"MICROBIAL INFECTION AND OM"

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"THE AVERAGE ABORIGINAL CHILD IN AUSTRALIA HAS 32 MONTHS' OF MIDDLE EAR DISEASE IN CHILDHOOD COMPARED WITH AN AVERAGE OF THREE MONTHS FOR THE NON-ABORIGINAL CHILD"

Dr Harvey Coates

CHARACTERISTICS OF THE PATHOGENSIS OF BACTERIAL RESPIRATORY AND MIDDLE EAR INFECTIONS

- The major bacteria responsible all exist as upper respiratory tract commensals without causing disease but data suggests they influence infection

- In acute infections a combination of host & environmental factors and pre-viral illness are major determinants of bacterial infection

CAUSATIVE BACTERIAL PATHOGENS IN ACUTE OTITIS MEDIA

MAJORS:

- *Streptococcus pneumoniae*
- Nontypeable *Haemophilus influenzae*
- *Moraxella. catarrhalis*

OTHERS:

- Group A *Streptococcus*
- *Staphylococcus aureus* including MRSAs
- *Pseudomonas aeruginosa*
- Klebsiella spp
- Proteus spp.
- *Alloiococcus otitidis*

PNEUMOCOCCUS

The recent genomic studies of *S. pneumoniae* demonstrate:

- A high degree of genomic plasticity in *S. pneumoniae*, which enhances their ability to adapt to clinical and public health interventions on a global scale.
- *In vivo* horizontal gene transfer that likely allows pneumococci to rapidly adapt to immune selection pressures encountered during colonization and infection.
- Comparative genome analyses that continue to reveal novel modes of resistance to antibiotics and other adaptive features.

NONTYPEABLE *HAEMOPHILUS INFLUENZAE*

Key themes from population genetics of *H. influenzae* are:

- Existing paradigms regarding the clonality of overt pathogens may not be applicable because of the significant host commensal niche
- Simultaneous infection with multiple strains/clones is probably more the rule than the exception
- Genetic exchange between subpopulations of *H. influenzae* is likely to be frequent and may be an important driver of dissemination and emergence of persistence determinants
- Laboratory identification and distinguishing between *H. influenzae* and *H. haemolyticus*.

MORAXELLA CATARRHALIS

Key themes regarding colonization by *M. catarrhalis* are:

- Is a common colonizer of infants and children, often being the most common colonizer among otitis media pathogens.
- Rate of colonization decreases with age.
- Geographic variability is seen in colonization and infection rates.
- Co- colonization with other otopathogens has been observed.
- Colonizing strains show genotypic and phenotypic diversity.

VIRUSES

MAJORS:

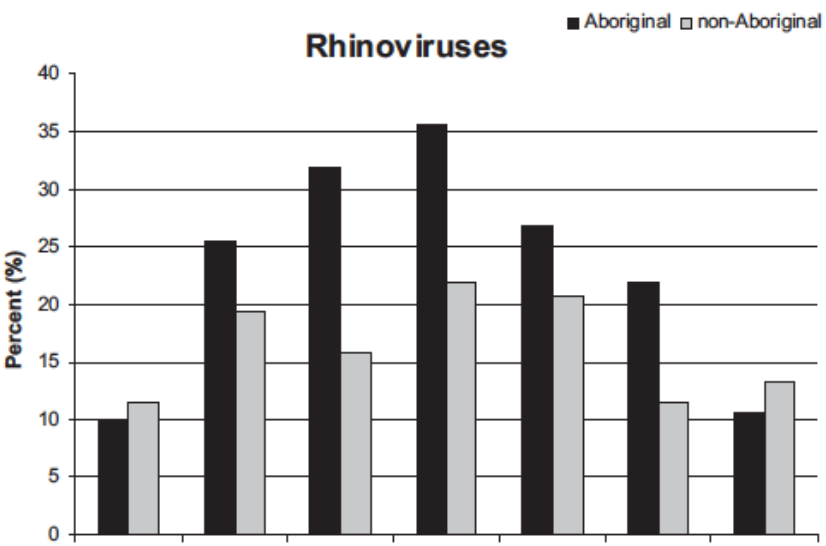
- RSV and adenoviruses still most common
- Parainfluenza virus
- Influenza A & B viruses
- Coronavirus
- Enterovirus

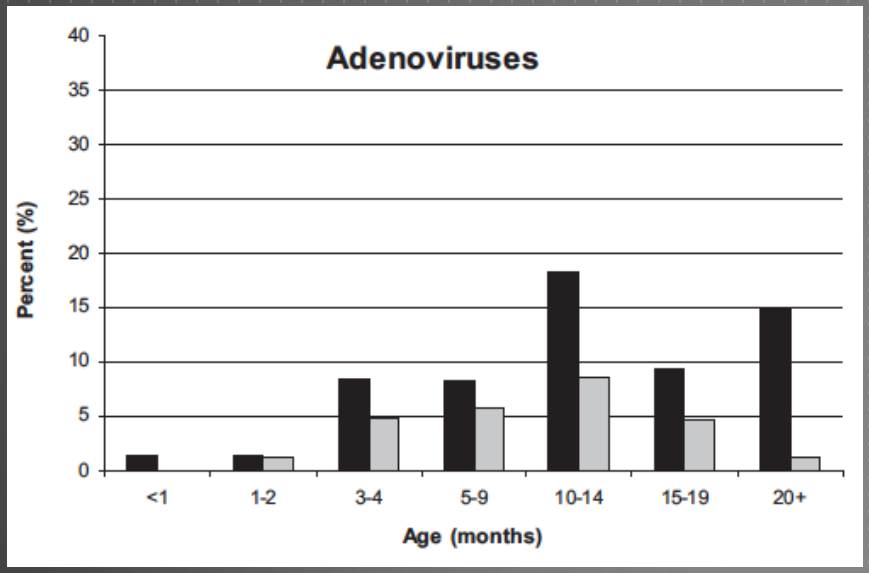
EMERGING OR RECENTLY ASSOCIATED:

