

## AEROBIC BACTERIAL FLORA OF THE NOSE: A REVIEW

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### ABSTRACT

The nose carries a variety of bacteria as part of the normal flora which can cause opportunistic infections under certain conditions and the nasal carriers are known to be a more potential source of spread of infection to others as compared to throat carriers of the same organism. The bacteria normally colonizing the nasal cavities are *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Corynebacterium* and *Neisseria* species. While the bacteria most commonly considered as nasal pathogens are Coagulase negative Staphylococci, viridians streptococci, *Hemophilus influenzae*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Klebsiella oxytoca* and various species of gram negative bacilli. Many pathogenic bacteria are developing multi-drug resistance due to irrational use of antibiotics and pose a problem in treatment. The growing concern over the advent of increasing antibiotic resistant organisms has prompted many researchers to look for alternate treatments and one such alternative is herbal remedies.

**Key words:** Opportunists, *S. aureus*, antibiotic resistance, nasal carriage, herbal remedies,

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### INTRODUCTION

One of the major connections between the interior of the body and the outside environment (along with the gastrointestinal tract) is the respiratory tract (Baron *et al.*, 1994). The principle function of the respiratory tract is gas exchange. It is, therefore, constantly exposed to the gaseous environment, which contains a suspension of particulate material including bacteria, viruses and spores (Inglis, 1996).

#### Physiological function of the nose:

The nasal cavities perform three important functions as the air passes through the nose;

- (i) warming of the air by the extensive surfaces of the conchae and septum,
- (ii) the complete humidification of the air even before it passes beyond the nose and
- (iii) the filtration of the air.

These functions together are called the air-conditioning function of the upper respiratory passage (Guyton, 1991). Although the entire respiratory tract is constantly exposed to air, the majority of particles are filtered out in the nasal hairs and by inertial impaction with mucus covered surfaces in posterior nasopharynx (Inglis, 1996) and transported by the cilia to the pharynx to be swallowed (Guyton, 1991). Once particles that have escaped the mucociliary sweeping activity enter the alveoli where alveolar macrophages ingest them and carry them to the lymphatics.

#### Role of the indigenous bacterial flora:

Along with the physiological defenses, normal flora of the nasopharynx and oropharynx help to prevent colonization of the upper respiratory tract by pathogenic microorganisms (Baron *et al.*, 1994) and possible disease through "bacterial interference" (Brooks *et al.*, 2002). The mechanism of bacterial interference is not clear. It may involve competition for receptors or binding sites on host cells, competition for nutrients, mutual inhibition by metabolic or toxic products, mutual inhibition by antibiotic materials or bacteriocins, or other mechanisms (Brooks *et al.*, 2002; Murray *et al.*, 1999). Suppression of the normal flora clearly creates a partial local void that tends to be filled by organisms from the environment or other parts of the body. Such organisms behave as opportunists and may become pathogens. On the other hand, the normal flora may produce disease under certain circumstances (Brooks, *et al.*, 2002) like previous damage by a viral infection, loss of some host immunity, or physical damage to the respiratory epithelium (e.g. from smoking) (Baron *et al.*, 1994).

#### Composition of the bacterial flora of the nose:

The bacteria most frequently and most consistently found in the nose are *Staphylococcus epidermidis* and *Staphylococcus aureus*; in the nasopharynx avirulent strains of *Streptococcus pneumoniae* and other alpha hemolytic streptococci predominate, but species of the genera *Staphylococcus*, *Corynebacterium*, *Neisseria*, *Branhemella*, *Hemophilus* (Pelczar *et al.*, 1986; Cheesbrough, 1994 and Brooks *et al.*, 2002), *Lactobacillus*, *Veillonella* and *Spirocheates* are also common (Baron *et al.*, 1994 and Murray *et al.*, 1999). *S. aureus* is carried in the nose of 40% or more of healthy people (Cheesbrough, 1994).

