

# PEDIATRIC NEWS

## San Antonio Military Pediatric Center



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### Housestaff Puzzler

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#### Housestaff Puzzler

**C**V is a 12yo African American male who presented to clinic for follow up of "scarlet fever." His symptoms started approximately 12 days prior with a generalized, pruritic, papular rash over his trunk. Over the next few days, he developed a fever up to 104°F. His father brought him to the clinic for evaluation on day 3 of the illness. The patient denied HA, cough, congestion, sore throat, nausea, vomiting, diarrhea, abdominal pain, myalgias, arthralgias, or dysuria. The rash had worsened and was intensely pruritic. He had been camping 2 weeks earlier but had no known tick or other insect bites. He was non-toxic appearing with normal vital signs. He had a mildly erythematous oropharynx, mild scleral icterus, and generalized erythroderma with

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### Obstructive Sleep Apnea

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**T**he syndrome of obstructive sleep apnea (OSA) was described more than a century ago. However, it was only in the 1970s that OSA in children was recognized. This frequent, albeit underdiagnosed, condition in children, if left untreated, may lead to substantial morbidity.

Estimates suggest that up to 2% of children may be affected by OSA; however, incidence of snoring in the general pediatric population has been estimated at 8-27%. African-American and Asian children are at higher risk of OSA presumably because of craniofacial characteristics. No sex differences exist in snoring or OSA prevalence among prepubertal children. In the older adolescent, as with adults, a male preponderance emerges. Peak incidence occurs at 2-8 years (coinciding with adenotonsillar tissue growth). Patients at increased risk include those with: craniofacial anomalies, neuromuscular disease, obesity, adenotonsillar hypertrophy, cerebral palsy, myelomeningocele, trisomy 21, hypothyroidism, and sickle cell disease.

#### Pathophysiology

Snoring and obstructive apnea represent a spectrum of symptoms of increased upper airway resistance. The ability to maintain upper airway patency during normal respiration is the result of equilibrium between the forces that promote airway closure and dilation. The 4 major predisposing factors for upper airway obstruction include anatomic narrowing, abnormal mechanical linkage between airway dilating muscles and airway walls, muscle weakness, and

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### Pneumococcal Disease: Beyond Prevnar

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**A**s a pediatrician-in-training, questions regarding the most common causes of various infections often arose. For children, the answer was most often Streptococcus pneumoniae, Nisseria meningitides and Haemophilus influenzae type B, although

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Pastia's lines and a few scattered petechiae on his extremities and in the groin area. Labs obtained included a throat culture (subsequently negative), Monospot (negative), CBC and LFTs. The CBC was significant for a white blood cell count of 15.7 with 55 segs, 15 bands, 7 lymphs, 6 monos, and 17 eosinophils. Hemoglobin was 12.4, hematocrit was 37.9, and platelets were 328. LFTs were significant for elevated AST, ALT, GGT, total bilirubin and direct bilirubin (see Table 1).

The patient was admitted for close observation because of the petechiae with a presumptive diagnosis of scarlet fever but with concerns for possible tick-borne illness. During admission, the patient received penicillin and steroids. Repeat LFTs showed a downward trend. Serum Streptozyme was positive despite a negative throat culture. The patient was discharged with oral penicillin to complete a full ten-day course, and Atarax for pruritus. Outpatient follow up was arranged for one week later.

The patient presented for the follow-up appointment on day 12 of the illness. He had finished the course of penicillin but continued to spike fevers (Tm 101°F) until 4 days ago. The rash had now started to desquamate. The patient also complained of three days of lower

leg myalgias. Physical exam was notable for diffuse desquamation of the trunk, arms, groin, back, palms, and thighs. Lower legs and feet were spared but appeared very dry. Musculoskeletal exam was normal. HEENT and neck exam were also completely normal (no oral lesions, clear conjunctivae, no cervical lymphadenopathy). There was no hepatosplenomegaly. The rest of the physical exam was normal.

