The Gram positive pathogen *Streptococcus pneumoniae*, (the pneumococcus), has contributed to our understanding of fundamental biology through the demonstration by Avery and co – workers more than 80 years ago, of DNA as the basis of the transforming principle of pneumococcal capsules, and therefore as the basis of heredity[1]. The pneumococcus has become the leading vaccine preventable cause of death and a successful and diverse human pathogen. More recently, the development of pneumococcal conjugate vaccine (PCV) has made possible the prevention of pneumococcal disease in infants, but also elucidated aspects of pneumococcal biology by the use of the vaccine as a probe to understand the burden of pneumococcal disease in children globally[2]; as infant mortality increases, the contribution of pneumonia and therefore of the pneumococcus to that mortality also increases[3, 4]. There is therefore significant optimism that the recent rollout of PCV under an advance market commitment will make a significant impact on the achievement of the millennium goal to reduce infant mortality by 2/3 by the year 2015.

Of particular interest is the impact of PCV on carriage as the vaccine has led to significant herd immunity in the US where is has reduced vaccine type invasive pneumococcal disease by more than 90% in adults through immunization of infants[5] Indeed 95% of the non – bacteremic pneumonia disease burden prevented in the USA by the immunization of infants has been seen in adults as the total burden of pneumonia in developed countries falls disproportionally on adults[6]. Immunization of infants has been shown to protect HIV infected adults from invasive disease due to the vaccine serotypes[7] although direct immunization of HIV infected adults with two doses of PCV has recently been demonstrated to be effective[8].

The impact of replacement on the reductions in disease burden post PCV introduction is the subject of much debate, but there is some consensus that the replacing strains tend to be less virulent, but are still able to cause a significant burden of disease in immunocompromized hosts.
The plasticity of a naturally transformable pathogen to respond to selective pressure through capsular switching and the accumulation of antibiotic resistance determinants has been highlighted recently by the publication of whole genome sequencing of 240 pneumococcal strains almost all identical in sequence at 7 housekeeping genes and defined as the Spanish clone – 1 of the Pneumococcal Molecular Epidemiology Network[9]. This study demonstrates that despite the close relationship between these strains, more than 70% of the genome is variant at each nucleotide position because of rampant homologous recombination, and in particular the organism has evolved to escape both antibiotic and vaccine pressure.

There are two large scale clinical trials ongoing which are testing PCV – one in Holland of PCV13 in adults and a PCV10 trial with a pneumonia endpoint in Argentina in infants. The results of both of these trials may become clear in 2011 – 12. A 15 valent pneumococcal conjugate vaccine is entering human clinical trials. A number of approaches to protein or whole cell based pneumococcal vaccines are entering phase I clinical trials in humans but will not be licensed for a number of years even if the trials are successful.

References

Based on global disease burden estimates, rotavirus is estimated to cause 527,000 (475,000 to 580,000) deaths among children less than 5 years of age. Although all countries are affected by rotavirus, the burden of deaths is greatest in developing countries. For example, in India, it is estimated that 122,270 die each year as a result of rotavirus. Previous rotavirus surveillance studies in Asia and other regions note that rotavirus accounts for ~50% of diarrheal hospitalizations among children less than 5 years of age. At present, two rotavirus vaccines are widely available and have been pre-qualified by the World Health Organization. Both vaccines (Rotarix and RotaTeq) are live-attenuated vaccines that are orally administered. Rotarix is licensed in a two-dose schedule and RotaTeq is licensed in a three-dose schedule. Both oral rotavirus vaccines can be given along with other routine infant immunizations. To date, these vaccines have shown efficacy against severe diarrhea in large-scale, multi-country, randomized controlled trials. Additional data on the clinical effectiveness and safety of these vaccines are expected within the next few years based on the uptake of these new vaccines in both developed and developing countries. As rotavirus vaccines are introduced into new populations, surveillance for laboratory-confirmed rotavirus diarrhea as well as monitoring for changes in circulating strains of rotavirus will remain an important public health activity for all countries. With new-generation rotavirus vaccines, the majority of deaths due to rotavirus are now vaccine-preventable. In addition, introduction of new rotavirus vaccines is highly likely to result in major reductions of rotavirus-associated hospitalizations in developed countries. The development and widespread introduction of safe and effective rotavirus vaccines into routine immunization programs will be a major public health achievement in the early 21st century.

Rotavirus vaccines
Paul Kilgore
International Vaccine Institute