Monitoring For Rotavirus Serotypes In The Americas

Jon Gentsch

Centers for Disease Control and Prevention, Atlanta, USA

* The findings and conclusions in this presentation are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC).
Introduction

- Rationale for rotavirus strain surveillance
- Introduction to serotypes
- Surveillance in the Americas
- Conclusions and future directions
Rotavirus Strain Surveillance in Vaccine Era

Vaccine Research

- Impact of vaccines on strain prevalence and evolution
  - Will immune selection over time result in emergence of strains that escape protection?
- Vaccine stability
  - Reversion to virulence
  - Transmission, gastroenteritis in unvaccinated
  - Reassortment with wild-type rotavirus

Virus Evolution

- Origin of new strains through reassortment
  - Role of animal rotaviruses
- Genetic variation in RV genes
Rotavirus Serotype Classification

RNA Segment

1. VP1
2. VP2
3. VP3
4. VP4
5. VP6
6. VP8
7. VP9
8. VP10
9. VP11
10. NSP1
11. NSP2
12. NSP3
13. NSP4
14. NSP5

Protein

VP2
VP4
Neutralization antigen

Subgroup antigen

VP6

VP7
Neutralization antigen

Subcore

VP4

G type

P type

Provided by MK Estes
Rotavirus Detection (e.g., IDEIA (Oxoid [Ely]))

Genotype positives using hemi-nested RT-PCR

Identify genotypes by electrophoresis

Methods: Processing Stool Samples for Strain Surveillance

Rotavirus Detection
(e.g., IDEIA (Oxoid [Ely]))

Genotype positives
using hemi-nested RT-PCR

Identify genotypes
by electrophoresis
Human Rotavirus Serotypes and Genotypes

- Four historically common strains globally (>30 yrs)
- $P[8]G9$ emerged since 1995
- Emerged since 2000

Data of K Banyai, PG types 2004-2008
Uncommon rotavirus genotypes: >20 G types, >30 P types and ~80 G-P combinations in humans

Uncommon G & P types
- G5-P[6], [8]
- G6-P[6], [9] & [14]
- G8-P[1], [14]
- G12-P[6], [8]
- G3-P[11], [14]
Occasionally some are regionally important

Adapted from Kirkwood et al
Rotavirus Serotypes: Lessons learned from surveillance

- Only few globally common strains
- Periodic emerging strains
- Huge diversity
- Large temporal and geographic variation
Surveillance in the United States

- National Rotavirus Strain Surveillance System (NRSSS)
- New Vaccine Surveillance Network (NVSN)
National Rotavirus Strain Surveillance System (United States, 1996-2008)
Number of Positive and Total Rotavirus Tests, United States, 2000-2008, 33 Continuously Reporting Labs

RotaTeq introduced
Longitudinal Variation of Rotavirus G Types in the United States (1996-2008)

RotaTeq introduced

Hull, Teel et al, in prep
Geographical Serotype Variation USA (2007-2008)

Seattle WA, N=61
- G9 39%
- G3 12%
- G2 15%
- other 3%

Omaha NE, N=40
- G3 91%
- G1 6%
- G2 3%

Fort Worth TX, N=23
- G3 96%
- G1 4%

Hull, Teel et al, in prep
P and G Genotypes of Rotavirus Strains in United States (NRSSS) (1996-97 TO 2006-07)

- P[8]G9: 15%
- P[8]G1: 30%
- P[8]G3: 35%
- Other: 7%

Hull, Teel et al, in prep


- P[8]G1: 30%
- P[8]G3: 35%
- P[8]G9: 15%
- Other: 7%

Hull, Teel et al, in prep
Genotyping by sequencing identified a major outbreak of genotype G12 in the United States (primers for G12 are not routinely present in multiplex RT-PCR)

From Payne et al, PIDJ, 2009
Surveillance in Latin America and the Caribbean

- Set up starting 2004 to assess disease burden and strains
- Strains received from rotavirus sentinel hospital surveillance network 2005-2007 analyzed at CDC
- Genotyping results from seven sites
Map of Countries Participating in the Rotavirus Surveillance Network in Latin America and the Caribbean

L Oliveira et al, JID 2009
Strains Circulating in Seven Latin American Countries (2005-2007)

**Adapted from**
L Oliveira et al, JID 2009
Regional Variation of Strains Circulating in the Latin American (2005-2007)

Adapted from L Oliveira et al, JID 2009
Are Vaccination Programs Impacting Prevalence of Common Strains?

- Vaccination of populations with Rotarix
  - Increased prevalence of P[4]G2 (Brazil, Australia)

- Vaccination with RotaTeq
  - Increased prevalence of P[8]G3 (Australia, United States)
Temporal Variation in Predominant Strain, Central America

2005
- El Salvador
  - P[8]G9
  - 94%
- Guatemala
  - P[8]G9
  - 96%
- Honduras
  - P[8]G9
  - 40%

2006
- El Salvador
  - 81%
- Guatemala
  - 72%
- Honduras
  - 68%

2007
- El Salvador
  - P[8]G1
  - 91%
- Guatemala
  - P[8]G1
  - 68%
- Honduras
  - P[8]G1
  - 68%

Adapted from Patel et al., EID 2008; L Oliveira et al., JID 2009
Rotavirus Genotypes in Nicaragua, 2007-2008

RotaTeq Vaccinated Population and increased P[8]G3

N=262, Patel et al, JAMA 2009
Conclusions and Future Directions

- No convincing evidence for immune selection, more likely natural variation

- Supported by continued moderately high field efficacy of Rotarix vs P[4]G2 (e.g., Brazil, Australia [Snelling 2009, Nakagomi 2009], RotaTeq vs P[8]G3 [e.g., Boom et al 2008])

- Long term effectiveness studies where serotype specific VE and overall disease trends can be assessed
  - Needed to discriminate observed trends from natural strain fluctuations, emergence of new strains etc
Epidemiological Surveillance of Ministries of Health from countries

Members of the NVSN and NRSSS networks in the United States