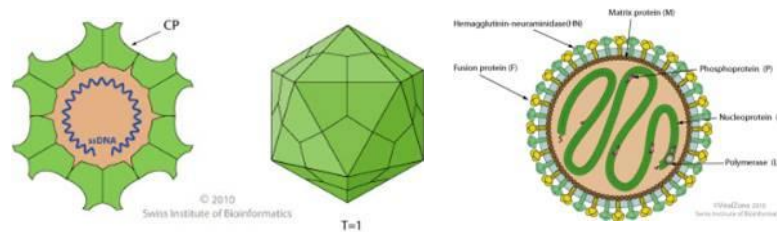


Chasing other viral causes of respiratory illness



“The science of influenza surveillance and control”
The 16th Public Health Summer School, 14 Feb 2012

Dr Richard Hall

Institute of Environmental Science & Research (ESR)
National Centre for Biosecurity & Infectious Disease (NCBID), Wallaceville, New Zealand.



Lecture plan

- Viruses that cause influenza-like illness
- Methods for detection
- Hidden viruses
- Emergence of new viruses
- Co-infection

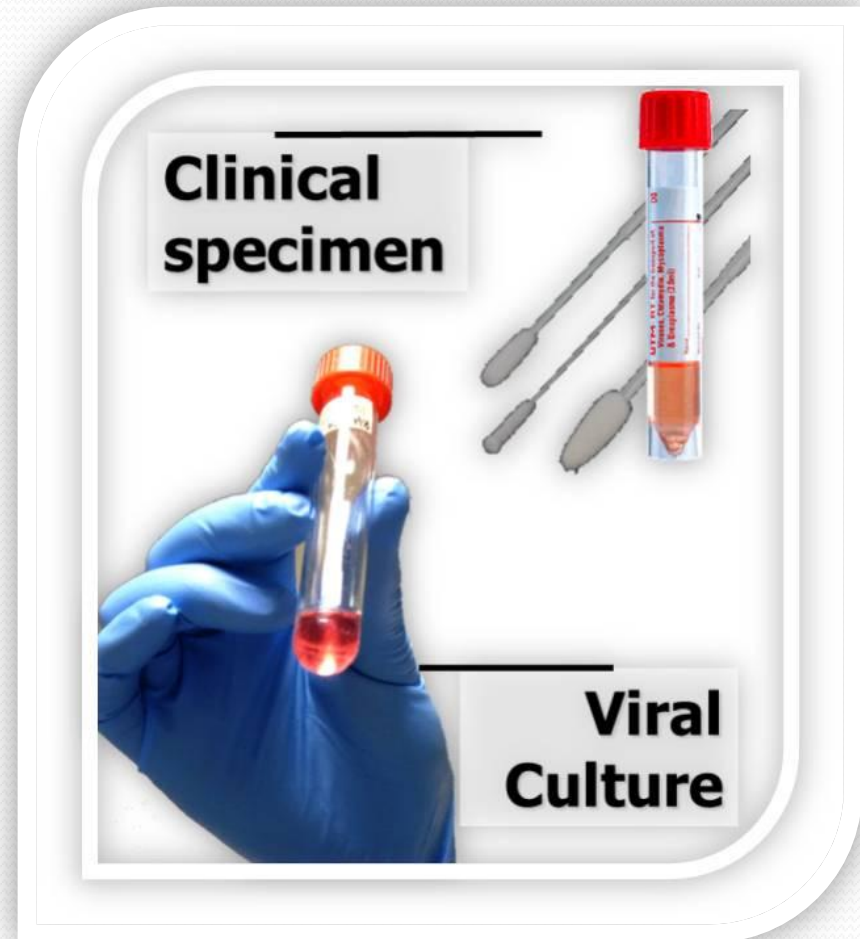
'Common Cold'

- Adenovirus (serotype B and C)
- Human Enterovirus (HEV)
- Human Rhinovirus (HRV)
- Coronavirus
- Respiratory Syncytial Virus (RSV)
- Human metapneumovirus (hMPV)
- Human parainfluenza virus (HPIV)
- Human bocavirus
- Influenza C