At this point, there were some definite concerns that this could represent atypical Kawasaki's disease. Repeat labs (see Table 1) revealed a marked elevation in platelet count (839) and a significantly elevated ESR of 100. LFTs continued to trend down. Hepatitis panel, EBV, and CMV titers were also negative. Cardiology was consulted; an echocardiogram revealed normal coronary arteries. The patient was instructed to return in one week for follow up.

At the next visit (day 19), the patient reported that the rash had resolved except for the lower legs and feet, which were now peeling. The patient's mother stated that he was now "walking like an old man" and complained of occasional lower back and ankle pain. Physical exam revealed resolution of the desquamation except on the lower legs and feet. Musculoskeletal exam demonstrated no bony tenderness, joint effusions, or joint tenderness. He had a definite antalgic gait that appeared worse upon initiation of

walking.

Repeat labs showed continued elevation of ESR at 100. LFTs had completely resolved except for a slightly elevated ALT and GGT. The platelet count was 1060. Creatine kinase was normal. An ultrasound of the liver and gallbladder was normal. After discussion with Cardiology, the patient was started on 160mg of aspirin per day (4mg/kg/day). Follow up echocardiogram one week later (day 25) showed a "prominent LMCA but normal for age."

### Discussion

Kawasaki syndrome (KS) is an acute vasculitis that primarily affects infants and young children between the ages of 1 and 8 years. The primary adverse sequela of this disease is the development of coronary artery aneurysms, which can be as common as 15-25% in untreated individuals. Classically, the diagnosis is based on the following clinical features:

- Fever for at least 5 days
- Four of the following five signs:
  - 1) Bilateral non-exudative conjunctival injection
  - 2) Changes of the oral mucosa (e.g., erythematous, dry, fissured lips; pharyngeal erythema; strawberry tongue)
  - 3) Changes of the hands and feet (e.g., redness and

Table 1 – laboratory values over 6 weeks

Date	WBC	Plts	ESR	AST	ALT	GGT	T Bili	DBili
4/3/01	15.7	328		80	279	265	2.9	2.1
4/4/01	15.9	377		67	197		2.3	1.8
4/12/01	15.6	839	100	70	123	229	0.7	0.4
4/18/01	8.5	1060	100	35	58	167	0.4	0.2
5/4/01	9.3	640	100			78		
5/25/01	6.4	429	43	22	20	50	0.3	0.1

- swelling, perinungal desquamation)
- 4) Polymorphous exanthem, primarily on the trunk (may be maculopapular, erythema multiforme, or scarlatiniform)
- 5) Cervical lymphadenopathy, node > 1.5cm
- Illness unexplained by other known disease process

When these features are evident, the diagnosis is very straightforward, and treatment with intravenous gamma globulin (IVGG) is instituted. Such treatment reduces the incidence of coronary dilatation to less than 5% and that of giant coronary aneurysms to less than 1%.

However, there are a significant number of patients who do not present in the typical fashion. One study indicated that 20% to 60% of patients with coronary aneurysms secondary to KS never meet the classic criteria. These patients include the very young as well as older children and adolescents. In the latter group, one study found a high frequency of delay in the diagnosis of coronary abnormalities because of “non-classic” Kawasaki features.

KS can mimic the clinical presentation of other illnesses, increasing the potential to misinterpret a non-classic presentation. The differential diagnosis of KS is broad and includes scarlet fever, staphylococcal scalded skin syndrome, Stevens-Johnson syndrome and other drug reactions, Rocky Mountain spotted fever, toxic shock syndrome, leptospirosis, juvenile rheumatoid arthritis, and measles. Fortunately, both clinical and laboratory data can help exclude these other possibilities.

