Health Protection Surveillance Centre

Decline in rotavirus notifications following vaccine introduction

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Rotavirus infection - background

- Most common cause of paediatric gastrointestinal infection globally
  - 25% of all diarrhoea in <5 years
  - >10,000 deaths in children <5 years annually in WHO European Region
  - In Ireland low mortality but high morbidity and associated costs

- Vomiting, fever and watery diarrhoea lasting 3-7 days

- 3 / 1,000 cases may require hospitalisation, average of 5 days length of stay

- Transmission is usually person-to-person, via the faecal-oral route

- Cases are infectious 2 days before symptoms and 10 days after symptoms begin

- Children <2 years of age are most susceptible to infection, also seen in elderly and immunocompromised adults

- Infection and vaccination confer immunity but re-infection can occur with milder illness
Rotavirus vaccine – background

• Currently 4 rotavirus vaccines available internationally: Rotarix™, RotaTeq™, Rotavac™ and RotaSiil™

• Since 2009 WHO recommendation to include in national immunisation programmes

• By 2018, 98 countries introduced vaccination, including 14 EU countries

• December 2016 vaccine introduced in Ireland in for babies born from October 2016
  – Rotarix™ oral, live, attenuated monovalent vaccine using human G1P[8] strain
  – two doses at 2 and 4 months, completed by 8 months
  – may shed virus for ~2 weeks after vaccination
  – vaccine effectiveness 89% for RV hospitalisation in high income countries

• Rotarix™ vaccination uptake ~90% nationally in Ireland
Rotavirus infection - laboratory diagnostics

- 2016 HPSC survey of diagnostic methods in microbiology laboratories:
  - Mix of antigen testing and PCR methods in use

- Rotarix™ vaccine RNA is also detectable & indistinguishable from wildtype in many available commercial and “in-house” assays
  - NVRL* introduced RT-PCR assay which discriminates between wildtype or Rotarix vaccine strain in December 2017
  - during first month of testing, 93% of detections in suspected clinical cases from the vaccine eligible age group were vaccine strain

- Genotyping project ongoing in NVRL to monitor strain diversity

*National Virus Reference Laboratory, University College Dublin
Rotavirus infection: sources of data

• Notifiable disease under the Infectious Disease Regulations
  – Prior to 2004 “Gastroenteritis in children under two years”
  – 2004 to 2010 all age groups under the “Acute Infectious Gastroenteritis”
  – 2011 to present day all age groups “Rotavirus infection”
  – Germany & Ireland are only EU countries to have as notifiable disease

• Laboratory & clinical data integrated in national web based system
  – ISO accreditation for information security

• Vaccination status is not currently reported on CIDR* for rotavirus cases

*Computerised Infectious Disease Reporting system
Annual number of rotavirus notifications and rate*, Ireland

*crude incidence rate per 100,000 population

Source: CIDR
Rotavirus annual rate by HSE area, Ireland

2018 regional rates:
• All HSE areas had >60% decrease
• highest CIR: HSE-M (17.8)
• lowest CIR: HSE-NW (7.8)

*crude incidence rate per 100,000 population

Source: CIDR
Annual number of rotavirus notifications by month of notification, Ireland

Seasonality:
- cases typically peak during March to May in Ireland.
- highest number of rotavirus notifications in 2018 during May (n=116) but the characteristic peak was absent
- Smallest peak: low ratio showing magnitude of seasonality decreased

Source: CIDR
Annual rotavirus rates* in children <10 years old, Ireland

Age groups:
- decrease of >75% in the <1 year old and 1-4 years old ASIRs compared to mean 2008-2017.
- 172 rotavirus notifications in the vaccine eligible cohort**

*ASIR: age specific incidence rate
** defined as having been born after 01/10/2016 and being aged two months or older at the time of notification

Source: CIDR
Conclusions

- High vaccination uptake ~90%
- Decrease observed in 2018 and hopefully sustained in 2019
- Laboratory methods are critical for interpretation of trends
Acknowledgements:

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• Further information available on HPSC website: http://www.hpsc.ie/a-z/gastroenteric/rotavirus/

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References

**Vaccine effectiveness:**
- **Hungerford et al. 2017.** *Population effectiveness of the pentavalent and monovalent rotavirus vaccines: a systematic review and meta-analysis of observational studies.* BMC. DOI 10.1186/s12879-017-2613-4
  - Vaccine effectiveness RV lab conf hospitalisations 89% in high income, VE 74% in middle income
  - Vaccine effectiveness all cause gastroenteritis community 40%
  - Vaccine effectiveness full dose 81%, partial dose 62%
  - Vaccine effectiveness against RV admission/ ED/ OP by country mortality <5yrs: 84% in low, VE 75% in medium, 57% high mortality
  - Vaccine effectiveness from random effects model 82%
  - Partial series effectiveness lower than full but partial of either RV1/5 provided considerable protection against severe RV disease for 1st 2yrs life

**Strain diversity:**
- **Leshem et al. 2014.** *Distribution of rotavirus strains and strain-specific effectiveness of the rotavirus vaccine after its introduction: a systematic review and meta-analysis.* Lancet. 10.1016/S1473-3099
  - Intro of vaccines “has not altered the regular variation in strains that would suggest selective pressure”
  - “dominance of strains changes fairly regularly”
  - “immunity after rotavirus vaccination and infection is polygenic”

**Herd immunity:**
- **Pollard et al. 2015.** *Estimating the herd immunity of rotavirus vaccine.* Vaccine DOI: 10.1016/j.vaccine.2015.06.064
  - Evidence that rotavirus vaccination confers a herd immunity effect among children <1yr in the US and Latin America.
  - Observed reductions in all cause diarrhoea hospitalisations were higher than the theoretical maximum reduction

**Cost effectiveness:**
- **Kotirim et al. 2017.** *Global economic evaluations of rotavirus vaccines: A systematic review.* Vaccine. DOI: 10.1016/j.vaccine.2017.04.051
  - Both found cost –effective for low-middle income, may not be cost effective for high income if vaccine is at market price

http://rotacouncil.org/vaccine_introduction/global_introduction_status