

Aetiology of Hospitalised Respiratory Infection in New Zealand

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Outline

- Determining the microbial causes of respiratory infections
- Current understanding of the aetiology of hospitalised respiratory tract infection in New Zealand

Aetiology of Respiratory Infections

- 1) Finding the microbial causes of respiratory infections can be challenging

Fundamental Issues in Determining the Aetiology of Respiratory Infections

a) Specimen collection

- It is not always possible to get a specimen from the site of infection

b) Some pathogens are difficult to culture

- e.g. *Mycoplasma pneumoniae*, *Legionella* spp., rhinoviruses

c) Differentiating innocent bystanders from true pathogens

- Some pathogens can also be colonisers
- Some pathogens may be detected for prolonged periods of time

Aetiology of Respiratory Infections

- 2) Much of existing dogma about the causes of respiratory infections is based on old data



- New diagnostics have disproportionately improved detection of viral respiratory pathogens



- A large proportion of respiratory infections still have no known cause despite intensive investigation

Aetiology of Respiratory Infections

- 3) There is increasing evidence of the importance of interaction between viruses and bacteria

Pathogens	Subjects (n)
Mixed viral and bacterial pathogens:	
Influenza A plus:	
<i>Streptococcus pneumoniae</i>	5
<i>Streptococcus pneumoniae</i> and <i>Chlamydia pneumoniae</i>	1
<i>Haemophilus influenzae</i>	1
<i>Legionella pneumophila</i>	1
<i>Pseudomonas aeruginosa</i>	1
Influenza B plus:	
<i>Staphylococcus aureus</i>	2
<i>Streptococcus pneumoniae</i>	1
<i>Legionella pneumophila</i>	1
Rhinovirus plus:	
<i>Streptococcus pneumoniae</i>	11
<i>Haemophilus influenzae</i>	2
Respiratory syncytial virus plus:	
<i>Streptococcus pneumoniae</i>	4
<i>Haemophilus influenzae</i>	1
<i>Moraxella catarrhalis</i>	1
<i>Pseudomonas aeruginosa</i>	1
Adenovirus plus:	
<i>Haemophilus influenzae</i>	2
<i>Streptococcus pneumoniae</i>	1
Parainfluenza virus plus:	
<i>Streptococcus pneumoniae</i>	3
<i>Haemophilus influenzae</i>	1
Coronavirus plus:	
<i>Streptococcus pneumoniae</i>	2
Multiple viral pathogens:	
Influenza A and adenovirus	1
Influenza A and coronavirus 229E	1
Influenza A and rhinovirus and <i>Haemophilus influenzae</i>	1
Influenza A and rhinovirus and <i>Streptococcus pneumoniae</i>	1
Rhinovirus and respiratory syncytial virus	1
Respiratory syncytial virus and coronavirus 229E and <i>Haemophilus influenzae</i>	1
Adenovirus and coronavirus 229E	1
Total	49

