Clinical Complications of Respiratory Viruses – rhinoviruses, influenza, hMPV

Michael Nissen FRACP FRCPA FFS

Queensland Paediatric Infectious Diseases Laboratory

Royal Children's Hospital & Pathology Qld.

Brisbane, Australia

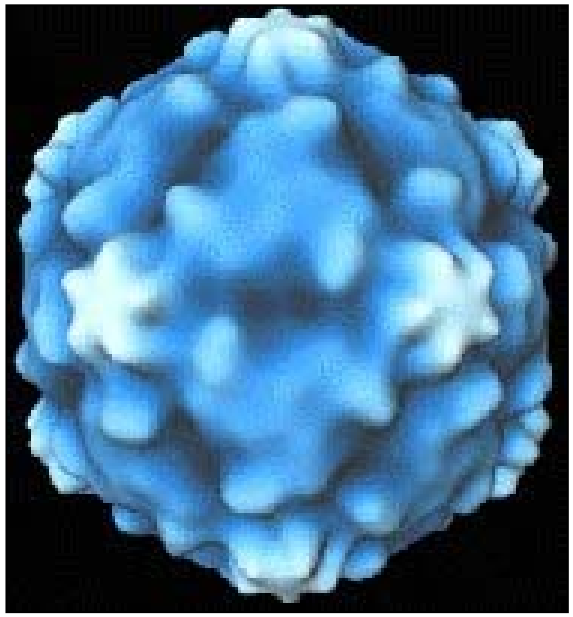
introduction

- Respiratory viral infections (RVIs) due to rhinoviruses, influenza, human metapneumovirus (hMPV) commonly cause mild illness in immunocompetent children and adults.
- RVIs rarely cause significant morbidity or mortality.
  - Complications are more common in the very young, very old, and those with underlying lung diseases.
- RVIs increasingly recognized as pathogens in haematopoietic stem cell transplants (HSCT) and solid organ transplants (SOTs) patients.
- Clinical microbiology laboratory is under increasing pressure to urgently test respiratory specimens for RVI's and interpret the results, particularly in immunocompromised patient groups.
- This can be problematic where the role and management of these viruses in causing serious disease is still being elucidated.

human rhinovirus

- Properties *(Picornaviridae)*
  - +ssRNA, 7-8 kb
  - Virion acts as mRNA, transcribed as a polyprotein and cleaved progressively to yield S & NS proteins
  - Acid-labile (ph<5)
  - 3 species: A, B, C
  - Rhinoviruses serotypes1-100
- Epidemiology
  - Year-round infection
  - Peaks in autumn & spring
  - 3-4 serotypes circulate simultaneously
- Pathogenesis
  - Predilection to replicate @ 33^{o}C
  - Acquired immunity type specific and correlates with locally synthesized IgA antibodies
- Clinical Features
  - "common cold"
  - ↑ recognition in LRTI & wheezing/asthma
- Diagnosis
  - EIA, PCR, culture

- Treatment
  - ? Pleconaril



Rhinovirus 14

human rhinoviruses [HRV]

- Commonest pathogen affecting mankind
- First isolated in 1950s
- Commonest “cold” virus in the first years of life
- Initially considered a mild nuisance rather than a true disease
- Cause 50% of respiratory tract infections (RTIs)
- Complications include:
  - Otitis media
  - Sinusitis
  - Exacerbations of asthma
  - Pneumonia in immunocompetent & immunocompromised
- RT-PCR has increased identification in RTIs
- Greater appreciation of role of HRV in Upper & Lower RTIs

HRV-pneumonia

OPEN ACCESS Freely available online

PLoS one

Human Rhinovirus Infections in Rural Thailand: Epidemiological Evidence for Rhinovirus as Both Pathogen and Bystander

Alicia M. Fry[1]*, Xiaoyan Lu[2], Sonja J. Olsen[3], Malinee Chittaganpitch[4], Pongpun Sawatwong[5], Somrak Chantra[5], Henry C. Baggett[5], Dean Erdman[2]

1 Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, **2** Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, **3** Division of Emerging Infections and Surveillance Services, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America, **4** National Institute of Health, Thailand Ministry of Public Health, Nonthaburi, Thailand, **5** International Emerging Infections Program, Thai MOPH-U.S.CDC Collaboration, Nonthaburi, Thailand

PLoS ONE | www.plosone.org

March 2011 | Volume 6 | Issue 3 | e17780

- From September 1, 2003-August 31, 2005, tested hospitalized patients with acute lower respiratory illness and outpatient controls without fever or respiratory symptoms for HRVs with polymerase chain reaction and molecularly-typed select HRVs.
- Compared HRV detection among hospitalized patients and controls and estimated enrollment adjusted incidence.

HRV-pneumonia

- HRVs were detected in 315 (16%) of 1919 hospitalized patients and 27 (9.6%) of 280 controls.
- Children had the highest frequency of HRV detections
  - Hospitalized: <1 year: 29%, 1-4 year: 29%, ≥ 65 years: 9%;
  - Controls: <1 year: 24%, 1-4 year: 14%, ≥ 65 years: 2.8%).
- Enrollment adjusted hospitalized HRV detection rates were highest among persons aged <1 year (1038/100,000 persons/year), 1-4 years (457), and ≥ 65 years (71).
- All three HRV species were identified
  - HRV-A was the most common species in most age groups including children aged <1 year (61%) and all adult age groups.
  - HRV-C was the most common species in the 1-4 year (51%) and 5-19 year age groups (54%).
- Compared to controls,
  - hospitalized adults (≥ 19 years) and children were more likely to have HRV OR]: 4.8, and
  - hospitalized children were more likely to have HRV-A (OR 1.7) or HVR-C (OR 2.7)

HRV-adult bone marrow transplants

Rhinovirus Infections in Myelosuppressed Adult Blood and Marrow Transplant Recipients

S. Ghosh, R. Champlin, R. Couch, J. Englund, I. Raad, S. Malik, M. Luna, and E. Whimbey

Clinical Infectious Diseases 1999;29:528–32

From the Department of Medical Specialties, the Department of Blood and Marrow Transplantation, and the Department of Pathology, The University of Texas M. D. Anderson Cancer Center, and the Department of Microbiology and Immunology, The Baylor College of Medicine, Houston, Texas

- Outcomes for 22 myelosuppressed adult BMT recipients with HRV who were hospitalized.
- 15 patients (68%), illnesses remained confined to the upper respiratory tract.
- 7 patients (32%) developed fatal pneumonia.
  - profound respiratory failure at mean of 12 days (range, 3-21 days) after the onset of symptoms.
- In 6 of 7 cases, HRV was isolated before death from a BAL or ETA.
- 5 patients underwent autopsies,
  - 1 revealed disseminated aspergillosis
  - 4 revealed interstitial pneumonitis and/or ARDS and no other organisms.