**Types of upper respiratory tract diseases:**

There are a vast majority of upper respiratory tract illnesses, of which acute coryza (common cold) is by far the most common, which is caused by viruses (Edward *et al.*, 1995). Complications result from secondary bacterial infections, often aided by the obstruction of respiratory passages (e.g., sinus ostia, bronchioles). They include purulent sinusitis, otitis media, bacterial pneumonia and tonsillitis. Serious bronchial obstruction may occur in patients with underlying bronchopulmonary disease (Edward *et al.*, 1995).

**Bacteria associated with Infections:**

The organisms infecting the nasal cavity are mainly the same as those infecting the throat and the two regions are often infected simultaneously. Nasal swabs are more often taken to detect healthy carriers than to diagnose infection; deep nasal swabs being taken for *S. pyogenes* and diphtheria bacillus and swabs from the skin of the anterior nares for *S. aureus*. Nasal carriers are more dangerous source of spread of infection than are throat carriers of the same organism, as they disseminate in much larger numbers of organisms into the environment than the latter (Collee *et al.*, 1989).

In a study, 46% patients suffering from chronic sinusitis revealed Coagulase Negative Staphylococci, Viridans Streptococci in 36% patients, *S. aureus* in 23%, group D Streptococci in 13%, Corynebacterium in 13%, Hemophilus influenzae in 8%, and *S. pneumoniae*, group A Streptococci, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella oxytoca*, *Propionobacterium acnes*, Actinomyces and anaerobic gram negative bacillus in 2% patients each (Orobello *et al.*, 1991). Sinusitis occurs in upto 5% of patients with upper respiratory tract infections. The maxillary sinus is the most commonly affected and the most common organisms isolated include *S. pneumoniae*, *H. influenzae* and *M. cararrhalis*. Other pathogens include *S. pyogenes* and gram-negative bacilli and anaerobes. Complications are rare but include orbital abscess, meningitis, cerebral abscess and cavernous sinus thrombosis (Collee *et al.*, 1989).

**GRAM POSITIVE COCCI:*****Staphylococci:***

The Staphylococci are the causative agents of many opportunistic human and animal infections and are considered among the most important pathogens isolated in the clinical microbiology laboratory (Yugueros *et al.*, 2000). Nasal colonization with *S. aureus* is common, occurs in 15-44% of the general population and is usually without ill effects (Shuter *et al.*, 1996) and this carriage is a major risk factor for infection (Lina *et al.*, 2003). Although *S. aureus* can be cultured from multiple sites of the skin and mucosal surfaces of carriers, the primary reservoir of staphylococci is thought to be the vestibulum nasi (anterior nares), i.e., the nostrils of the nose (Kluytmans *et al.*, 1997). Carriage of *S. aureus* appears to play a key role in the epidemiology and pathogenesis of infection. In healthy subjects, over time, three patterns of carriage can be distinguished: about 20% of people are persistent carriers, 60% are intermittent carriers, and approximately 20% almost never carry *S. aureus* (Kluytmans *et al.*, 1997; Vanden Bergh *et al.*, 1999). *S. aureus* is one of the most frequently identified pathogens in clinical laboratories (Merlino *et al.*, 2000; Kluytmans *et al.*, 2002) causing both nosocomial and community-acquired infections (Fang and Hedin, 2003). The consequences of these infections, specially when bacteremic are often devastating (Shuter, 1996). *S. aureus* has been found to be associated with various infections, particularly those involving the respiratory tract. It is the first pathogen to appear in cystic fibrosis respiratory infection and is also involved in acquired respiratory diseases (e.g., chronic bronchitis and nosocomial infections) (Mongodina *et al.*, 2000); also an etiologic agent of septicemia, meningitis, endocarditis, osteomyelitis, septic arthritis, toxic shock syndrome and food poisoning (Van Leeuwen *et al.*, 2000). Surgical site infections (SSI) caused by *S. aureus* are an important complication of surgery and *S. aureus* nasal carriage has been proven to be a main risk factor for the development of SSI (Ahmed *et al.*, 1998). Elimination of carriage has been found to reduce the infection rates in surgical patients and those on hemodialysis. Therefore, it appears to be an attractive preventive strategy in patients at risk (Kluytmans *et al.*, 1997). In 1990, Santos *et al.*, investigated the behaviour of *S. aureus* strains from simultaneous areas of healthy carriers working in different nursing categories in a general teaching hospital. They determined the propagation of *S. aureus* from the recognized source of colonization (the nasal cavity). They observed that a higher percentage of right-handed nursing workers had positivity for *S. aureus* in the nasal cavity and right hands. They used phage typing for identification of isolates obtained from the anatomical areas and suggested that the areas were colonized by *S. aureus* strains, probably of nasal origin.