Polymicrobial Infections in 304 Adults with Community-Acquired Pneumonia

- Documented bacterial/viral co-infections are common

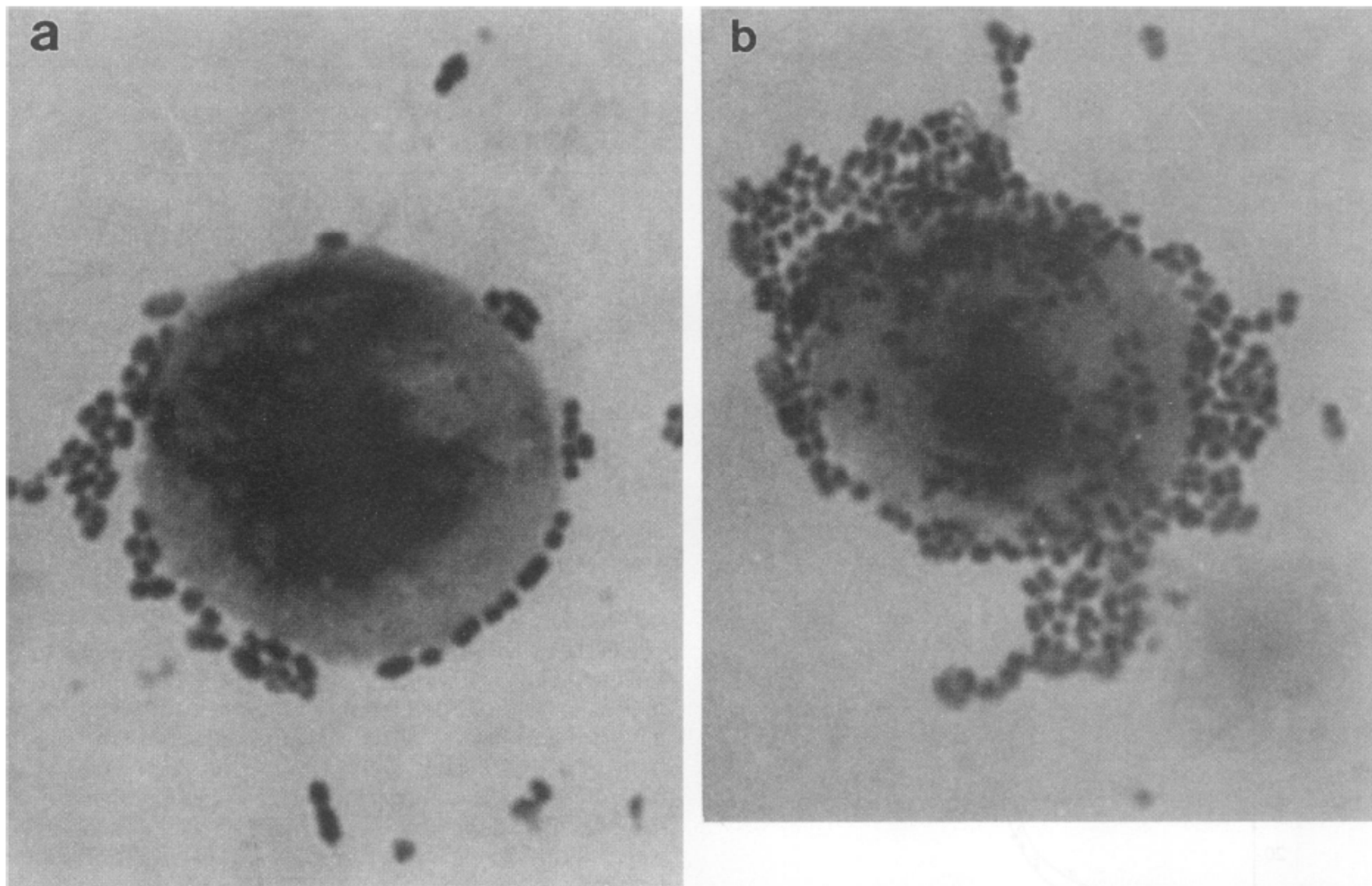
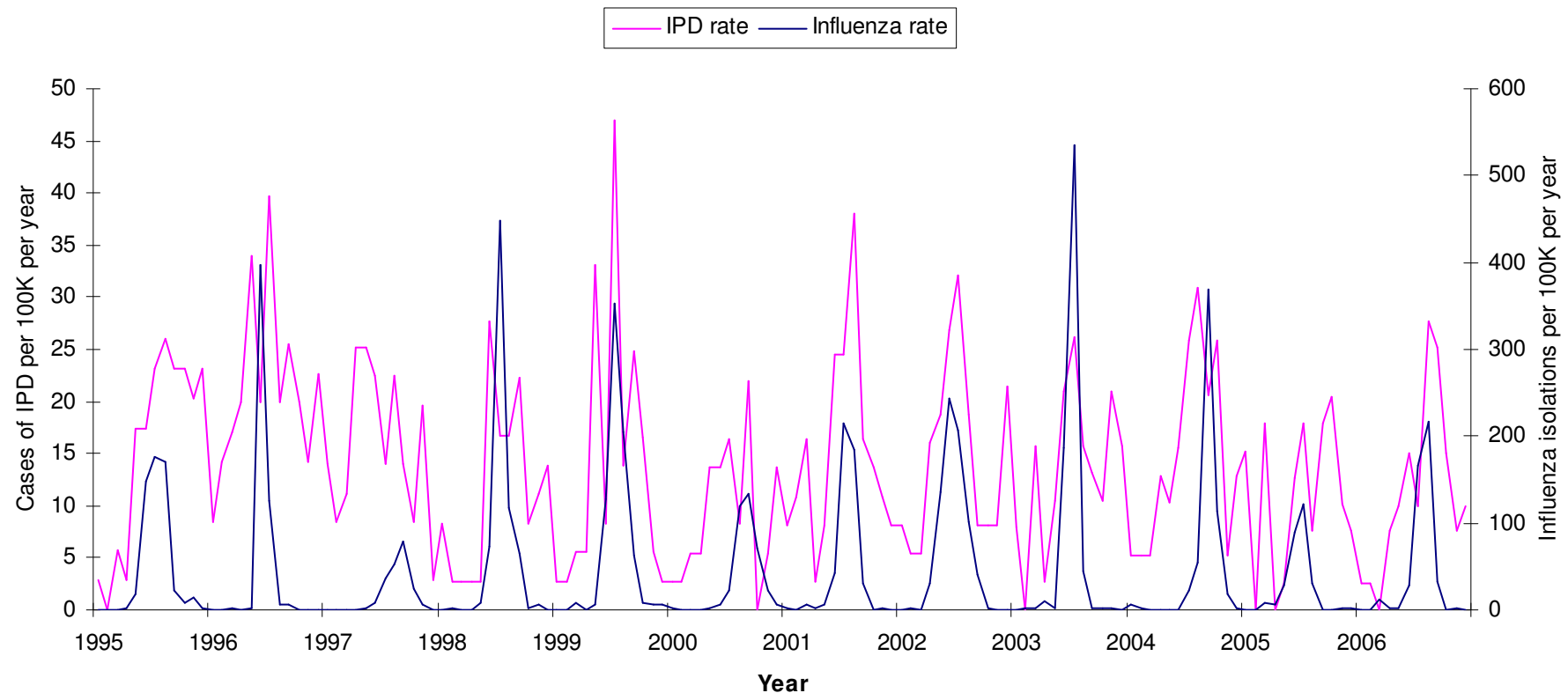