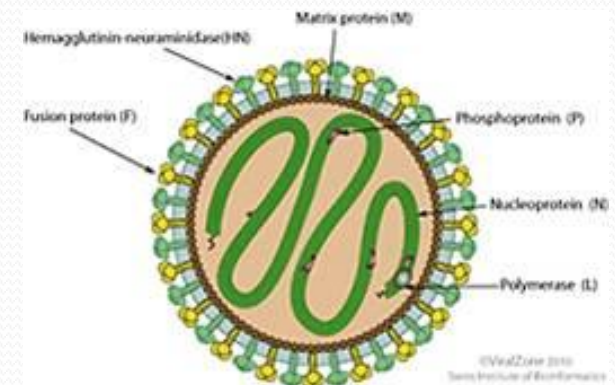
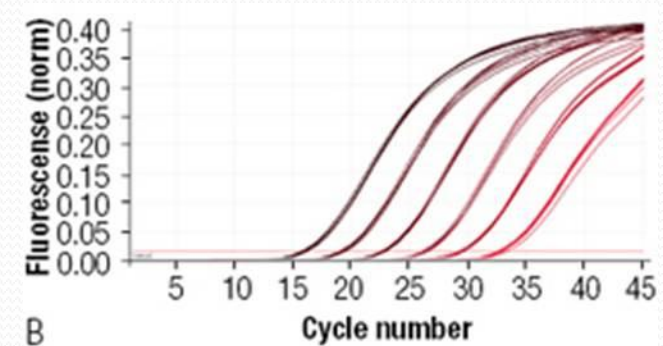
Diagnostics for 'common cold'

- Viral culture
- Serology



Detection of viral genome

- Molecular diagnostics
 - Real-time Polymerase Chain Reaction (PCR)
- Nucleic Acid Amplification Tests
 - Rapid (TAT 24 hours)
 - Specific (exact sequence match)
 - Sensitive (detection of 1 virus)



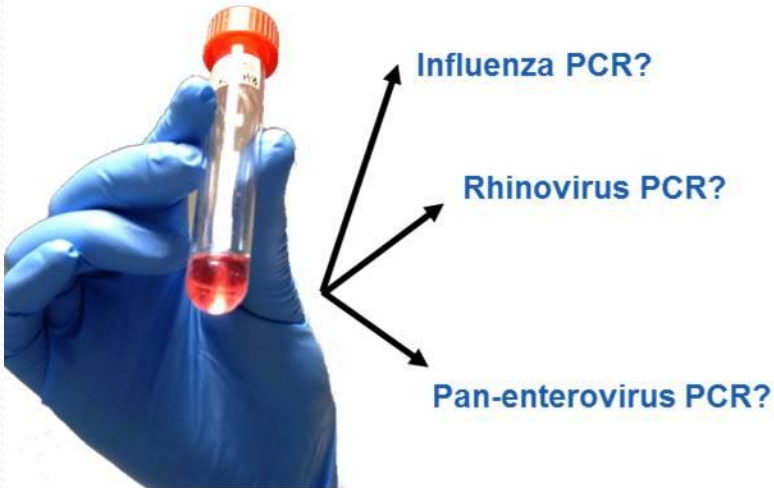
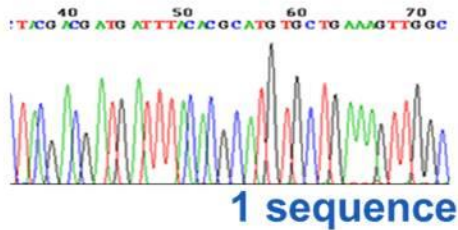
New Molecular Methods

- ‘Multiplex’ = detection of multiple agents in single test
- Published real-time PCR (single/multiple)
- FilmArray Respiratory Panel (Idaho Tech.)
- xTAG Respiratory Virus Panel (Luminex)

