

Colonization and infection of the respiratory tract: What do we know?

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Distinguishing colonization from infection is an important factor in making the correct diagnosis in a wide variety of paediatric conditions. For example, in this issue of *Paediatrics & Child Health*, Al-Mutairi and Kirk (pages 25-30) describe the difficulty in distinguishing bacterial tracheitis from other causes of upper airway obstruction. Part of this difficulty is that growth of bacteria from the trachea can occur because of contamination of specimens by organisms that are colonizing the upper respiratory tract.

Colonization implies that the patient has a sufficiently high concentration of organisms at a site that they can be detected, yet the organism is causing no signs or symptoms. This differs from contamination, where the organism was never present in the site from which it has been detected, but was introduced into the specimen from another site or from contamination in the laboratory. A carrier is a person who is colonized with an organism and may transmit the organism to other people. Colonization can persist for days to years, with resolution influenced by the immune response to the organism, competition at the site from other organisms and, sometimes, use of antimicrobials.

Table 1 summarizes the most common organisms isolated from the respiratory tract and their significance. The most important factor in determining if a patient is colonized or infected with an organism is the clinical picture. For example, in the upper respiratory tract, up to 20% of children are colonized with group A streptococcus (GAS) (1), with the highest concentration of organisms being in the oropharynx. Throat cultures should only be done in children who have symptoms of GAS pharyngitis (sore throat in the absence of cough, rhinitis or laryngitis) because culturing all children with sore throats results in these carriers being treated with antibiotics that will not improve their symptoms. Antibiotics are far less successful in eradicating the organism in the carrier state than in a patient with symptomatic GAS pharyngitis (1); therefore, their use cannot be justified as a measure to reduce transmission of the organism.

Bacterial pharyngitis in the developed world is usually due to beta-hemolytic streptococci. However, many other organisms can be present in the pharynx. Infants and toddlers commonly become colonized with *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae*, *Neisseria meningitidis*

and/or *Moraxella catarrhalis*, with the highest concentration of organisms usually being in the nasopharynx (2). Colonization with these organisms occurs earlier in life if children attend a childcare centre or live in overcrowded conditions (2). Clearance of one serotype of *S pneumoniae* is often followed by colonization with another serotype, and it has been suggested that children may be colonized with multiple serotypes simultaneously, with the predominant type growing in cultures (3). A small percentage of children will develop invasive disease following colonization with *S pneumoniae* or *N meningitidis*. This risk appears to be highest immediately after colonization, likely because the patient has not yet produced antibodies to the organism (2). An inflamed nasopharynx (such as that which occurs with influenza or smoking) may increase the risk of invasive disease following colonization with *N meningitidis* (4). If a child develops an upper respiratory tract infection while colonized with *S pneumoniae*, *H influenzae* or *M catarrhalis*, they may develop acute otitis media or sinusitis with the colonizing strain. Antibiotics may eradicate the strain, but they may also increase the risk of the child being colonized with a different organism that is resistant to the antibiotic that was chosen (2).

Approximately one-third of adults are persistently colonized with *Staphylococcus aureus* (5), with the highest concentration of organisms in the respiratory tract being in the nasopharynx. Colonization of the skin and the nasopharynx can occur shortly after birth. Colonization with *S aureus* precedes most invasive diseases caused by *S aureus* (osteomyelitis, cellulitis or pneumonia), but such conditions are so rare that eradication could never be justified in an attempt to prevent them. Eradication may be useful in preventing infection of indwelling venous catheters or wound infections in patients undergoing invasive procedures (6). Other possible indications for eradication are if a health care worker is a carrier of methicillin-resistant *S aureus* (MRSA), or if an MRSA carrier has a chronic severe disease and is therefore likely to spend long periods in strict isolation if they remain colonized. However, the reason to attempt eradication is for infection control purposes, because the risk of invasive disease is very low.

Viruses and fungi can also be detected in the upper respiratory tract. Traditional respiratory viruses (adenovirus, influenza, parainfluenza virus, respiratory syncytial virus and

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TABLE 1
The most common organisms isolated from the respiratory tract and their significance

