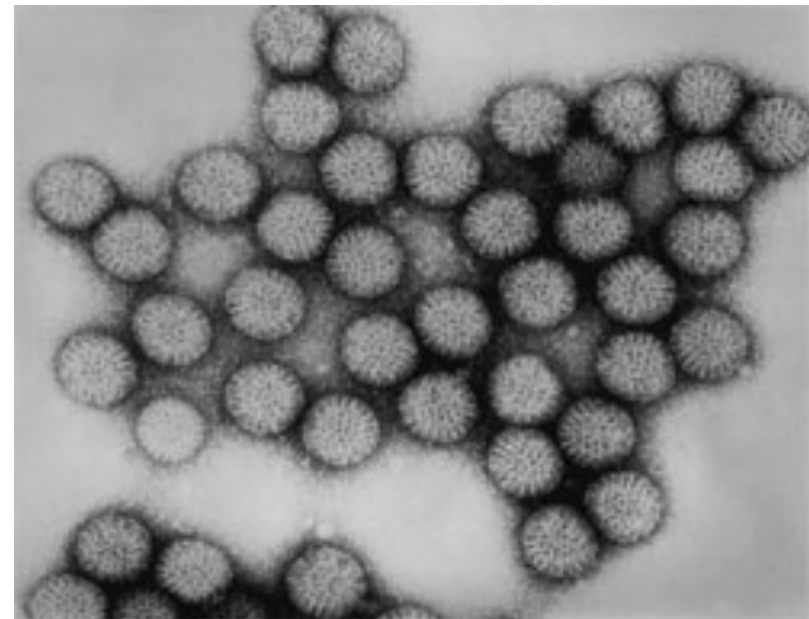
Rotavirus

- First identified as cause of **diarrhea** in 1973
- Most common cause of **severe gastroenteritis** in infants and children
- Nearly universal infection by age 5 years
- Responsible for up to **500,000 diarrheal deaths each year** worldwide



Rotavirus

- Reovirus (RNA)
- **VP7** and **VP4** proteins define **virus serotype** and induce neutralizing antibody
- From 1996-2005, **five predominant strains** in U.S. (**G1-G4, G9**) accounted for 90% of isolates
- **G1 strain accounts for 75% of infections**
- Very stable and may remain viable for weeks or months if not disinfected





Rotavirus Pathogenesis

- Entry through mouth
- Replication in epithelium of small intestine
- In severe infections — **rotavirus antigen detectable in serum**
- Infection leads to **isotonic diarrhea**



Rotavirus Immunity

- Antibody against VP7 and VP4 probably important for protection
- **First infection usually does not lead to permanent immunity**
- Reinfection can occur at any age
- **Subsequent infections generally less severe**



Rotavirus Clinical Features

- Short incubation period (usually less than 48 hours)
- First infection **after age 3 months generally most severe**
- May be asymptomatic or result in **severe dehydrating diarrhea** with fever and vomiting
- Gastrointestinal symptoms generally resolve in **3 to 7 days**



Rotavirus Complications

- Severe diarrhea
- Dehydration
- Electrolyte imbalance
- Metabolic acidosis
- **Immunodeficient children may have more severe or persistent disease**



Rotavirus Epidemiology

- **Reservoir**
 - Human —GI tract and stool
- **Transmission**
 - Fecal-oral, fomites
- **Temporal pattern**
 - Fall and winter (temperate areas)
- **Communicability**
 - 2 days before to 10 days after onset of symptoms



Rotavirus Disease in the United States

- Estimated **3 million cases per year** in the pre-vaccine era
- **95% of children infected by 5 years of age**
- Annually responsible for:
 - more than 400,000 physician visits
 - more than 200,000 emergency dept visits
 - **55,000 to 70,000 hospitalizations**
 - 20 to 60 deaths
- Annual direct and indirect costs are estimated at approximately \$1 billion
- Highest incidence among children 3 to 35 months of age



GARV Epidemiology in Europe, 2007

- 231 deaths
- More than 87.000 children hospitalized
- Around 700.000 medical examination

Diarrhoea related to rotavirus seemed most serious than diarrhoea related to other virus and bacteria

Giaquinto C, et al. Prospective study of the burden of acute gastroenteritis and rotavirus gastroenteritis in children less than 5 years of age, in Padova, Italy. *Infection*. 2008 Aug;36(4):351-7.



GARV Epidemiology in Italy

October 2004 - September 2005, 2,846 children <5 years of age with AGE included in 7 European countries

Italy - the city of Padua and the surrounding residential towns (n = 757)

Table 1. Study-area populations and the number of hospitals, emergency departments, and primary care physicians participating in the study.