In addition, there are a wide variety of other features associated with KS that can assist the clinician

in making the diagnosis and instituting the appropriate treatment. Laboratory features include the following:

- Elevated WBC (PMN predominance)—typical during first 1-2 weeks
- ESR elevation—typical during first week and may persist 4-6 weeks
- Normocytic anemia—common in acute KS, severe in patients with prolonged fever or coronary disease
- Thrombocytopenia—generally associated with development of severe coronary disease and myocardial infarction
- Thrombocytosis (often in excess of 1 million/mcL)—occurs during second and third week of illness
- ANA, RF—not detectable in KS
- Sterile pyuria—approximately 33% of patients during first week
- Elevated AST/ALT (often 2- to 3-fold)—typical during first week
- Mild CSF pleocytosis—typical during first week; usually associated with normal protein and normal glucose

Other “non-classic” clinical features include myocarditis, extreme irritability (mostly in infants), aseptic meningitis, arthralgia and arthritis, mild hepatic dysfunction, gallbladder hydrops, diarrhea, pneumonitis (seen on X-ray but not clinically), and otitis media.

### Treatment

During the first 10 days of illness, patients with KS are treated with a 2g/kg dose of IVGG in addition to 80 to 100 mg/kg/day of aspirin. Once the fever has resolved, the aspirin is reduced to 3-5 mg/kg/day. The exact mechanism of action of IVGG in KS is unknown. Aspirin has both anti-inflammatory and

antithrombotic effects. Studies in Japan have shown that this treatment decreases the prevalence of coronary abnormalities from 15-25% to 2-4%.

Prolonged fever is a risk factor for more severe coronary disease; thus, treatment with IVGG should be considered in a patient who presents with fever for greater than 10 days, even though studies with IVGG have only been conducted within the first 10 days of illness. However, if a patient presents with desquamation and a history consistent with KS, and if he has been afebrile for many days, treatment with IVGG should not be instituted because IVGG is unlikely to prevent coronary disease once the acute inflammatory response has resolved.

### Prognosis

In general, patients with KS who are treated with IVGG and aspirin within 10 days of onset are at low risk for developing permanent sequelae. Patients are kept on daily aspirin until follow-up echocardiograms (at 2-3 weeks and 6-8 weeks following the onset of illness) are normal, and laboratory values (particularly the CBC and ESR) have normalized. After 2 months, it is unlikely for patients with normal coronaries to develop long-term coronary abnormalities.

The patient in the case presentation did not meet the classic criteria for KS. Only after serial exams and laboratory studies did the diagnosis become clear. Over several weeks, the patient’s desquamating rash and arthralgias resolved. Although the follow-up echocardiogram on day 25 of illness showed a “prominent LMCA”, it was still within normal limits. A subsequent exam 6 weeks later was also normal, so aspirin therapy was discontinued. The platelet count and ESR normalized over time.

## Summary

Kawasaki syndrome is the most common cause of acquired heart disease in children in the United States. If untreated with IVGG, as many as 1 in 4 children with KS develop coronary artery aneurysms. All pediatricians must develop an understanding of the classic clinical signs in affected patients as well as a high index of suspicion in children who may not meet the classic criteria but who have other associated findings.

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abnormal neural regulation.

A smaller cross-sectional area of the upper airway is associated with decreased ability to maintain airway patency. Under conditions of flow limitation, maximal inspiratory flow will be determined by the pressure changes upstream (nasal) to a collapsible site of the upper airway, and flow will be independent of downstream (tracheal) pressure generated by the diaphragm. This explains why, for example, snoring and obstructive apnea worsen during a common cold (increased nasal-upstream resistance). Anatomic factors, both congenital and acquired, play a significant role in the pathogenesis of pediatric OSA.

Malposition of specific dilating muscles is likely to have major consequences upon the mechanical dilating efficiency. Therefore, even without weakness, the mechanical

disadvantage imposed by muscle shortening or by displacement of the muscle insertion upon the pharyngeal wall diminishes the ability to stiffen the airway, leading to increased collapsibility.

In neuromuscular disorders, upper airway obstruction frequently is observed during sleep as muscle tone decreases, dropping outward pressure of the pharyngeal wall.