Site of detection	Organism	Significance
Nasal cavity	<i>Staphylococcus aureus</i>	<ul style="list-style-type: none"> - colonization of the nasal cavity occurs in about 30% of children and adults - this sometimes leads to impetigo in the nasal cavity, but otherwise is a benign condition - increases the risk of indwelling venous catheter or wound infections with <i>S aureus</i> - a patient with colonization but no infection may require isolation if the organism is methicillin-resistant
Oropharynx/ nasopharynx	Group A streptococcus	<ul style="list-style-type: none"> - present in up to 20% of children (1) - most commonly represents colonization, which is a benign condition - less commonly causes pharyngitis or local suppurative infections, with rheumatic fever being a rare sequelae if untreated - the relationship between Group A Streptococcus invasive disease and pharyngeal colonization is not clear
	Group C/G streptococci	<ul style="list-style-type: none"> - most commonly represents colonization, but can cause single cases and outbreaks of symptomatic pharyngitis - poststreptococcal glomerulonephritis has been described, but it is not clear that antibiotics decrease the incidence of this rare complication, so treatment is only recommended in the face of persistent symptoms
	<i>Streptococcus pneumoniae</i>	<ul style="list-style-type: none"> - present in a large percentage of infants and toddlers (range of 6% to 100% [3]) - persists for weeks to months - growth from the oropharynx/nasopharynx is of no significance, but about 15% of children will develop clinical infections within one month of acquiring a new strain (2) - a child who develops a viral upper respiratory tract infection while colonized may develop pneumococcal acute otitis media or sinusitis - colonization can be followed by bacteremia, with the risk being highest soon after acquisition of a new strain - bacteremia may resolve spontaneously but can lead to serious invasive disease (pneumonia, meningitis, septic arthritis)
	Nontypeable <i>Haemophilus influenzae</i> and <i>Moraxella catarrhalis</i>	<ul style="list-style-type: none"> - present in a large percentage of infants and toddlers - growth from the oropharynx/nasopharynx is of no significance, but a child who develops a viral upper respiratory tract infection while colonized may develop acute otitis media or sinusitis with these organisms
	<i>Neisseria meningitidis</i>	<ul style="list-style-type: none"> - present in about 5% to 15% of individuals in nonendemic areas (higher in endemic areas or during an epidemic) (4) - growth from the oropharynx/nasopharynx is of no significance, but colonization can be followed by bacteremia, which may resolve spontaneously but more commonly leads to serious invasive disease (septic shock, meningitis, septic arthritis)
Herpes simplex virus	<ul style="list-style-type: none"> - can result in vesicular lesions in the oropharynx, but asymptomatic shedding is more common - shedding occurs at times of stress, and therefore is often isolated from the mouth or pharynx of intensive care patients - growth in the absence of lesions is only of significance in an immunocompromised host or in an infant less than 30 days of age 	
<i>Candida</i> species	<ul style="list-style-type: none"> - normal mouth flora - results in thrush if concentration is too high - not thought to be a cause of upper respiratory tract disease except in the immunocompromised host, where laryngitis and tracheitis can occur 	
Lower respiratory tract	Group A streptococcus	<ul style="list-style-type: none"> - despite colonization of the pharynx being common, it is rare for lower respiratory tract specimens to be contaminated; therefore, isolation from the lower respiratory tract should usually be treated
	<i>S aureus</i> , <i>S pneumoniae</i>	<ul style="list-style-type: none"> - common contaminants from the upper respiratory tract (where they are colonizing organisms), but also common causes of lower respiratory tract disease - significance depends on the clinical picture and the results of investigations (Figure 1)
	Nontypeable <i>H influenzae</i> , <i>M catarrhalis</i> , and <i>Enterococcus</i> species	<ul style="list-style-type: none"> - common contaminants from the upper respiratory tract (where they are colonizing organisms) and rare causes of lower respiratory tract disease in children - usually require no treatment
	<i>N meningitidis</i>	<ul style="list-style-type: none"> - usually a pathogen if isolated from the lower respiratory tract, therefore, it should be treated
	Enterobacteriaceae and nonfermenting Gram-negative bacilli	<ul style="list-style-type: none"> - colonize the upper respiratory tract in children who have been in intensive care or have received frequent courses of antibiotics, so often contaminate lower respiratory tract specimens - however, can cause pneumonia, especially in ventilated patients - significance depends on the clinical picture and the results of investigations (Figure 1) - a colonized patient may require isolation if the organism is resistant to multiple antibiotics
	Herpes simplex virus	<ul style="list-style-type: none"> - rare cause of lower respiratory tract disease, even in immunocompromised hosts - if grown from lower respiratory tract specimens, usually originated in the upper respiratory tract
<i>Candida</i> species	<ul style="list-style-type: none"> - usually not from the lower respiratory tract (might originate in the oropharynx, or in the esophagus in an immunocompromised host with fungal esophagitis) - can cause lower respiratory tract disease in immunocompromised hosts 	

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TABLE 1 – continued

Site of detection	Organism	Significance
	<i>Aspergillus</i> species	- can be contaminants, but can result in rapidly progressive invasive disease; therefore, lung biopsy is often done if the clinical picture fits
Any respiratory tract site	Viridans group streptococci, Nonhemolytic streptococci, coagulase-negative staphylococci, Nonpathogenic <i>Neisseria</i> species, <i>Corynebacterium</i> species, <i>Lactobacillus</i> species, <i>Micrococcus</i> species, <i>Stomatococcus</i> species, and <i>Bacillus</i> species	- part of normal upper respiratory tract flora and not thought to be causes of lower respiratory tract disease - most laboratories would not report because therapy is not indicated
	<i>Pneumocystis jiroveci</i> (<i>carinii</i>)	- usually a pathogen, but can occasionally be detected in well normal hosts
	<i>Mycoplasma pneumoniae</i>	- usually a pathogen, but carrier state has been described
	<i>Pasteurella</i> species	- can cause sinusitis, bronchitis or pneumonia but can also be part of normal flora - significance depends on clinical picture
	<i>Mycobacterium tuberculosis</i> , <i>Chlamydia pneumoniae</i> , <i>Chlamydia trachomatis</i> , <i>Bordetella pertussis</i> , adenovirus, influenza, parainfluenza virus, respiratory syncytial virus, coronavirus, human metapneumovirus and rhinovirus	- a carrier state has not been described, so identification of these organisms by any means is probably always indicative of active or recent infection, although the spectrum of disease can vary widely