FIG. 2. Examples of adherence of *S. pneumoniae* CCUG 10175 to an uninfected A549 cell (a), an A549 cell infected with adenovirus type 5 (b), and an A549 cell infected with adenovirus type 9 (c).

Rates of Invasive Pneumococcal Disease and Influenza in Christchurch, NZ 1995-2006



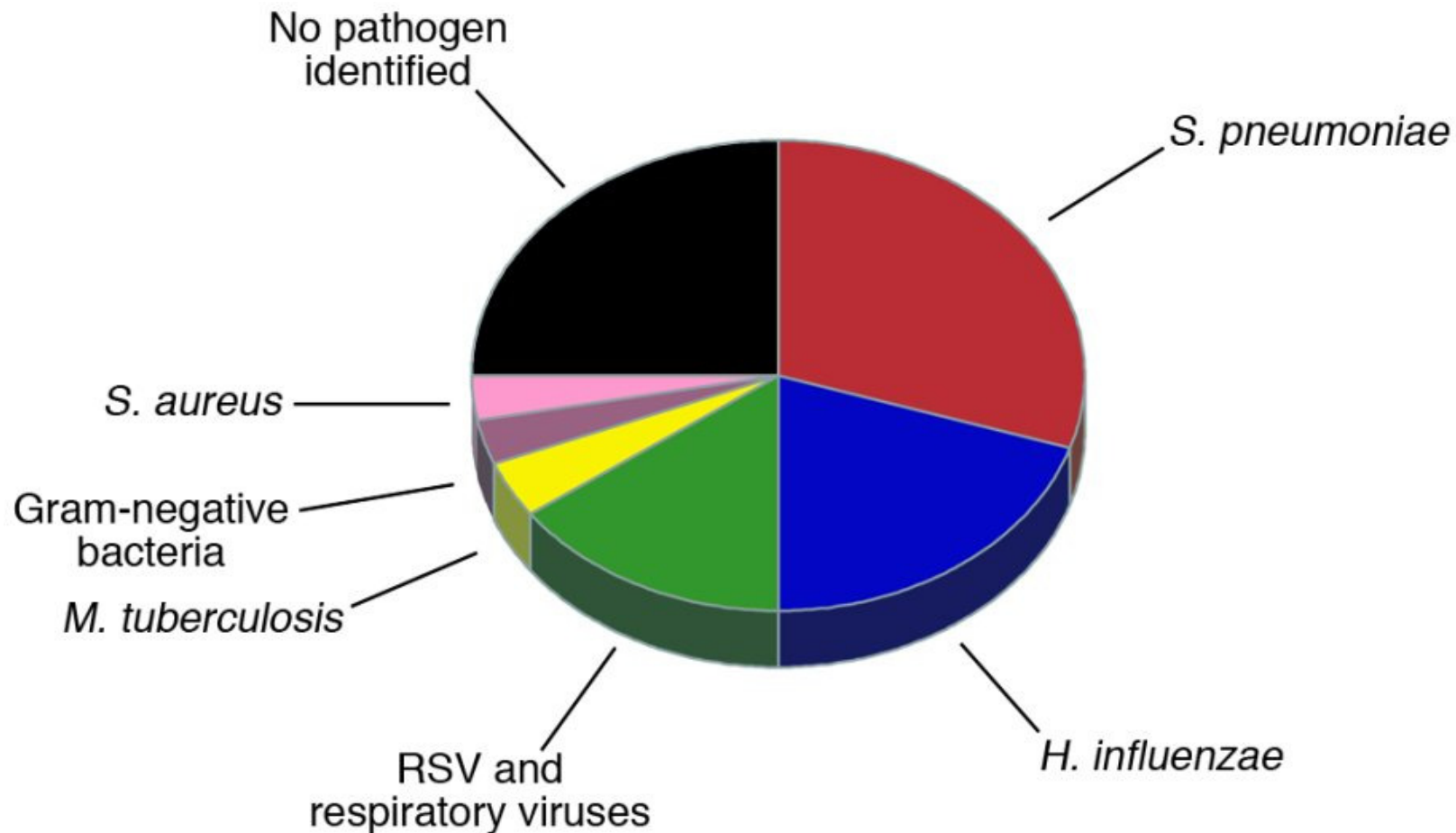
Aetiology of Respiratory Infections

- 4) Most published data on the aetiology of respiratory infection is from hospital-based studies

Aetiology of Respiratory Infections

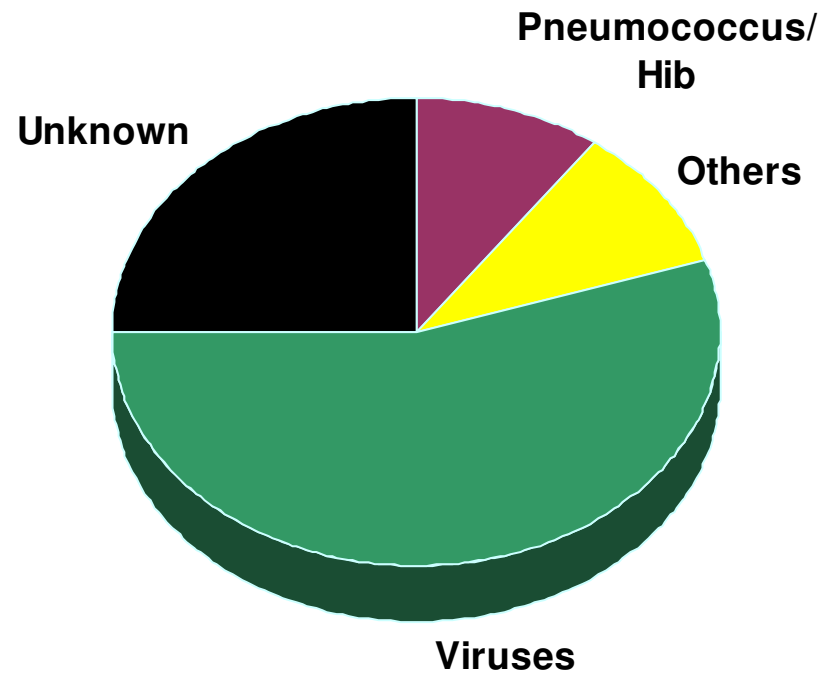
- 5) There is a publication bias towards rich countries