HRV-paediatric bone marrow transplants

Clin Transplant 2012 DOI: 10.1111/j.1399-0012.2012.01607.x

Clinical Transplantation

Respiratory viral infections during the first 28 days after transplantation in pediatric hematopoietic stem cell transplant recipients

Lee JH, Jang J-H, Lee SH, Kim Y-J, Yoo KH, Sung K-W, Lee NY, Ki C-S, Koo HH. Respiratory viral infections during the first 28 days after transplantation in pediatric hematopoietic stem cell transplant recipients. Clin Transplant 2012 DOI: 10.1111/j.1399-0012.2012.01607.x. © 2012 John Wiley & Sons A/S.

Ji Hyun Lee[a], Ja-Hyun Jang[a], Soo Hyun Lee[b], Yae-Jean Kim[b], Keon Hee Yoo[b], Ki-Woong Sung[b], Nam Yong Lee[a], Chang-Seok Ki[a,*], Hong Heo Koo[b,*]

HRV-paediatric bone marrow transplants

- Focused on the first 28 d after transplantation in pediatric HSCT recipients
- 176 pediatric HSCT recipients,
  - 84 with respiratory symptoms within 1 yr after HSCT were tested by viral culture or multiplex PCR.
- Within 28 d after HSCT, 9 patients were infected with RVs;
  - Incidence of a first episode of RV infection within 28 d after HSCT was 5.1%.
  - 8 patients recovered without complications.
  - 1 patient died of adenovirus (AdV) pneumonia with pulmonary hemorrhage;
- Mortality rate of RV infection within 28 d after HSCT was 0.57%.
- In the 9 patients with RV infection, 5 different types of RV were identified, either alone or with another RV.
  - HCV
  - HRV
  - RSV combined with CoV;
  - AdV combined HRV;
  - PIV.

HRV-lung transplants

Chronic Rhinoviral Infection in Lung Transplant Recipients

Am J Respir Crit Care Med Vol 174, pp 1392-1399, 2006

Laurent Kaiser, John-David Aubert*, Jean-Claude Pache*, Christelle Deffernez, Thierry Rochat, Jorge Garbino, Werner Wunderli, Pascal Meylan, Sabine Yerly, Luc Perrin, Igor Letovanec, Laurent Nicod, Caroline Tapparel, and Paola M. Soccal

Central Laboratory of Virology, Division of Infectious Diseases, Department of Internal Medicine; Department of Pathology; Division of Pulmonary Medicine, Department of Internal Medicine; Clinic of Thoracic Surgery, Department of Surgery, University Hospitals of Geneva, Geneva; Division of Pulmonary Medicine, Department of Medicine; Institute of Microbiology and Division of Infectious Diseases, Department of Pathology, University Hospital of Lausanne, Lausanne; and Division of Pulmonary Medicine, University Hospital, Bern, Switzerland

- The incidence of chronic HRV and potential clinical impact was assessed prospectively in a cohort of 68 lung transplant recipients during 19 mo by screening of bronchoalveolar lavages.
- Describe 3 lung transplant recipients with graft dysfunctions in whom HRV was identified in upper and lower respiratory specimens over a 12-mo period.
- The persistence of a unique strain in each case was confirmed by sequence analysis of the 5'NCR and VP1 gene.
- In the index case, HRV was detected in the lower respiratory parenchyma.
- In the cohort of lung transplant recipients, rhinoviral infections were documented in bronchoalveolar lavage specimens of 10 recipients, and 2 presented with a persistent infection

Rhinovirus C and Respiratory Exacerbations in Children with Cystic Fibrosis

Table 1. Respiratory viruses and clinical status of 103 children with cystic fibrosis , Brazil, 2006–2007

Virus	No. samples collected during routine visits, n = 266	No. samples collected during respiratory exacerbations, n = 142	Total no. (%) samples
Rhinovirus	91	48	139 (34.1)
Enterovirus	13	11	24 (5.9)
Human bocavirus	14	9	23 (5.6)
Human coronavirus	13	6	19 (4.7)
Respiratory syncytial virus	7	8	15 (3.7)
Influenza A	1	3	4 (1.0)
Human metapneumovirus	1	2	3 (0.7)
Influenza B	1	0	1 (0.2)
Parainfluenza 1	0	1	1 (0.2)
Parainfluenza 2	0	1	1 (0.2)
Parainfluenza 3	0	1	1 (0.2)
Adenovirus	0	1	1 (0.2)