- Human metapneumoviruses (hMPV) high association in < 3 years of age
- Human bocavirus (hBoV) occurs frequently in conjunction with other viruses and seems to persist for a long time in the respiratory tract. Detected in middle ear fluids
- Human rhino-enterovirus

VIRAL DIAGNOSTICS

- Molecular detection methods and diagnosis of viral infections have been rapidly evolving→ discovery of new viral pathogens
- Important aspects in diagnostics include tissue sample type, sample collection technique, detection method used, and interpretation of results
  - Use of flocked swabs to obtain NPS sample seems to be as sensitive as nasal aspirates, but easier to perform
  - a combined nose and throat swab specimen is nearly as sensitive as nasopharyngeal aspirate samples and yet less laborious .
- The use of nucleic acid amplification methods is continuously evolving;
  - In-house or commercial multiplex PCR techniques enable rapid testing for numerous viruses simultaneously
  - viral RNA/DNA can be detected from asymptomatic patients, over a prolonged period, or more viruses may be detected simultaneously
  - virus quantification needed to determine the dominant virus or to associate presence of the specific virus with clinical symptoms





The interaction between Respiratory Viruses and Pathogenic Bacteria in the upper respiratory tract of asymptomatic Aboriginal and non-Aboriginal children

- 1006 nasopharyngeal aspirates
- 42% of samples from Aboriginal and 32% from non-Aboriginal children were virus positive
- Rhinovirus (23.6 & 16.5%) then adenovirus (8.5 & 3.5%) were most common
- Proportion by age show the higher rates in aboriginal children for rhinoviruses

Moore *et al. 2010* Pediatr. Infect. Dis.J 29:540-5

TABLE 2. Associations Between Isolation of Bacterial OM Pathogens and Rhinoviruses in Asymptomatic Aboriginal and Non-Aboriginal Children

Subjects	OR*	95% CI	OR†	95% CI
Aboriginal children				
M. catarrhalis	2.67	1.60–4.44	1.94	1.05–3.57
S. pneumoniae	1.91	1.15–3.17	1.29	0.75–2.23
H. influenzae	2.91	1.76–4.83	2.24	1.24–4.07
Non-Aboriginal children				
M. catarrhalis	1.43	0.86–2.38	1.15	0.64–2.08
S. pneumoniae	1.49	0.90–2.46	1.37	0.80–2.34
H. influenzae	1.64	0.89–3.04	1.44	0.74–2.79

*Adjusted for age, age^2, gender, proportion of rhinovirus-positive specimens per child.

†Adjusted for age, age^2, gender, proportion of rhinovirus-positive specimens per child, identification of adenovirus, isolation of the 2 other bacterial OM pathogens.

OR indicates odds ratio; CI, confidence interval.

Aboriginal:
The strongest positive association was between rhinoviruses and NTHi

When adjusted for other bacteria and adenovirus as well, all remained significant except *S.pneumoniae*

Non-aboriginal
No significant positive associations

Aboriginal:
The strongest positive association was between adenovirus and NTHi

When adjusted for other bacteria and rhinovirus as well, *S.pneumoniae* had a negative association with adenovirus

Non-aboriginal
Strong significant positive association for *M. catarrhalis*

TABLE 3. Associations Between Isolation of Bacterial OM Pathogens and Adenoviruses in Asymptomatic Aboriginal and Non-Aboriginal Children

Subjects	OR*	95% CI	OR†	95% CI
Aboriginal children				
M. catarrhalis	1.96	0.84–4.52	1.83	0.65–5.18
S. pneumoniae	0.75	0.41–1.36	0.39	0.18–0.84
H. influenzae	3.29	2.19–8.40	3.30	1.19–9.09
Non-Aboriginal children				
M. catarrhalis	5.71	1.67–19.61	5.75	1.74–19.23
S. pneumoniae	1.81	0.88–3.68	1.17	0.51–2.68
H. influenzae	0.87	0.36–2.11	0.44	0.16–1.24

*Adjusted for age, age^2, gender, proportion of adenovirus-positive specimens per child.

†Adjusted for age, age^2, gender, proportion of adenovirus-positive specimens per child, identification of rhinovirus, isolation of the 2 other bacterial OM pathogens.

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CONCLUSION

- As detection techniques improve, the complexity of the composition of the microbial flora in OM increases
- Our knowledge is increasing
- We understand more BUT
- Are we closer to eliminating the problems???