Study area characteristic	Belgium ^a	France ^b	Germany ^c	Italy ^d	Spain ^e	Sweden ^f	United Kingdom ^g
Location	Antwerp	Dijon and SAs	Rostock and SAs	Padua and SAs	Gandia, Denia, and SAs	Västerbotten County	Wirral Peninsula
Total population	250,243	242,073	432,740	392,827	305,000	256,875	312,293
Children <5 years of age evaluated	14,193 (5.7)	13,108 (5.4)	15,844 (3.7)	16,000 (4.1)	14,856 (4.9)	12,763 (5.0)	17,488 (5.6)
Setting							
Hospital	2	2	2	1	2	2	1
Emergency department	2	6	2	1	3	3	1
Primary care ^h	22	22	34	13	23	13	12
Children seen by study PCPs ⁱ	5369 (37.83)	2693 (20.54)	5574 (35.18)	6338 (39.61)	6956 (46.82)	4784 (37.48)	3011 (17.22)

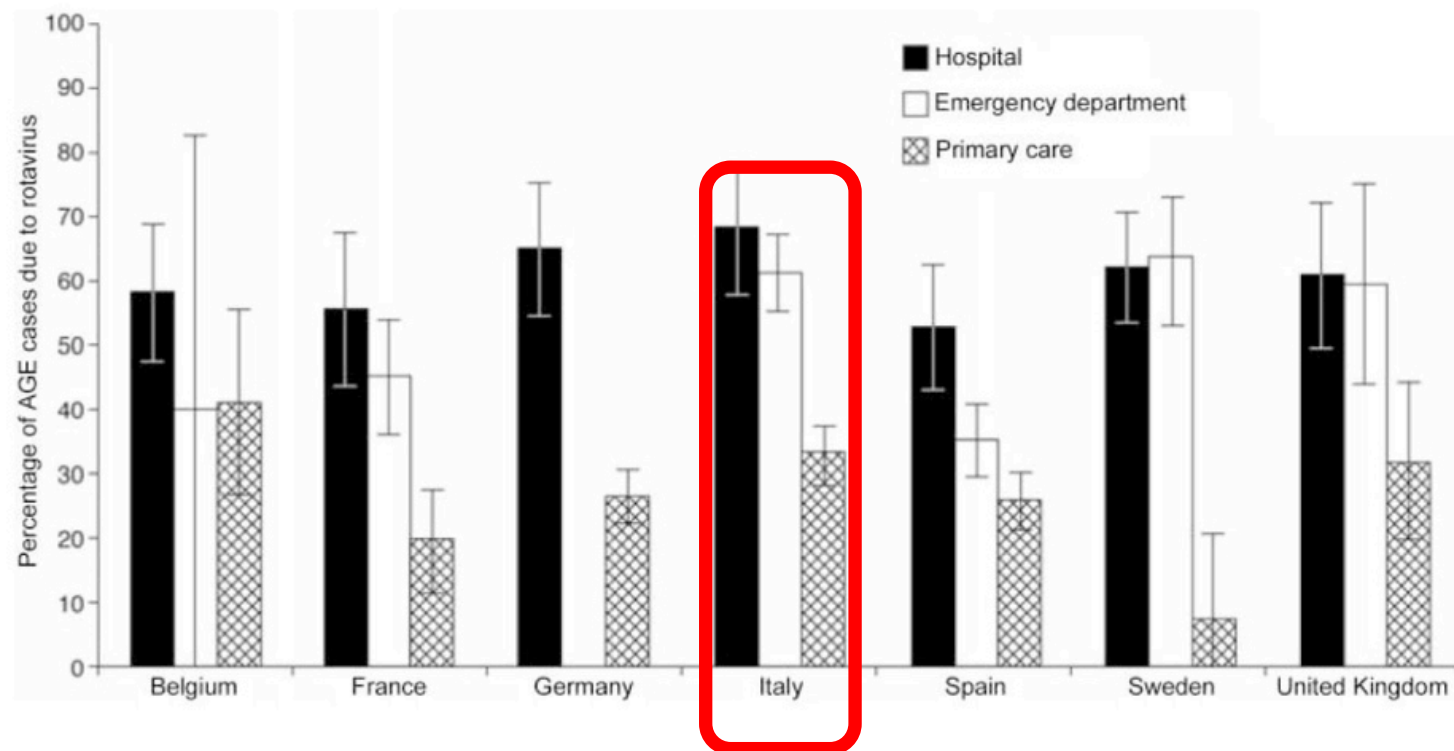
NOTE. Data are no. (%) of children, unless otherwise indicated. PCPs, primary care physicians; SAs, surrounding areas.