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 16, No. 6, June 2010

HRV-cystic fibrosis

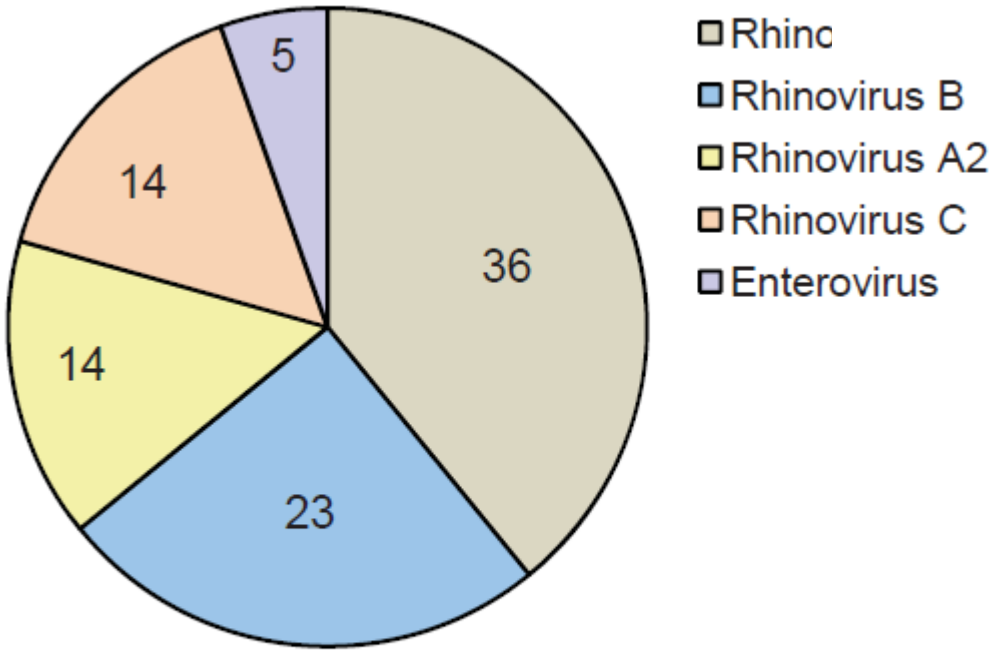


Figure 1. Results of 5′ noncoding region sequencing of 93 samples with identification of human rhinovirus by real-time reverse transcription–PCR, obtained from samples from 103 children with cystic fibrosis, Brazil, 2006–2007.

Table 2. Virologic test results and respiratory exacerbation outcome for 103 children with cystic fibrosis, Brazil, 2006–2007*

Virus	OR (95% CI)	p value
Any respiratory virus	1.063 (0.979–1.154)	0.144
Rhinovirus	1.020 (0.931–1.117)	0.666
Any respiratory virus except rhinoviruses	1.195 (1.043–1.369)	0.010
Rhinovirus A2 or C (excluding samples not sequenced)	1.213 (1.024–1.436)	0.025

*Estimates from binomial, generalized linear models. OR, odds ratio; CI, confidence interval.

HRV type C-asthma

Original article

A novel group of rhinoviruses is associated with asthma hospitalizations

E. Kathryn Miller, MD, MPH,[a] Kathryn M. Edwards, MD,[a] Geoffrey A. Weinberg, MD,[b] Marika K. Iwane, PhD, MPH,[c] Marie R. Griffin, MD, MPH,[d] Caroline B. Hall, MD,[b] Yuwei Zhu, MD, MS,[e] Peter G. Szilagyi, MD, MPH,[b] Laura-Lee Morin, BS,[a] Luke H. Heil,[a] Xiaoyan Lu, MS,[c] and John V. Williams, MD,[a,f] for the New Vaccine Surveillance Network *Nashville, Tenn, Rochester, NY, and Atlanta, Ga*

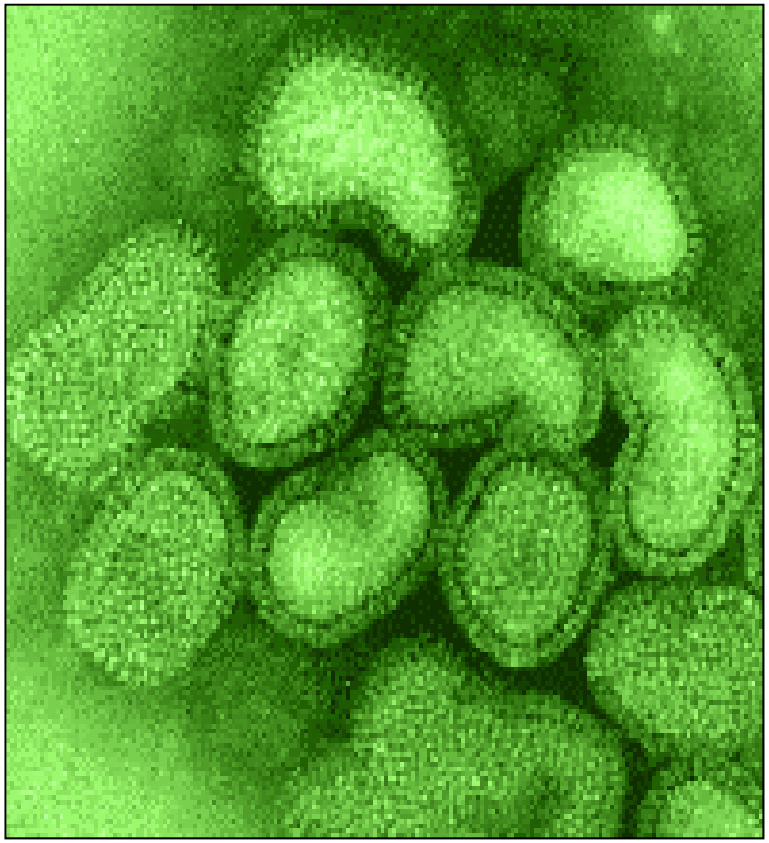
J Clin Virol. 2009 Sep;46(1):85-9. Epub 2009 Jul 5.