Diminished arousal as well as laryngeal reflexes to mechanoreceptor and chemoreceptor stimulation, with reduced afferent inputs into central neural regions underlying inspiratory inputs, may be present in children with OSA. For example, chemoreceptor stimuli, such as increased PaCO<sub>2</sub> or decreased PaO<sub>2</sub>, stimulate upper airway dilating muscles.

## Mortality/Morbidity

Despite the misleadingly benign clinical presentation, the pathological consequences of OSA in children may be severe. These morbidities stem from the 4 consequences of upper airway obstruction during sleep: sleep fragmentation, increased work of breathing, alveolar hypoventilation, and intermittent hypoxemia.

### Sleep fragmentation

Reports of decreased intellectual function in children with adenotonsillar hypertrophy date from 1889 when Hill reported on "some causes of backwardness and stupidity in children." Schooling problems and ADHD-like symptoms have been reported in case studies of children with OSA and, in fact, may underlie more extensive behavioral disturbances, such as restlessness, aggressive behavior, excessive daytime sleepiness, and poor test performance. Recent studies suggest long-term performance deficits in untreated OSA patients, though short-term improve-

ment is seen after treatment.

### Increased work of breathing

A major consequence of OSA is arterial hypertension. Although the pathophysiological mechanisms of elevation in arterial tension remain debatable, it appears that intermittent arousal, hypoxemia, and increases in cardiac afterload during the obstructive apneic event lead to enhanced sympathoadrenal discharge and sympathetic tone even while awake.

The most prominent clinical manifestation of increased work of breathing in children with OSA is failure to thrive (FTT), with an incidence as high as 50%. Significant catch-up growth has been reported after tonsillectomy and adenoidectomy (T&A), even in obese children with OSA. The causes of poor growth include anorexia and dysphagia, resulting from tonsillar and adenoid hypertrophy, diminished or altered patterns of nocturnal growth hormone secretion, hypoxemia, acidosis, and increased work of breathing during sleep.

### Alveolar hypoventilation

Children with snoring and OSA are a classic example of intermittent alveolar hypoventilation, which is elicited by increased upper airway resistance, concurrent with diminished or insufficient compensatory mechanisms developing during sleep.

### Intermittent hypoxemia

A serious consequence of intermittent hypoxia is elevation of pulmonary artery pressure due to pulmonary vasoconstriction, such that chronic intermittent nocturnal hypoxemia will lead to development of pulmonary hypertension and cor-

pulmonale. Another potentially very serious consequence of intermittent hypoxia may involve its long-term deleterious effects on neuronal and intellectual function.

### Diagnosis

The clinical presentation of a child with OSA syndrome is nonspecific and requires increased awareness by the primary care physician. Indeed, the medical history usually is normal, unless the pathophysiology of sleep-associated airway obstruction is related to one of the various conditions delineated below. Significant relationships with family history of snoring, allergies, and environmental exposure to smoking exist. For the otherwise healthy child, the principal parental complaint will be snoring during sleep. History of loud snoring three or more nights per week should increase suspicion of OSA. Occasionally, parents will comment on breathing difficulties during sleep, unusual sleeping positions, morning headaches, daytime fatigue, irritability, poor growth and weight gain, and behavioral problems. Nevertheless, even when the diagnostic interview is conducted by a sleep specialist, the accuracy of OSA prediction is poor and does not exceed a 50-60% sensitivity and specificity, particularly in distinguishing OSA from benign snoring.

Physical examination generally is normal while awake, with the exception of findings related to predisposing conditions noted below. Growth charts may reveal FTT or obesity. Examine the nasal passages for mucosal swelling, cobblestone pattern of the mucosa, polyps, and reduced nasal airflow. Also evaluate the size and position of tonsils and uvula, noting particularly hypertrophy or malformation. Unfortunately, while tonsillar hypertrophy may contribute to the

severity of OSA, the data available to date have not established a clear relationship between tonsillar size and frequency or severity of apneic events. Furthermore, though more prevalent in patients with OSA, tonsillar hypertrophy is also common in healthy children without OSA, with a prevalence as high as 57%. Look at the palate for evidence of cleft or pharyngeal narrowing or compression. The relative position of the chin with respect to the maxilla is helpful in the identification of mild micrognathia or retrognathia. Cardiac examination may reveal the presence of a prominent pulmonic second heart sound suggestive of pulmonary hypertension.