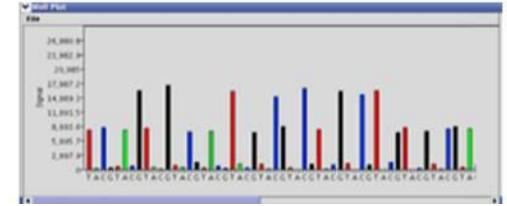


Next-generation Sequencing

Sanger Sequencing



Next-generation Sequencing



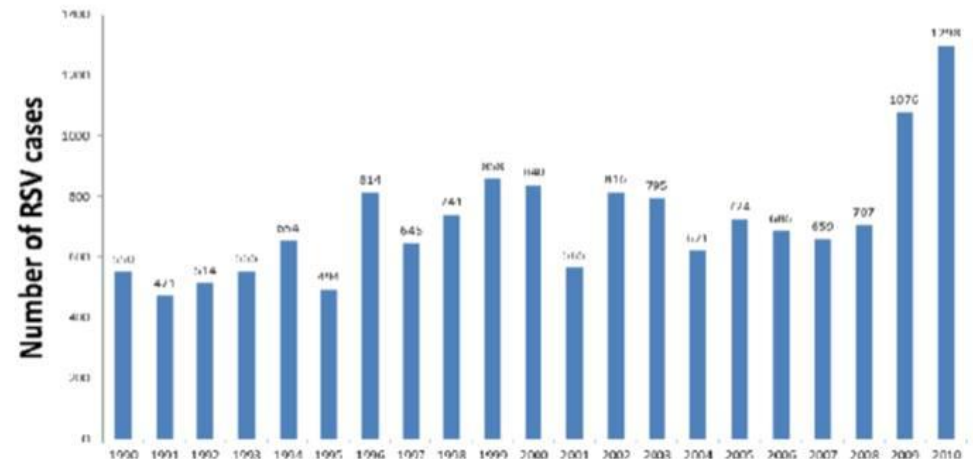
Millions of Sequences



Surveillance

- In New Zealand, ESR - Virology Reports
 - <http://www.surv.esr.cri.nz/virology/virology.php>
- Enterovirus, Adenovirus, RSV

Fig 1 Annual laboratory-confirmed RSV cases, 1990-2010



Surveillance

Scandinavian Journal of Infectious Diseases, 2012; 44: 9–17

informa
healthcare

ORIGINAL ARTICLE

Seasonal variations of 15 respiratory agents illustrated by the application of a multiplex polymerase chain reaction assay

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MAGNUS LINDH³ & JOHAN WESTIN³

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Seasonal variations of respiratory agents 15