HRV-C & asthma

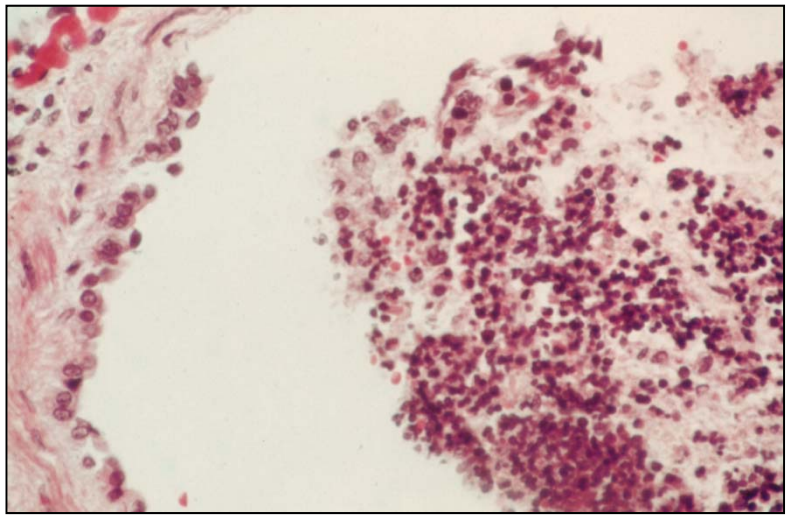
- A prospective population-based surveillance in 2 US counties among children <5 yoa hospitalized with acute RTI or fever from Oct 2001-Sept 2003.
- Nasal/throat swabs were obtained and tested for HRVs, as determined by means of RT-PCR & characterized by partial sequencing.
- 1052 children enrolled and tested during 2 yrs.
  - 167 (16%) had HRVs detected.
  - 147 samples successfully sequenced,
  - 77 HRV-Cs, 64 HRV-As, 6 HRV-Bs.
- Children with HRV-Cs significantly more likely than HRV-A to have underlying high-risk conditions, such as asthma (42% vs 23%, *P=0.023*) and to have had a discharge diagnosis of asthma (55% vs 36%, *P=0.022*).
- HRV-C detected in 7% of children hospitalized for fever or respiratory conditions and constituted almost 50% of all HRV-associated hospitalizations.
- Suggests this novel group causes a substantial burden of pediatric disease.

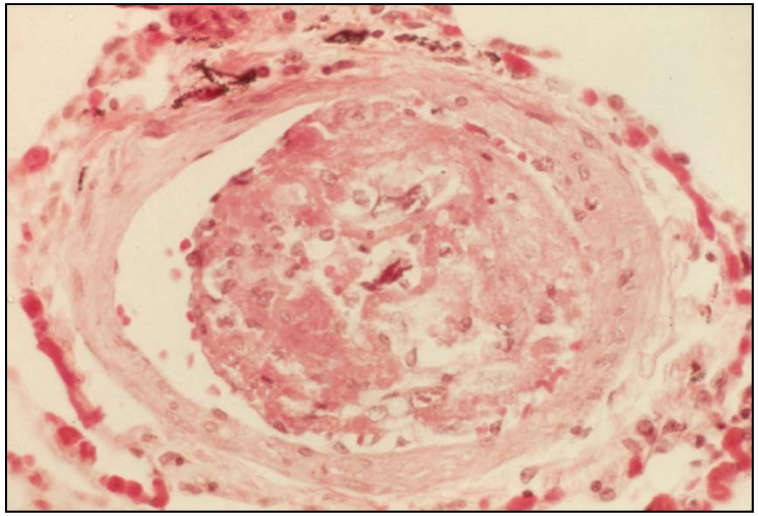
influenza

- Properties
  - Belong to family *Orthomyxoviridae*
  - 3 genera A,B,C
  - -ssRNA, 13.6 kb, 8 segments
- Epidemiology
  - Antigenic “drift” & “shift”
  - Seasonality
  - B less pathogenic
- Pathogenesis
  - Transcription/replication in cell nucleus
  - Incubation 1-4 days
  - Large no. of virions shed



Influenza





- Clinical Features
  - Abrupt onset of fever, sore throat, cough, myalgia, headache, malaise.
  - Duration 3-7 days
  - Complications vary with age: croup, pneumonia, OM
  - Increaed risk;
    - Prexisitng heart/lung/renal/CNS diseases
    - Pregnancy
    - Immunosuppression
  - 2^0 bacterial pathogens: *S. aureus, S. pneumoniae, H. influenzae.*