Causes of Pneumonia in Children from Developing Countries

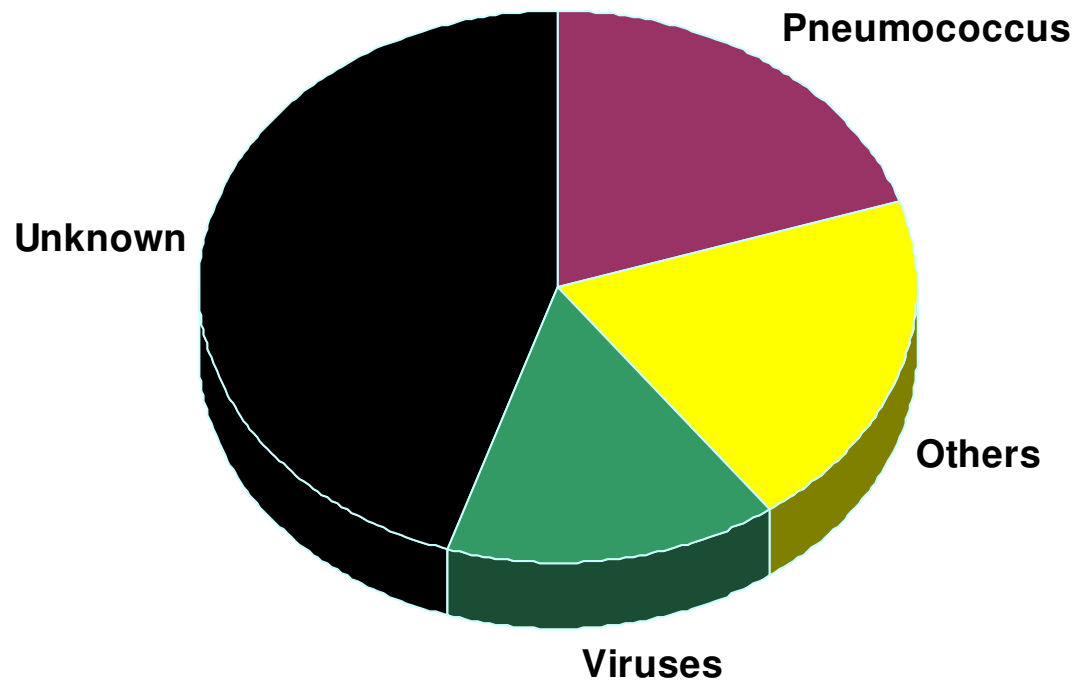


J. Clin. Invest. **118**:1291–1300 (2008)

Causes of Pneumonia in Children from Developed Countries



Causes of Hospitalised Pneumonia in Adults from Developed Countries



Causes of Community-Acquired Pneumonia in Adults (New Zealand)

*Table 4 Microbiological diagnosis**

<i>Organism</i>	<i>Number</i>	<i>Percentage</i>
<i>Streptococcus pneumoniae</i>	100	39
<i>Mycoplasma pneumoniae</i>	41	16
<i>Legionella</i> spp	27	11
<i>Haemophilus influenzae</i>	28	11
Influenza A	12	5
<i>Chlamydia pneumoniae</i>	8	3
<i>Moraxella catarrhalis</i>	8	3
<i>Staphylococcus aureus</i>	7	3
Enterobacteriaceae	4	2
<i>Pseudomonas</i> sp	3	1
Others**	13	5

Unknown cause = 29%

Thorax 1996;51:1010–1016

Viral Pneumonia in Adults

Table 1 Viral pathogens identified in adults with community-acquired pneumonia

Virus	All subjects* (n = 304)	Subjects with full array of viral diagnostic tests* (n = 225)
Rhinovirus	31 (10)	30 (13)
Influenza A	23 (8)	22 (10)
Influenza B	6 (2)	5 (2)
RSV	12 (4)	8 (4)
Adenovirus	11 (4)	10 (4)
Parainfluenza	6 (2)	2 (1)
Coronavirus 229E	4 (1)	3 (1)
Coronavirus OC43	2 (1)	2 (1)
Metapneumovirus	0 (0)	0 (0)
Total	95	82

Data shown as number (%).

*More than one virus was detected in some patients.

RSV, respiratory syncytial virus.

Causes of Community-Acquired Pneumonia in Children (Finland)

Microbe	All children (n = 76) No (%)
Bacteria	
<i>Streptococcus pneumoniae</i> †	35 (46)
<i>Haemophilus influenzae</i>	22 (29)
<i>Moraxella catarrhalis</i>	21 (28)
<i>Staphylococcus aureus</i>	9 (12)
<i>Mycoplasma pneumoniae</i> ¶	2 (3)
Other bacteria**	3 (4)
Normal/mixed flora	11 (14)
Negative	2 (3)
Total	60 (79)
Viruses	
Rhinovirus	22 (29)
Human bocavirus	14 (18)
Human metapneumovirus	10 (13)
Respiratory syncytial virus	3 (4)
Enteroviruses	2 (3)
Parainfluenzae type 3 virus	1 (1)
Influenza A virus	1 (1)
Influenza B virus	1 (1)
Adenovirus	0 (0)
Parainfluenzae type 1 virus	0 (0)
Parainfluenzae type 2 virus	0 (0)
Total	42 (55)

“Unknown cause” = 10%

Thorax 2009;**64**:252–257

Other Respiratory Tract Infections

- Pertussis
 - High hospitalisation rates in New Zealand
 - Small proportion of adults with pneumonia have evidence of recent pertussis
- Bronchiolitis
 - RSV, human metapneumovirus, bocavirus, others
- Pulmonary tuberculosis
- Immunocompromised host
 - Pneumocystis pneumonia

What About the “Unknown” Section of the Aetiology Pie?

- Most likely this is mainly comprised of known pathogens that have not been detected
- Novel pathogens likely to play a small role

Summary

- Determining the causes of respiratory infections is challenging
- Recent improvements in diagnostics have emphasised the importance of viruses and viral/bacterial coinfection
- Pneumococcus remains an important respiratory pathogen
- Conjugate vaccines against *H. influenzae* type b and pneumococcus have altered the aetiology spectrum of pneumonia