rhinovirus) are almost always pathogens if detected anywhere in the respiratory tract, although they sometimes result in only minor signs or symptoms. Furthermore, there is some evidence that parainfluenza virus can persist for weeks following acute infection (7). Herpes simplex virus can cause stomatitis, but reactivation of this and other herpes viruses, such as Epstein Barr virus and cytomegalovirus, can result in asymptomatic shedding in the pharynx and mouth, which is of no significance. *Candida* species can be part of normal gastrointestinal flora from mouth to anus, with thrush occurring when the concentration of organisms in the mouth is high. Growth of *Candida* from the upper respiratory tract usually implies that a sample is contaminated with mouth flora.

It is thought that the lower respiratory tract should be sterile and, therefore, any organism detected there is a pathogen. However, molecular techniques allow for the detection of much lower concentrations of organisms than traditional culture techniques (8), and it may eventually become evident that asymptomatic colonization also occurs in the lower respiratory tract. When attempts are made to obtain samples from the lower respiratory tract, it is always possible for them to be contaminated with organisms that are causing colonization in the upper respiratory tract. Sputum is difficult to obtain from paediatric patients, and adult studies have shown the sensitivity and specificity to be sufficiently low such that some experts recommend obtaining

sputum from adults with suspected bacterial pneumonia only in selected circumstances (9). For patients with severe pneumonia, there is no consensus on the relative value of samples obtained by endotracheal aspirate, bronchoalveolar lavage or a protected brush specimen (10), but all are superior to sputum. Direct lung aspiration is rarely done but has been described as a useful technique in children with bacterial pneumonia (11). The ultimate way to determine if an organism is a pathogen is to obtain a lung biopsy, because contamination of such specimens is exceedingly rare. However, even that may not confirm a diagnosis if the patient has already received antimicrobials, or if cultures are not requested for the correct organism (such as mycobacteria). One problem with all techniques is that the sensitivity is limited by the fact that the area that is sampled may not be the one with the highest concentration of organisms. However, one basic principle that applies to specimens obtained from all lower respiratory sites is that an organism that is seen on a Gram stain is present in higher concentration than one detected only on culture; therefore, it is more likely to be a pathogen. Also, because polymicrobial lower respiratory tract infections are rare, it is more likely that the true pathogen has been identified if there is heavy growth of a single organism than if there is mixed growth.

The significance of specific organisms detected in the lower respiratory tract is shown in Table 1. Most of the time, one must put together the pieces of the puzzle that

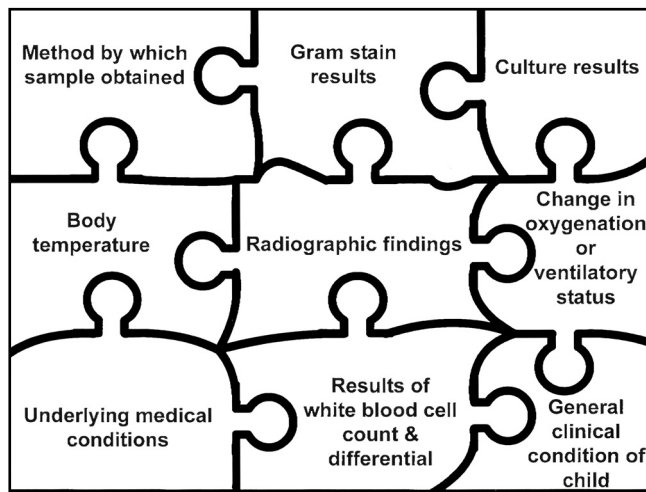


Figure 1) Diagnosis of lower respiratory tract infection in the paediatric patient. All the factors shown in the puzzle must be considered in deciding if a child has a lower respiratory tract infection and in choosing antimicrobial agents

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constitute the clinical picture (Figure 1) to determine if antimicrobials should be started.

The difficulty in detecting anaerobes means that clinicians are seldom faced with determining the significance of these isolates in respiratory tract samples. A more common dilemma is whether to add empiric anaerobic coverage for respiratory tract disease. When proper isolation techniques are employed, anaerobes are isolated from persistent otitis media (12), sinusitis (12), bacterial tracheitis (13) and paediatric pneumonia (14). It remains unclear when anaerobes are pathogens and when they are contaminants or colonizing organisms, but treatment should be considered if they are the predominant organism grown from a sterile or lower respiratory site.

In summary, to determine the significance of an organism isolated from the respiratory tract, one must consider the site from which the organism was isolated, the method of obtaining the sample, the Gram stain results, the other organisms isolated from the same site and, most importantly, the clinical picture.