The only currently available tool for definitive diagnosis of OSA is an overnight polysomnographic evaluation in the sleep laboratory. This includes multiple channels aiming to monitor sleep state, as well as cardiac and respiratory parameters. The adult criteria that are usually employed for the diagnosis of OSA do not apply to children. In fact, the finding of 10-15 obstructive apneic events per hour of sleep, which would be considered to represent a mild adult OSA patient in whom treatment may not even be contemplated, represents a sleep-related respiratory disturbance corresponding to a severely affected child definitely in need of therapeutic intervention. Thus, an apnea-hypopnea index (AHI) of more than 5 events per hour clearly is considered to represent an indication for treatment in children. An AHI of fewer than 3 events per hour is considered as not requiring any intervention, and in children with an AHI of more than 3 but fewer than 5 events per hour, the cost-benefit ratio of treatment remains to be determined.

### Treatment

Although OSA has multiple etiologies in children, once the

diagnosis of OSA has been established and its severity assessed, T&A usually is the first line of treatment. T&A alone may not suffice in high-risk patients and polysomnographic evaluation 6-8 weeks after may confirm the need for additional treatment. In fact, cure rates in normal children may only be about 80%. Temporary palliation using supplemental oxygen may be implemented until surgery, provided that sufficient attention is given to the possibility that severe hypercapnia may develop.

A higher risk for surgical complications exists in children < 2 years old, with severe OSA, with craniofacial syndromes, or with other conditions contributing to the OSA. For example, the presence of pulmonary hypertension and right ventricular dysfunction has been linked to arrhythmias during anesthesia induction. Thus, in these patients, preoperative echocardiographic assessment is indicated. Similarly, for all of the risk categories mentioned above, a high risk of post-surgical upper airway obstruction exists in an obtunded patient in whom the anesthetic effects on upper airway tone and reflexes still are compromised. Finally, the development of idiopathic pulmonary edema following the relief of upper airway obstruction also has been noted. Therefore, in high-risk patients, overnight cardiorespiratory monitoring in the PICU is warranted. Additional surgical options may be warranted in specific patients. Tracheostomy remains a last resort.

In the context of allergic rhinitis or conditions associated with decreased nasal airflow, efforts to improve nasal patency may be of partial benefit. Thus, use of antihistamines and topical intranasal steroids may reduce the severity of OSA. Systemic steroids have no proven efficacy.

In recent years, noninvasive positive-pressure ventilation, with

CPAP or bilevel PAP, has become a safe and viable alternative to further surgery or tracheostomy in children with unresolved OSA after T&A. An important aspect of these interventions involves the patient-machine interface. The use of nasal prongs, nasal masks, or facemasks requires individualized, case-by-case consideration. Particular care to ensure that the mask fits snugly and is comfortable to the patient is essential for ensuring successful intervention. Masks currently are available in several sizes and for particular clinical conditions, such as craniofacial syndromes. Custom-made masks can be ordered to fit the facial contours. Inappropriately fit masks inevitably leak, causing eye irritation, and efforts to seal these leaks frequently will result in pressure sores on the bridge of the nose. Many techniques may be used to secure the mask. Again, the importance of the patient's comfort cannot be overemphasized. Nevertheless, mid-facial hypoplasia may develop with long-term use, particularly in children with neuromuscular weakness. Finally, implement adequate parental training and behavioral techniques designed to improve the acceptance and tolerance to these devices in order to increase compliance.