GARV Epidemiology in Italy

Van Damme P, et al. Multicenter Prospective Study of the Burden of Rotavirus Acute Gastroenteritis in Europe, 2004–2005: The REVEAL Study. *JID* 2007;195 (Suppl 1): S4

Observed percentage (and 95% confidence interval) of cases of acute gastroenteritis (AGE) due to rotavirus, by study area and setting





Rotavirus Vaccines

RV5 (RotaTeq)

- contains **five reassortant** rotaviruses developed from **human and bovine parent rotavirus strains**
- vaccine viruses suspended in a buffer solution
- contains no preservatives or thimerosal



Rotavirus Vaccines

RV1 (Rotarix)

- contains **one strain of live attenuated human rotavirus** (type G1PA[8])
- provided as a lyophilized powder that is reconstituted before administration
- contains no preservatives or thimerosal



Rotavirus Vaccine Efficacy

- Any rotavirus gastroenteritis: 74%-87%
- Severe gastroenteritis: 85%-98%

Both vaccines significantly reduced physician visits for diarrhea, and reduced rotavirus-related hospitalization



Rotavirus Vaccine Recommendations

- Similar estimates of efficacy and safety between RV1 and RV5
- No preference for one vaccine over the other
- **Routine vaccination of all infants without a contraindication**



Rotavirus Vaccine Recommendations

- 2 (RV1) or 3 (RV5) **oral doses** beginning as early as **6 weeks of age**
- maximum age for first dose is 14 weeks 6 days
- maximum age for any dose is 8 months 0 days
- minimum interval between doses is 4 weeks
- ACIP did not define a maximum interval between doses
- It is not necessary to restart the series or add doses because of a prolonged interval between doses



Rotavirus Vaccine Recommendations

- ACIP recommends that providers **do not repeat the dose if the infant spits out or regurgitates the vaccine**
- Any remaining doses should be administered on schedule
 - Doses of rotavirus vaccine should be separated by at least 4 weeks.
- Complete the series with the same product whenever possible
- **If product used for a prior dose or doses is not available or not known, continue or complete the series with the product that is available**
- If any dose in the series was RV5 (RotaTeq) or the vaccine brand used for any prior dose is not known, a total of 3 doses of rotavirus vaccine should be administered
- **Infants documented to have had rotavirus gastroenteritis before receiving the full course of rotavirus vaccinations should still begin or complete the 2- or 3-dose schedule**



Rotavirus Vaccine Contraindications

- Severe allergic reaction to a vaccine component (including latex) or following a prior dose of vaccine
 - latex rubber is contained in the RV1 oral applicator
- History of intussusception
- Severe combined immunodeficiency (SCID)



Rotavirus Vaccine Precautions

- Altered immunocompetence, (except severe combined immunodeficiency, which is a contraindication)
 - Limited data do not indicate a different safety profile in HIV-infected versus HIV-uninfected infants
 - HIV diagnosis not established in infants due for rotavirus vaccine
 - Vaccine strains of rotavirus are attenuated
 - **These considerations support rotavirus vaccination of HIV-exposed or infected infants**
- Acute, moderate or severe gastroenteritis or other acute illness



Rotavirus Vaccine - Conditions Not Considered to be Precautions

- Pre-existing **chronic gastrointestinal conditions**
 - no data available
- ACIP considers the **benefits of vaccination** to outweigh the theoretic risks



Rotavirus Vaccine and Preterm Infants

ACIP supports vaccination of a preterm infant if:

- **chronological age is at least 6 weeks**
- clinically stable
- vaccine is administered at time of discharge or after discharge from neonatal intensive care unit or nursery



Immunosuppressed Household Contacts of Rotavirus Vaccine Recipients

- Infants living in households with persons who have or are suspected of having an **immunodeficiency** disorder or impaired immune status **can be vaccinated**
- Protection provided by vaccinating the infant outweighs the small risk of transmitting vaccine virus



Pregnant Household Contacts of Rotavirus Vaccine Recipients

Infants living in households with pregnant women should be vaccinated

- majority of women of childbearing age have preexisting immunity to rotavirus
- **risk for infection by vaccine virus is considered to be very low**



Rotavirus Vaccine Adverse Events

Intussusception

- Postlicensure-evaluation RV1 — **1-3 excess cases per 100,000 first doses**, possible risk for RV5 cases too small to confirm
- VAERS — reports show events cluster in 3-6 days following RV5
- Vaccine Safety Datalink — **no increased risk of intussusception** — unable to assess RV1



Rotavirus Vaccine Adverse Reactions

- RV5
 - Diarrhea 18.1%
 - Vomiting 11.6%
 - Also greater rates of otitis media, nasopharyngitis and bronchospasm
- RV1
 - Irritability 11.4%
 - Cough or runny nose 3.6%
 - Flatulence 2.2%



Reduction in Pediatric Rotavirus-related Hospitalizations After Universal Rotavirus Vaccination in Belgium

Marc Raes, et al. *Pediatr Infect Dis J* 2011;30: e120–e125

Number of rotavirus-positive tests in the 2 years prevaccination and the 2 years postvaccination in children 5 years of age, hospitalized patients