There are currently 27 distinct species in the genus Staphylococcus and 23 of these species are Coagulase Negative (Hebert, 1990). The Coagulase Negative Staphylococcal species constitute a major component of the normal microflora of humans (Drancourt and Raoult, 2002). The natural habitat of many species of Coagulase Negative Staphylococci (CoNS) include the skin and nares of humans. The pathogenic role of several of the species

of CoNS is now well-established and CoNS are recognized as one of the most frequent causes of nosocomial infections (Hebert, 1990; Ben-Ami *et al.*, 2003). In recent times, CoNS have emerged as significant pathogens and nosocomial infections caused by CoNS are becoming increasingly important in most countries. Because of their ubiquitous nature and relatively low virulence, CoNS other than *S. epidermidis* and *S. saprophyticus* have long been considered clinically insignificant. However, *S. hominis*, *S. haemolyticus* and *S. warneri* are increasingly reported as causes of nosocomial infection (Leven *et al.*, 1995; Murray *et al.*, 1999). CoNS have increasingly been recognized as the cause of bacteremia in patients with neutropenia and indwelling prosthetic devices. In immunocompromised patients, bacteremia caused by CoNS has far reaching clinical consequences (Sloos *et al.*, 2000). CoNS are a major cause of foreign-body infections. The infection rate has been correlated with the increase in the use of prosthetic and indwelling devices and the growing number of immunocompromised patients in hospitals. The need exists for the accurate identification of CoNS, so that precise delineation of the clinical disease produced by this group of bacteria and the determination of the etiologic agent can be accomplished (Murray *et al.*, 1999).

### **Streptococci:**

*Streptococcus pneumoniae* is a human pathogen of major importance. It causes both mucosal and invasive diseases including otitis media, sinusitis, pneumonia, arthritis, septicemia and meningitis (Sluiter *et al.*, 1998; Overweg *et al.*, 1999 and Greiner *et al.*, 2001). Pneumococci are often part of the normal nasopharyngeal flora. Specially in young children, pneumococcal colonization often occurs. Colonization is an important risk factor: children colonized with *S. pneumoniae* more often develop acute otitis media than children who are not colonized (Overweg *et al.*, 1999; Sluiter *et al.*, 1998). Organisms are presumably passed from person to person via respiratory secretions and aerosols. *S. pneumoniae*, also called the “pneumococcus”, is the second most common cause of bacterial meningitis, often preceded by pneumonia. Pneumococcal pneumonia is the most common type of community-acquired bacterial pneumonia; the fatality rate of uncomplicated pneumococcal pneumonia is still relatively high (5% to 7%), even with prompt institution of appropriate therapy (Baron *et al.*, 1994).

### **GRAM POSITIVE BACILLI**

#### ***Corynebacterium:***

*Corynebacterium* species most likely to be encountered in the clinical laboratory include *C. diphtheriae*, *C. ulcerans*, *C. pseudodiphtheriticum*, *C. xerosis*, *C. minutissimum*, *C. jeikeium*, *C. matruchotii* and *C. urealyticum*. Most species are harmless saprophytes and many are part of the normal human skin and mucous membrane flora. *C. diphtheriae* is the agent of diphtheria, and *C. jeikeium* and *C. urealyticum* are relatively common causes of infection in immunocompromised host. They are considered as major pathogens of humans (Baron *et al.*, 1994).