### Prognosis

In children with enlarged tonsils and adenoids leading to OSA, T&A usually results in complete cure, even though no definitive studies have demonstrated this issue clearly. The outcome of those complex patients requiring extensive surgical management obviously depends on the severity of the condition leading to upper airway compromise. With the emergence of noninvasive ventilation as an alternative option for these children, upper airway obstruction during sleep can be managed conservatively and successfully in most children. In

those children with FTT, treatment of OSA will lead to resolution of the somatic growth disturbance. Similarly, pulmonary hypertension will resolve. Although major improvements in neurobehavioral outcomes are expected, there currently are insufficient data to support a complete recovery in some of the cognitive abilities impacted by OSA.

Neurobehavioral disturbances and diminished learning capabilities, stunted growth, altered respiratory load response patterns, and pulmonary hypertension are major consequences of OSA in childhood. Early diagnosis and prevention of such morbidities are fundamental aspects of adequate pediatric care in the community.

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nobody in training had ever seen the latter. The reason behind this was the institution of the HiB vaccine in early 1980's. This vaccine has virtually eliminated disease states attributed to this organism and thrust pneumococcus into the forefront as the most grievous bacterial infectious disease predator of children. Prior to 2000, the only vaccine available was the 23-valent pneumococcal vaccine (Pneumovax), which was composed of capsular polysaccharide antigens of 23 pneumococcal serotypes. This covered 88% of serotypes known to cause bacteremia and meningitis in adults and 100% of cases of bacteremia and meningitis in children.<sup>1</sup> Unfortunately, polysaccharide antigens have little immunogenicity in children under 2-3 years of age. In February 2000, a new heptavalent pneumococcal vaccine (Prevnar) was approved for use in the routine childhood immunization schedule. Since it was based on technology similar to the HiB vaccine (polysaccharide-protein conjugate vaccine), this is useful in children under 2 years of age.

I often get questions where a provider will state that they are not worried about pneumococcus because the patient has been immunized. While the technology is similar to the HiB vaccine, not all disease was expected to be eradicated as with *Haemophilus influenzae* for a few reasons. Many studies have looked at which serotypes cause disease in young children. The most glaring weakness of the vaccine is that it only covers the 7 most common serotypes associated with invasive disease (14, 6B, 19F, 18C, 23F, 4, and 9V). These serotypes account for 80% of invasive isolates for children < 6 years old but only 50% of isolates for children > 6 y/o.<sup>1</sup> Additionally,



geographic and ethnic differences have been noted. Less invasive disease in Native Americans and Alaskans can be attributed to the covered serotypes.<sup>2</sup> The latest data suggests a brighter picture. It noted that 85.4% of pneumococcal isolates were due to vaccine associated strains.<sup>3</sup> Furthermore, studies in other countries have noted that serotypes 1 and 5 play a much greater role as a cause of invasive disease. In the most recent study in the United States, only 2.5% of invasive infections are due to these serotypes.<sup>4, 5</sup>

The big question to be addressed is what difference has this vaccine made in practice and how can it help you make clinical decisions. I will attempt to address the following areas: 1. Invasive Disease 2. Bacteremia 3. Pneumonia 4. Otitis Media

#### Invasive Disease

The primary initial studies were conducted by the Kaiser Permanente group in California. They defined invasive disease as an acute illness cultured from a normally sterile site. They randomized 37,830 patients to receive or not receive Prevnar. They found that patients were 97.4% protected against vaccine strains when fully immunized (3 doses) and 93.9% protected after having received at least one dose of vaccine. Statistical significance was detected for serotypes 19F, 14, 18C and 23F. No increase in non-vaccine covered strains were detected.<sup>1</sup>

#### Bacteremia

Not a large amount of material exists looking solely at bacteremia as a cause of disease. Approximately, 65% of all patients with invasive disease will have bacteremia. In a recent study of occult bacteremia, 97.7% of all pneumococcal cases of occult bacteremia were caused by vaccine-associated serotypes.<sup>6</sup> The

overall incidence of occult bacteremia was 1.9% of 5901 patients who met criteria for occult bacteremia.<sup>7</sup> In our population, we have recently reviewed the data from the first year with regard to bacteremia. We have found a reduction in the first year following routine immunization of 50% and 62% compared to the previous two years. Additionally, we found no cases in children who had received prior immunization and 60% of cases were caused by potentially vaccine preventable strains. While universal immunization was attempted, it was not achieved.