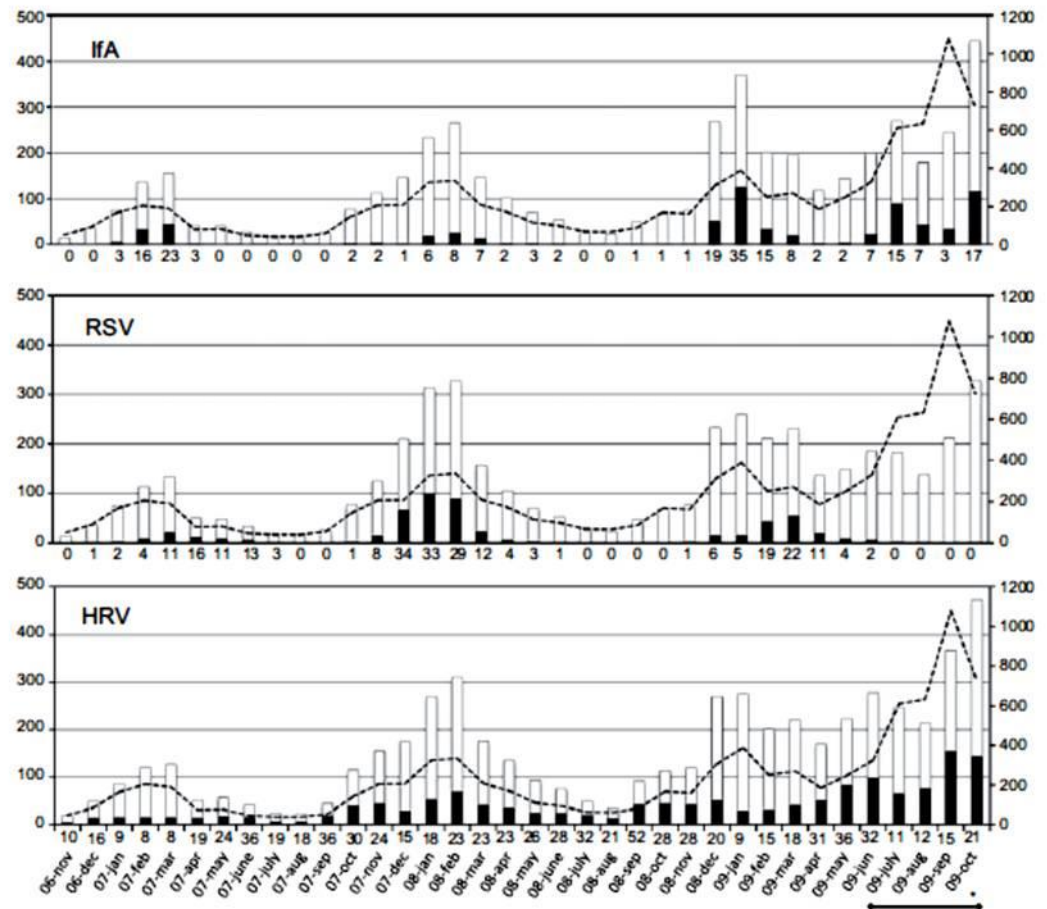


Figure 4. Multiplex real-time PCR each month from November 2006 through October 2009 ($n = 7853$). Number of samples positive for influenza A (IfA), respiratory syncytial virus (RSV), and human rhinovirus (HRV) depicted in black columns; number of total positive

We thought we knew it all...

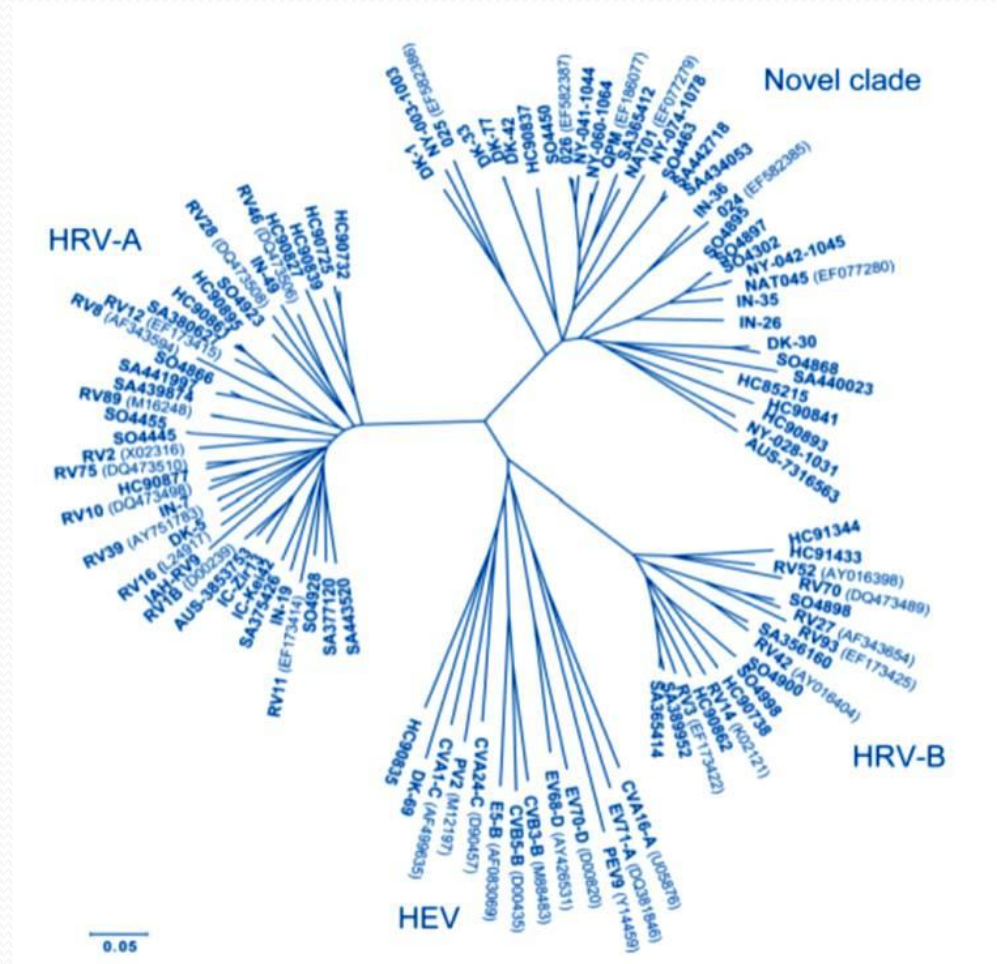
- Rhinoviruses
 - Cause 50% of 'common cold'
 - Can exacerbate asthma or COPD
 - Grow at lower temperature (32°C)
 - Closely related to enteroviruses
 - Difficult to inactivate