### **GRAM NEGATIVE COCCI**

#### ***Neisseria:***

*Neisseria meningitidis* can be cultured from upto 40% of human nasopharyngeal swab samples (Claus *et al.*, 2002). It is primarily a commensal bacterium colonizing the human nasopharynx (Alber *et al.*, 2001) which may cause meningococcal disease (Claus *et al.*, 2002). Colonization of the human nasopharynx is a feature of some species of *Neisseria*, and is a prerequisite of invasive meningococcal disease. The likelihood of colonization by *N. meningitidis* varies widely between humans, and very few develop invasive disease (Townsend *et al.*, 2002). The great majority of meningococcal infections are harmless colonizations of the throat or nasopharynx, but some of these lead to life-threatening meningitis and septicemia, which may occur separately or in combination (Bygraves *et al.*, 1999). Humans can be colonized by commensal *Neisseria* including *N. lactamica*, which rarely causes disease. Colonization by *N. lactamica* is frequent in infants but declines to relatively low rates in teenagers and adults (Townsend *et al.*, 2002).

### **GRAM NEGATIVE BACILLI**

#### ***Hemophilus:***

The organisms belonging to genus *Hemophilus* cause upper respiratory tract infections; suppurative infections, primarily in areas adjacent to the respiratory tract; and systemic infections, particularly meningitis (Baron *et al.*, 1994). *Haemophilus influenzae* is a common commensal of the human respiratory tract (Reilly *et al.*, 1999) and the most important human pathogen among the *Haemophilus* species (Baron *et al.*, 1994). This organism is the etiologic agent of a variety of local and invasive infections in both children and adults (Reilly *et al.*, 1999). It is associated with acute, contagious conjunctivitis, acute and chronic otitis media, epiglottitis, cellulites and other infections. Other *Haemophilus* species, which include *H. parainfluenzae*, *H. haemolyticus*, *H. aphrophilus*, *H. paraphrophilus* and *H. segnis*, are normal flora of humans, occasionally causing upper and lower respiratory tract infections. These

organisms may also occasionally enter the blood stream from a mucosal focus, disseminating to cause systemic disease, including endocarditis, metastatic abscesses (specially brain abscess), septic arthritis and osteomyelitis. They have also been known to infect tissue adjacent to the mucosa, causing jaw infections, dental abscesses and appendicitis (Baron *et al.*, 1994).

#### **Moraxella:**

Moraxella species are members of normal flora of the upper respiratory tract and occasionally cause bacteremia, endocarditis, conjunctivitis, meningitis or other infections (Brooks *et al.*, 2002). The recognition of *Moraxella catarrhalis* as an important cause of the upper respiratory tract has been protracted, mainly because it is a frequent commensal organism of the upper respiratory tract (Greiner *et al.*, 2003). *M. catarrhalis* has been isolated as the causative agent of disease, including septicemia, meningitis, endocarditis, otitis media, conjunctivitis, sinusitis, laryngitis, pneumonia and bronchitis (Baron *et al.*, 1994).

#### **Klebsiella:**

*Klebsiella pneumoniae* is present in the respiratory tract of about 5% of normal individuals. It causes a small proportion (about 3%) of bacterial pneumonias. *K. pneumoniae* can produce extensive hemorrhagic necrotizing consolidation of the lung. It occasionally produces urinary tract infection and bacteremia with focal lesions in debilitated patients (Brooks *et al.*, 2002). *K. pneumoniae* and *K. oxytoca* cause hospital acquired infections (Westbrook *et al.*, 2000; Brooks *et al.*, 2002 and Hansen *et al.*, 2004). *K. ozaenae* and *K. rhinoscleromatis* are rarely associated with inflammatory conditions of the upper respiratory tract (Brooks *et al.*, 2002; Hansen *et al.*, 2004).

#### **Antibiotic resistance:**

Antibiotics are used to treat bacterial infections that work by binding to specific target molecules in bacterial cells and alter certain metabolic activities like inhibiting cell wall synthesis; altering the permeability of cytoplasmic membrane; inhibition of nucleic acid and protein synthesis or inactivation of enzyme system. If bacteria can prevent an antibiotic from interacting with its target site, they will manifest resistance to that agent (Pelczar *et al.*, 1986).