#### Pneumonia

Pneumonia results can be looked at with regard to any clinical pneumonia, clinical pneumonia with abnormal chest x-ray, and clinical pneumonia with chest x-ray remarkable for a consolidation of > 2.5 cm. Reduction was noted in all three subgroups. The most remarkable was a 73.1% reduction in children with pneumonia and a consolidation >2.5 cm. The clinical pneumonia subgroups were less impressive with rates of reduction of 11.4% and 33 % respectively.<sup>8</sup>

#### Otitis Media

Finally, it was hoped that the "holy grail" of the immunization would be in the prevention of otitis media in young children. Prevention of otitis media would serve as a major advancement in the improvement of health care for children. This vaccine also covers serotypes that have often been associated with otitis media. One study found that 71% of samples obtained by tympanocentesis were vaccine-covered serotypes while another found 60%.<sup>9, 10</sup> The results, while statistically significant, have not been overwhelming. The Kaiser Group noted a reduction in all cases of otitis media of 6.4%.<sup>8</sup> Patients

with frequent infection or infections requiring tympanostomy tube placement showed a greater response of 9.1% and 20.3% respectively. The Finnish group found similar outcomes. They enrolled 1662 infants in a randomized prospective study. They found a similar reduction of 6% of all cases of otitis media. Since this study was a myringotomy study, pneumococcal culture and serotyping was possible. A reduction of 34% was estimated for all pneumococcal serotypes and 51% for those covered by the vaccine.<sup>10</sup>

#### Cost Savings

One study prior to the institution of routine immunization indicated that based on the prevention of bacteremia and meningitis, 222 lives per million children would be saved at a cost of 0.08 to 2.42 per child.<sup>11</sup> The Kaiser Group also analyzed their data in order to determine cost efficacy. They found that in a cohort of 3.8 million patients, they would prevent 12,000 cases of meningitis and bacteremia, 53,000 cases of pneumonia and 1 million cases of otitis media. This would save \$342 million in medical and \$415 million in work-loss costs. This is noted to be cost effective if the price of the immunization was \$46 per dose (the approximate cost to the military).<sup>12</sup>

#### What does the future hold?

From the data which has been compiled, it is obvious that invasive disease due to pneumococcus will likely decrease in incidence. Unfortunately, this immunization will not likely have the dramatic effect that HiB had in altering our daily practice. Some theories suggest that increased efficacy could be obtained if herd immunity occurs after mass immunization resulting in less pneumococcal colonization in children in general. Other scenarios

exist which could decrease the efficacy of the immunization program. Most obvious is the fact that the immunization has been in short supply and very few children are receiving the entire 3 shot series. While protection can be seen following one immunization, it is decreased versus the full series. Additionally, multiple studies have shown that in our population the 7 serotypes covered by the immunization are the most common causes of invasive disease. Other populations have not shown the same serotype prevalence. Immunizations to cover 9 and 11 different serotypes are also under development for these populations. A study from Israel using the 9-valent vaccine shows a decrease in respiratory tract infections in day-care attendees, a group well known to have pneumococcal colonization and resistance. They noted a decrease of 15%, 16% and 17% for URI, LRI and otitis media in this group known to have a high number of these infections.<sup>13</sup> In the future, we may see some of the present serotypes replaced by other serotypes as carriage rates are decreased by immunization. If that is the case, immunizations may need to be tailored to a specific population over time.<sup>14</sup>

In summary, the newest vaccine, Prevnar, is very effective at preventing invasive disease in our patients. It is well documented to prevent cases of meningitis, bacteremia and pneumonia in children. While it will help to decrease the number of cases of otitis media, it should not be called the "Ear Infection" vaccine based on present data. Long-term efficacy will need to be followed to insure that the immunization continues to be protective.

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