influenza hospitalisations

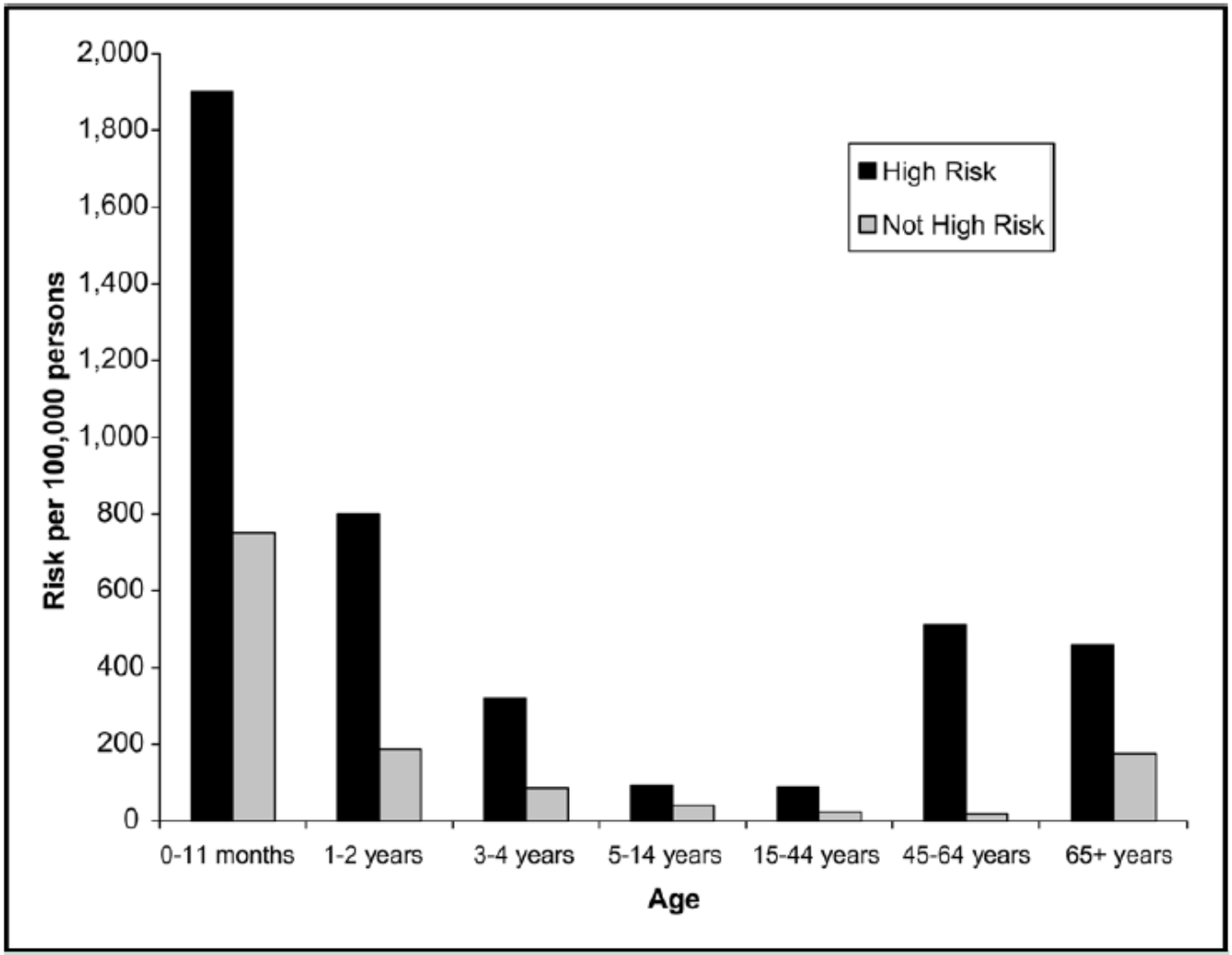


Figure Annual risk of hospitalization for high-risk and non–high-risk persons.

Complications of Viral Influenza

Michael B. Rothberg, MD, MPH,[a,c] Sarah D. Haessler, MD,[b,c] Richard B. Brown, MD[b,c]

The American Journal of Medicine (2008) 121, 258-264

influenza A/H1N1/California

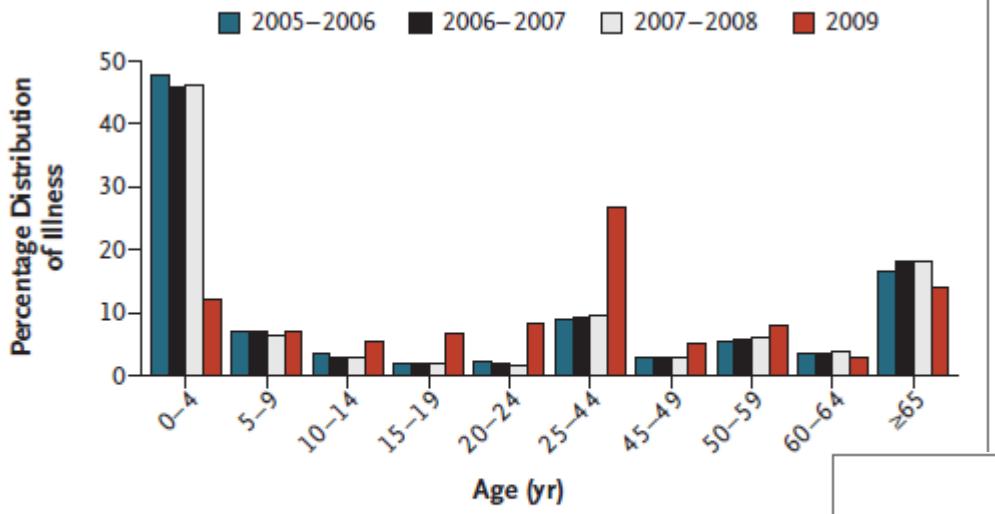


Figure 3. Percentage Distribution of Illness from Severe Pneumo during the 2009 Study Period, as Compared with Influenza Seas from 2005 through 2008, in Mexico, According to Age Group.

Severe Respiratory Disease Concurrent with the Circulation of H1N1 Influenza

Gerardo Chowell, Ph.D., Stefano M. Bertozzi, M.D., Ph.D., M. Arantxa Colchero, Ph.D., Hugo Lopez-Gatell, M.D., Ph.D., Celia Alpuche-Aranda, M.D., Ph.D., Mauricio Hernandez, M.D., Ph.D., and Mark A. Miller, M.D.

N ENGL J MED 361;7 NEJM.ORG AUGUST 13, 2009

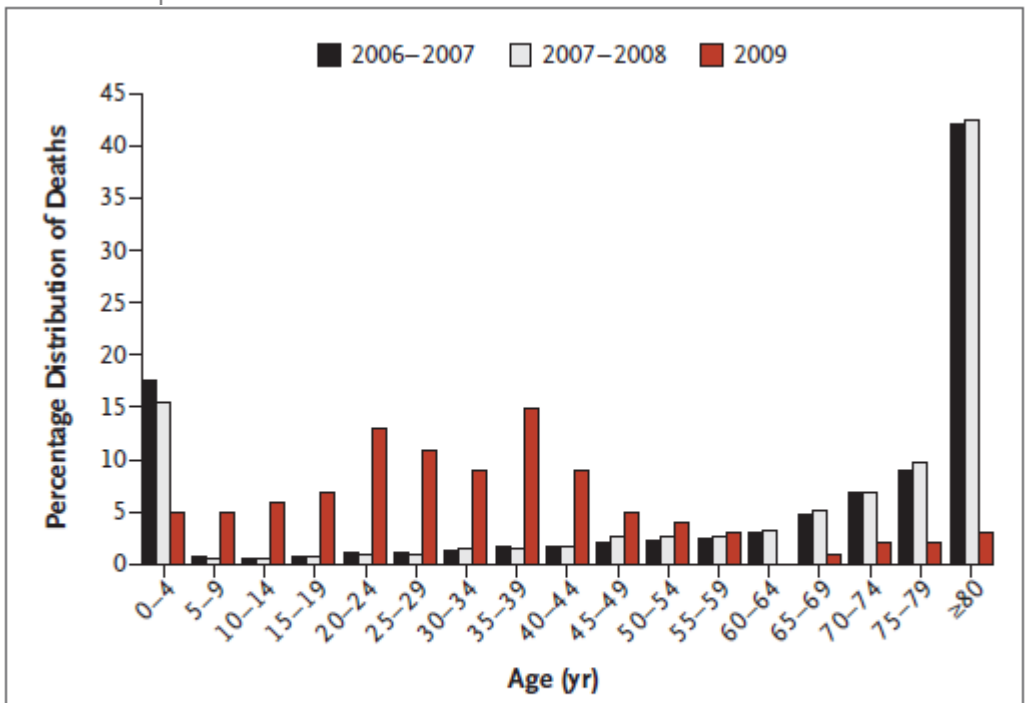


Figure 2. Percentage Distribution of Deaths from Severe Pneumonia during the 2009 Study Period, as Compared with Influenza Seasons from 2006 through 2008, in Mexico, According to Age Group.

influenza ICU admissions

Complications of seasonal and pandemic influenza

Michael B. Rothberg, MD, MPH; Sarah D. Haessler, MD

Crit Care Med 2010 Vol. 38, No. 4 (Suppl.)