The composition of bacterial flora is affected by the administration of antimicrobial agents and may reduce the risk of respiratory tract infections by eliminating the potential pathogens (Brook and Gober, 2005). Brook and Gober (2005) demonstrated a reduction in recovery of potential pathogens from nasopharynx following antimicrobial therapy with amoxicillin and cefdinir.

On the other hand, it has been proved by a number of studies that indiscriminate use of antibiotics results in the development of antibiotic resistance (Coutinho *et al.*, 2009). Clinically important bacteria involved in respiratory tract infections are rapidly developing resistance to common therapeutic options and use of antibiotic agents can select resistant microorganisms (Perez-Trallero *et al.*, 2001), resulting in infections by antibiotic resistant strains which make treatment troublesome.

*S. aureus* acquires antibiotic resistance with remarkable proficiency, and strains for which vancomycin is the only effective therapeutic agent have emerged (Booth *et al.*, 2001). The organism is also highly versatile in its capacity to colonize and establish infections in a wide range of body sites, which makes it a leading cause of infections in hospitalized patients. Infections by antibiotic resistant *S. aureus* are serious; difficult to treat and sometimes life threatening. Methicillin resistant *S. aureus* (MRSA) is an important pathogen and a major cause of nosocomial infections (Watanabe *et al.*, 2000 and Sakoulas *et al.*, 2001). Resistance to methicillin was first discovered in 1960, shortly after the introduction of the drug into clinical practice. Since then, MRSA has become a widely recognized cause of morbidity and mortality throughout the world (Hookey *et al.*, 1998). Data from around the world verify the escalating incidence of infections caused by MRSA. Infections with MRSA are serious and often life-threatening (Wenzel *et al.*, 1991). Since methicillin resistance is now wide spread in hospitals all over the world, therapy has become cumbersome. A new and even more threatening development is the emergence of strains with a reduced susceptibility to glycopeptides. Therefore, the control of *S. aureus* in hospitals has now become more important than ever before (Kluytmans *et al.*, 2002).

Until the beginning of the 1980s the majority of pneumococcal strains were susceptible to penicillin, which was the treatment of choice. However, in recent years there have been reports of strains with structural changes to penicillin binding proteins, reducing susceptibility not only to penicillin, but also to all other beta-lactam antibiotics (Anton *et al.*, 2001). The emergence of drug resistant *S. pneumoniae* threatens to complicate the management of pneumococcal infections (Hofmann *et al.*, 1995). The increasing rate of antibiotic resistance in *S. pneumoniae* complicates the elimination of pneumococcal strains from the middle ear (Sluiter *et al.*, 1998).

There are other bacteria like *H. influenzae*, *B. catarrhalis*, *K. pneumoniae* and *Ps. aeruginosa* which are considered nasal pathogens causing nosocomial infections and tend to develop antibiotic resistance. If used rationally, antibiotics can cure most bacterial infections. However, there is an increasing tendency globally for bacteria to become resistant to antibiotics (Gakuu, 1997). Most reports regarding drug-resistant organisms have been linked to day-care centers and the indiscriminate use of antibiotics (Hofmann *et al.*, 1995).

### Alternate Medicine:

The growing concern over the advent of increasingly antibiotic resistant organisms has prompted many individuals to look for alternate treatments. One such alternative is the herbal remedies, which are being marketed with mounting zeal. Used for centuries as folk remedies, herbs are enjoying a surge of public interest. Scientific experiments since the late 19<sup>th</sup> century have documented the antimicrobial properties of some spices, herbs and their components (Zaika, 1988). Researchers have been testing herbs for activity against pathogenic organisms and the results support the notion that plant essential oils and extracts may have a role as pharmaceuticals and preservatives. Many therapeutic plants have not only shown antimicrobial activity but also demonstrated resistance-modifying capability (Gibbons, 2004).

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