Hidden ILI virus

- 250 year old virus that causes 33% of 'common colds' only discovered in 2006.
- Human Rhinovirus C

Briese et al. (2008) Global distribution of a novel rhinovirus genotype. *EID* 14 (6), p944.



Coronaviruses

- Cause 10 – 30% of all ‘common colds’
- Human coronavirus strains 229E, NL63, HKU1, OC43
- Usually mild URTI
- Associated with otitis media, pneumonia and exacerbation of asthma



Emergent ILI

- Severe-acute respiratory syndrome associated coronavirus (SARS)
- Biphasic illness.
 - Myalgia, cough, dyspnoea, fever with diarrhea and other gastrointestinal symptoms.
 - Respiratory distress syndrome (ventilation and intensive care).
- Emerged late in 2002
- 10.9% mortality rate



Emergent ILI

- Adenovirus 14p1
- First isolated during ARD outbreak in military camp in Netherlands in 1955
- Absent for 50 years
- Emerged in 2006
- Lackland Air Force Base, TX



Kajon et al. (2010) JID 202: 93.

Co-infection

Journal of Infection (2011) 63, 260–266



BIAA
British Infection Association

www.elsevierhealth.com/journals/jinf

Rate and influence of respiratory virus co-infection on pandemic (H1N1) influenza disease[☆]

Frank P. Esper^{a,b,*}, Timothy Spahlinger^c, Lan Zhou^{a,c}

Table 1 Presence of respiratory viruses in H1N1 and non H1N1 positive respiratory samples.

Virus	H1N1 Positive (N = 229)	H1N1 Negative (N = 267)
	# (%)	# (%)
RhinoVirus	19 (8.3%)	35 (13.1%)
Coronaviruses ^a	5 (2.2%)	3 (1.1%)
Adenovirus	2 (0.9%)	6 (2.2%)
HPIV1	1 (0.4%)	16 (5.9%)
HPIV2 ^a	2 (0.9%)	1 (0.4%)
HPIV3	0 (0.0%)	1 (0.4%)
WU Polyoma	1 (0.4%)	0 (0.0%)
RSV	1 (0.4%)	13 (4.9%)
HBoV1	0 (0.0%)	2 (0.7%)
Total ^a	30 (13.1%)	77 (28.8%)

^a 1 Patient coinfectd with HPIV2 and coronavirus.

Table 3 Breakdown of clinical severity score attributes between mono and coinfectd H1N1 patients.

	Vent	Admit	Admit ≥ 5d	O2 ≤ 87%	O2 Given
H1N1 Monoinfected (N = 199)	8.5%	69.8%	28.1%	9.0%	31.0%
H1N1 with co-infection (N = 30)	23.3%*	60.0%	26.7%	20.0%	33.3%
Non-rhinovirus co-infections (N = 11)	45.5%*	72.7%	27.3%	36.4%*	54.5%
Rhinovirus (N = 19)	10.5%	52.6%	26.3%	10.5%	21.1%

*P < 0.05 compared to H1N1 mono-infection.

The **16th**
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7 – 24 February 2012



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