Table 1. Demographic characteristics of 1047 patients admitted to intensive care for 2009 pandemic H1N1 infections in five countries

Country	US	Spain	Canada	Mexico	Australia/ New Zealand	Total	%
Number admitted to ICU	67	32	168	58	722	1047	
Age, mean	29	40	32	42	40	38	
Female, %	NR	27	67	55	52		50
Obesity BMI >30[a]	NR	10	56	21	172	259/859	30
Morbid obesity BMI >40	NR	4	NR	8	NR	12/90	13
Comorbid illness							
Asthma/COPD	19	9	54	4	231	317/1032	31
Renal insufficiency	NR	1	11	4	NR	16/258	6
Diabetes	NR	1	35	10	112	158/958	16
Pregnancy	6	2	13	1	66	88/1047	8
Immune suppression	12	NR	33	2		47/293	16
Congestive heart failure	NR	1	12	1	74	88/961	9
Neurologic disease	12	1	26	1	NR	40/325	12
No major comorbid conditions	22	15	117	37	495	664/1012	66

H1N1 pregnancy

Table 1. Characteristics of Women Who Were Hospitalized with or Died from 2009 H1N1 Influenza, as Reported to the California Department of Public Health during the Period from April 23 to August 11, 2009, According to Pregnancy Status.*

Characteristic	Pregnant (N=94)	Postpartum (N=8)	Nonpregnant (N=137)	P Value
Age — no. (%)				<0.001†
15–19 yr	14 (15)	0	24 (18)	
20–24 yr	29 (31)	1 (12)	24 (18)	
25–29 yr	29 (31)	5 (62)	26 (19)	
30–34 yr	16 (17)	2 (25)	22 (16)	
35–39 yr	4 (4)	0	26 (19)	
40–44 yr	2 (2)	0	15 (11)	
Median age (range) — yr	26 (16–42)	28 (22–33)	28 (15–44)	0.02‡
Chronic coexisting illness — no./total no. (%)¶	32/93 (34)	2/8 (25)	82/137 (60)	<0.001†
Chronic lung disease	16/93 (17)	0	45/135 (33)	0.007†
Asthma	15/93 (16)	0	38/135 (28)	0.04†
Other**	2/93 (2)	0	14/135 (10)	0.02‖
Metabolic disease	14/90 (16)	1/8 (12)	29/130 (22)	0.21†
Diabetes mellitus	2/90 (2)	0	19/130 (15)	0.002‖
Gestational diabetes	8/90 (9)	1/8 (12)	NA	
Renal disease	3/90 (3)	0	8/130 (6)	0.53‖
Other††	1/90 (1)	0	2/130 (2)	1.00‖
Immunosuppressive disorder	4/91 (4)	0	25/136 (18)	0.002‖
Cancer or transplantation-related	3/91 (3)	0	20/136 (15)	0.006‖
HIV or AIDS	1/91 (1)	0	2/136 (1)	1.00‖
Other‡‡	0	0	8/136 (6)	0.02‖
Chronic cardiac disease§§	3/92 (3)	0	14/133 (11)	0.07‖
Neurologic disorder¶¶	1/91 (1)	1/8 (12)	13/131 (10)	0.009‖
Other chronic coexisting illness	6/89 (7)	1/8 (12)	34/134 (25)	<0.001†
Hypertension	5/94 (5)	1/8 (12)	23/137 (17)	0.009†
Hyperlipidemia	0	0	4/137 (3)	0.15‖
Gastrointestinal disease‖‖	2/85 (2)	0	17/123 (14)	0.006‖

N ENGL J MED 362;1 NEJM.ORG JANUARY 7, 2010

TABLE 2. Outcomes for live births to pregnant women with 2009 pandemic influenza A (H1N1) severe illness (i.e., ICU admission or death) — United States, April 15, 2009–August 10, 2010

Outcome	Delivery during maternal hospitalization for 2009 H1N1 illness		Delivery after discharge from 2009 H1N1 illness hospitalization		Estimated % in U.S. population
	No.	(%)	No.	(%)	
Gestational age at delivery (wks)					
Very preterm (<32)	17	(22.1)	0	—	
Preterm (32–36)	32	(41.6)	10	(20.8)	
Very preterm and preterm (<37)	49	(63.6; CI = 51.8–74.3)	10	(20.8; CI = 10.5–35.0)	12.3*
Term (≥37)	28	(36.4)	38	(79.2)	
Unknown/Missing	8	—	6	—	
Small for gestational age					
≤10th centile for gestational age†	3	(4.1; CI = 0.0–11.5)	13	(25.0; CI = 14.0–39.0)	10.0†
>10th centile for gestational age	70	(95.9)	39	(75.0)	
Unknown/Missing	12	—	2	—	
Birthweight (g)					
Low (<2,500)	32	(43.8; CI = 32.2 –56.0)	10	(19.2; CI = 9.6–32.5)	8.2*
Normal (≥2,500)	41	(56.2)	42	(80.8)	
Unknown/Missing	12	—	2	—	
Admission to neonatal ICU					
No admission	22	(30.6)	39	(78.0)	
Admission	50	(69.4; CI = 57.5–79.8)	11	(22.0; CI = 11.5–36.0)	6.1§
Unknown/Missing	13	—	4	—	
5-minute Apgar scores					
Low (≤6)	21	(29.2; CI = 19.1–41.1)	1	(2.0; CI = 0.1–10.7)	1.6¶
Normal (>6)	51	(70.8)	49	(98.0)	
Unknown/Missing	13	—	4	—	
Total	**85****	**100.0**	**54****	**100.0**	

A newly discovered human pneumovirus isolated from young children with respiratory tract disease

BERNADETTE G. VAN DEN HOOGEN[1], JAN C. DE JONG[1], JAN GROEN[1], THIJS KUIKEN[1], RONALD DE GROOT[2], RON A.M. FOUCHIER[1] & ALBERT D.M.E. OSTERHAUS[1]

[1]Departments of Virology and [2]Pediatrics, Erasmus Medical Center, Rotterdam, the Netherlands
Correspondence should be addressed to A.D.M.E.O.; email: osterhaus@viro.fgg.eur.nl

From 28 young children in the Netherlands, we isolated a paramyxovirus that was identified as a tentative new member of the *Metapneumovirus* genus based on virological data, sequence homology and gene constellation. Previously, avian pneumovirus was the sole member of this recently assigned genus, hence the provisional name for the newly discovered virus: human metapneumovirus. The clinical symptoms of the children from whom the virus was isolated were similar to those caused by human respiratory syncytial virus infection, ranging from upper respiratory tract disease to severe bronchiolitis and pneumonia. Serological studies showed that by the age of five years, virtually all children in the Netherlands have been exposed to human metapneumovirus and that the virus has been circulating in humans for at least 50 years.

NATURE MEDICINE • VOLUME 7 • NUMBER 6 • JUNE 2001

HMPV clinical features

Human Metapneumovirus, Australia, 2001–2004

Theo P. Sloots,*†‡§[1] Ian M. Mackay,*†‡[1]
Seweryn Bialasiewicz,*† Kevin C. Jacob,*†‡
Emily McQueen,*† Gerald B. Harnett,¶
David J. Siebert,§ I. Brent Masters,*
Paul R. Young,‡ and Michael D. Nissen*†‡§

We examined 10,025 respiratory samples collected for 4 years (2001–2004) and found a 7.1% average annual incidence of human metapneumovirus. The epidemic peak of infection was late winter to spring, and genotyping showed a change in predominant viral genotype in 3 of the 4 years.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 12, No. 8, August 2006

HMPV clinical features

Human Metapneumovirus, Australia, 2001–2004

Table 2. Signs and symptoms noted with human metapneumovirus infection (N = 273)

Clinical feature	%
Cough	63
Rhinorrhea	61
Crackles/crepitations	60
Fever	57
Respiratory distress	48
Anorexia	45
Vomiting	39
Wheezing	38
Irritability	31
Tachypnea	30
Lethargy	26
Pharyngitis/tonsillitis	24
Dry mouth	23
Diarrhea	18
Otitis media	15
Noisy breathing	14
Rash	10
Conjunctivitis	7
Cyanosis	4
Apnea	2
Hoarseness	1

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 12, No. 8, August 2006

HMPV clinical features

TABLE 1. Frequency of Symptoms Among Children With HMV Infection

Symptom	Frequency, %
Cough[21,25,27,33]	67–92
Fever[25,27]	73–77
Rhinorrhea/nasal congestion[25,27,33]	64–77
Dyspnea/shortness of breath[21,25]	57–81
Wheeze[21,27]	40–51
Pharyngitis[33]	29

Sample sizes for these studies[21,25,27,33] was n = 1 n = 668, and n = 931, respectively.

Brodzinski H& RM Ruddy Pediatric Emergency Care & Volume 25,

TABLE 2. Frequency of Diagnoses Among Children With HMV Infection

Diagnosis	Frequency, %
Bronchiolitis[10,13,14,22,25,26,28,33]	10–67
Pneumonia/pneumonitis[10,13,14,22,25,28]	8–66.7
Recurrent wheeze[26]	45.5
Asthma/asthma exacerbation[10,14,22,25,33]	5.7–23
Croup[14]	18
Fever without a source[25]	11.5

Most studies showed a frequency of bronchiolitis in the 50% to 65% range.[13,14,22,26,33]

HMPV illness severity

Human Metapneumovirus, Australia, 2001–2004

- Severity score calculated at discharge
- Oxygen therapy
  - *Martinello RA et al., J Infect Dis 2002;186(6):839-42.*
  - *McIntosh ED et al., Pediatr Infect Dis J 1993;12(10):815-9.*
    - requiring ventilation : 2
    - oxygen therapy : 1
    - no oxygen : 0
- Intravenous or nasogastric fluids
  - *Smyth RL et al., Lancet 1999;354(9194):1997-8*
    - required IV/NG fluids : 1
    - no NG/IV fluids : 0
- Time until ready for discharge
  - *Wainwright C et al., N. Engl. J. Med. 2003;349(1):27-35.*
    - > 5 days : 2
    - < 5 days : 1
    - not admitted : 0

Overall severity score

Severe : 4-5
Moderate : 2-3
Mild : 0-1

Severity	#	%
Mild	156	49
Moderate	129	41
Severe	32	10

- 13 Deaths
  - 5 directly related
- 41 cases of nosocomial infection
- 17 cases in Transplant patients
  - 12 Solid
  - 5 BMT
- 9 families infected
- 3 children with multiple isolations
- Exacerbation of CPD infection

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 12, No. 8, August 2006

HMPV illness severity

Manifestation (%)	hMPV + (n=25)	RSV + (n=25)	95% CI of difference
Dyspnea	28	76	-72 to -23
Feeding difficulties	36	76	-65 to -15
Hypoxia	47	82	-62 to -7
Illness score	0.38	0.55	-0.2 to –0.03
Asthma hx	16	0	1.6 to 30
O_2 administration	36	64	-55 to -1
Antibiotic use	60	12	25 to 71
Hoarse voice*	91 (n=10)	42 (n=11)	p=0.01

van den Hoogen et al., 2003

** Peret T., CDC 2003*

HMPV in high risk populations

A Prospective Study Comparing Human Metapneumovirus with Other Respiratory Viruses in Adults with Hematologic Malignancies and Respiratory Tract Infections

JID 2005:192 (15 September) • 1061

John V. Williams,[1] Rodrigo Martino,[3] Núria Rabella,[4] Magdalena Otegui,[4] Rocio Parody,[3] Joshua M. Heck,[1] and James E. Crowe, Jr.[1,2]

Departments of [1]Pediatrics and [2]Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee; [3]Division of Clinical Hematology and [4]Department of Microbiology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Twenty-two (9%) of 251 episodes of respiratory infection tested positive for hMPV.

Sixteen (73%) of the illnesses occurred in hematopoietic stem-cell transplant recipients. Nine patients with hMPV developed LRI; 3 of these patients died.

HMPV in haematologic malignancies

Table 2. Characteristics of 156 respiratory virus infections, according to initial virus isolated.

Characteristic	Result in patients infected with: hMPV	Influenza virus	RSV	PIV1 or PIV3	Adenovirus	Rhinovirus	Enterovirus	Total
No. of infections	22	68	27	15	12	3	9	156
Nature of infection								
Primary viral isolate[a]	18 (82)	66 (97)	18 (67)	14 (93)	8 (67)	2 (67)	9 (100)	135 (87)
Superinfection[b]	4 (18)	2 (3)	9 (33)	1 (7)	4 (33)	1 (33)	...	21 (13)
Clinical presentation[c]								
URI	20 (91)	54 (79)	20 (74)	11 (73)	10 (83)	3 (100)	7 (78)	125 (81)
LRI	...	8 (12)	1 (4)	2 (13)	1 (8)	...	1 (11)	13 (9)
URI + LRI	1 (5)	5 (7)	6 (22)	2 (13)	1 (8)	...	1 (11)	16 (10)
LRI (pneumonia)	9 (41)	20 (29)	11 (41)	6 (40)	5 (42)	0	2 (22)	53 (34)
Initial LRI ± URI	1 (5)	13 (65)	6 (22)	4 (27)	2 (17)	...	2 (22)	28 (18)
URI progressing to LRI	8 (36)	7 (35)	5 (18)	2 (13)	3 (25)	...	...	25 (16)
Superinfection by another virus during episode								
RSV	4[f] (18)	7 (10)	...	...	1 (8)	...	...	12 (8)
Adenovirus	1 (5)	3 (4)	1 (44)	1 (7)	...	...	...	6 (4)
CMV	1 (5)	1 (1)	1 (4)	1 (7)	...	...	...	4 (3)
Influenza A	2 (9)	3 (4)	12 (44)	1 (7)	5 (42)	...	1 (11)	24 (15)
PIV1	...	...	...	...	1 (8)	1 (33)	1 (11)	3 (2)
Enterovirus/rhinovirus	1 (5)	...	...	2 (14)	...	...	...	3 (2)
Respiratory-tract coinfections								
Other respiratory virus	9 (41)[g]	14 (20)	14 (52)	5 (33)	7 (58)	1 (33)	2 (22)	52 (33)
Death attributed to virus (% of LRI episodes)	3 (33)	4 (20)	3 (27)	2 (33)	2 (40)	0	0	12 (23)
No other copathogens found	1	0	1	2	2	...	...	5
Other copathogens involved	2	4	2	...	...	...	...	6
Invasive aspergillosis	...	1	...	...	...	...	...	1
Gram-negative bacilli	2	1	1	...	...	...	...	4
Cytomegalovirus	...	2	1	...	...	...	...	3

HMPV in high risk populations

Human Metapneumovirus in Lung Transplant Recipients and Comparison to Respiratory Syncytial Virus

Peter Hopkins[1], Keith McNeil[1], Fiona Kermeen[1], Michael Musk[1], Emily McQueen[2], Ian Mackay[2,3], Terry Sloots[2], and Michael Nissen[2]

Am J Respir Crit Care Med Vol 178. pp 876–881, 2008

- 89 patients had199 visits for aspirate studies.
- A viral cause was determined for 62 visits in 47 patients (19 human metapneumovirus, 18 RSV, 13 parainfluenza, 9 influenza A, 2 adenovirus, and 1 influenza B).
- A significant percentage of patients with metapneumovirus (63%) and RSV (72%) developed graft dysfunction, with average declines in FEV1 of 30 6 12.4% and 25.9 6 11.2%, respectively.
- In these patients, bronchiolitis obliterans syndrome onset or progression occurred in no patients with human metapneumovirus compared with 5 of 13 (38%) patients with RSV at 6 months.

HMPV in lung transplants

TABLE 1. CHARACTERISTICS OF PATIENTS WITH RESPIRATORY VIRAL INFECTION

	hMPV	RSV
Subjects	19	18
Mean age, yr	47.9 ± 10.7	48 ± 8.3
Sex, male:female	11:8	12:6
Transplant type		
SLT	2	3
BSLT	16	14
HLT	1	1
Time post-transplant, d	1,505 ± 613	1,135 ± 523
Previous OB or BOS	n = 8 (42%)	n = 6 (33%)
BOS grade 1–2	5	2
BOS grade 3	3	4
Inspiratory squeaks	8	16
Hypoxemic at diagnosis*	2	2
Abnormal CXR	4	4
Clinical		
Self-limiting URTI	7 (37%)	5 (28%)
Graft dysfunction	12 (63%)	13 (72%)
Average decline in FEV_1		
Absolute volume, ml	511 ± 243	627 ± 154
Percentage	30 ± 12.4	25.9 ± 11.2

HMPV in lung transplants

TABLE 2. CLINICAL OUTCOMES IN THE FIRST 6 MONTHS AFTER DIAGNOSIS

Outcome	hMPV	RSV
Number with graft dysfunction, n	12/19	13/18
Recovery of lung function, n (%)	11/12 (91.5)	11/13 (84.6)
Time to return, d*	29.5 ± 11	22.2 ± 8
Duration of ribavirin	9.9 ± 3.5 d	11.6 ± 5.1 d
BOS		
New onset	0	2
Progressive	0	3
Death	0%	15%


Acknowledgements to Qpid Laboratory, SASVRC, RCH
Unofficially sponsored by Lowes


RCH Foundation Building
Royal Children's Hospital
Thank you
Questions?