Paediatric Focus

Volume 2 No 1 February 2011

Sponsored in the interests of continuing medical education by Pfizer

Editorial

Editor
Professor Robin Green
Professor and Head
Department of Paediatrics
and Child Health,
University of Pretoria

Let me start this editorial with a belated 'Happy New Year'. May this year bring forth all those dreams and ambitions and allow your goals to be met.

I want to use this column to continue my journey through the concept of rational use of antibiotics to limit the problem of emerging resistance of micro-organisms. I want to tackle the issue of unnecessary hospitalisation of children for illnesses that could just as easily and effectively be managed at home. Apart from incurring unnecessary cost, the risk of hospitalisation of children, is that of subjecting a child to the possibility of a hospital-acquired infection. This is a real possibility today.

A recent review has suggested that the problem is more common than realised.[1] Both developed and under-developed countries face the burden of healthcare-associated (hospital-acquired) infections. In a World Health Organization (WHO) cooperative study (55 hospitals in 14 countries), almost 9% of hospitalised patients had nosocomial infections.[1] That is nearly one in ten kids admitted are worse off because of an illness, we as doctors, subject them too.

Healthcare-associated infections result in many sequelae including increased length of stay, morbidity, mortality and increased healthcare costs. In 2002, an estimated 1.7 million healthcare-associated infections occurred in the United States, resulting in 99,000 deaths.[1] In 2009, the CDC estimated that the overall annual direct medical costs of healthcare-associated infections ranged from $28-45 billion.[1]

Bloodstream infections, followed by pneumonia and urinary tract infections are the most common healthcare-associated infections in children.[1] Among children, infants, extremely low birth weight (≤ 1000 g) neonates and children in either the PICU or NICU have higher rates of healthcare-associated infections.[1]

So what can we do. Well without sounding contrite, avoiding admission of children to hospital who don't need to be there, is the obvious answer. Most Guidelines for managing childhood illnesses have a table of who needs admission and under what circumstances. In private practice it seems sometimes easier to admit rather than chance treatment at home. However I think it is time we looked at this issue more carefully, especially in light of the dilemma today of causing greater harm. Ethical principles tell us to avoid doing harm and I certainly believe that a decision to admit a child must now be balanced for risk. I would like to remind you of some of the Guideline recommendations for admission of children with respiratory tract diseases. Table 1 is the recommendation for Community Acquired Pneumonia and Table 2 is that for Bronchiolitis. In essence both recommend admission if a child is hypoxic and requires oxygen. Requirement for an antibiotic is not a reason for admission. Most antibiotics can be given orally and at home.

Table 1. Indications for admission to hospital – children with CAP.[2]

- All children < 2 months old
- When older than 2 months with:
  - Impaired level consciousness
  - Inability to drink/eat
  - Cyanosis
  - Grunting
  - Severe chest-wall indrawing
  - Oxygen saturation < 90%
  - Severe malnutrition
  - Poor social circumstances
  - Clinical deterioration on home therapy

Table 2. Indications for hospitalisation of an infant with bronchiolitis.[3]

- Oxygen saturation <90% (inland) or 92% (coast)
- Severe respiratory distress (cyanosis, grunting, or lower chest wall recession)
- Poor feeding
- Apnoea
- Premature infants with associated risk factors
- Underlying medical condition (congenital heart disease, chronic lung disease, Down syndrome) or risk factor for severe disease
- Severe malnutrition
- Family unable to provide appropriate care

I have often heard it said that parents want an antibiotic and preferably a systemic antibiotic. This is a fallacy. Parents want to know what is going on and the few minutes taken to educate parents can be used instead of writing the admission documents or prescription for an antibiotic.

Again let me take you through the articles in this issue. We have for you a wonderful review by Marta Nunes and Shabir Madhi on the impact of pneumococcal disease on HIV infection and in turn the impact of pneumococcal vaccines on HIV-infected children.

Theunis Avenant takes us through a new concept - Antibiotic Stewardship - and what we can do to limit antimicrobial resistance. Elsabe Klinck, a well-known expert in medical and legal issues, highlights the need for informed consent. Finally another congress feedback report. Refiloe Masekela has penned her impressions of Barcelona and some of the paediatric session at the ERS in 2010.

I wish you a great read and a prosperous 2011.

References:

1. Mirza A. Hospital-acquired infections. eMedicine Specialities. http://emedicine.medscape.com/article/967022-overview.
2. Zar HJ, Jeena P, Argent A, Gie R, Madhi SA. Diagnosis and management of community-acquired pneumonia in childhood - South African Thoracic Society Guidelines. S Afr Med J 2005;95(12 Pt 2):977-81.
3. Green RJ, Zar HJ, Jeena PM, Madhi SA, Lewis H. Guideline for the diagnosis, management and prevention of bronchiolitis in South Africa. S Afr Med J 2010;100:320-325.

jeanetteverster photography

Cover photo: "Arnan"
by Jeanette Verster Photography
www.jeanetteverster.com

Sponsor: Pfizer
Editor: Professor R J Green
Production Editors: Ann Lake, Helen Gonçalves
Design: Jane Gouveia
Queries: Ann Lake Publications 011 802 8847
Website: www.annlakepublications.co.za
Email: lakeann@mweb.co.za

2011 Congresses

Congress	Location	Date	Contact/URL
European Paediatric Orthopaediatric Society 30th Annual Meeting 2011 (EPOS 2011)	MCH Messe Basel, Basel, Germany	6 - 9 April	www.epos2011.org/epos2011/home.html
ASEAN Paediatric Congress 2011, (APC 2011)	Suntec Singapore International Convention Centre, Singapore	14 - 17 April	www.apc2011.com.sg/
ECCMID: European Society of Clinical Microbiology and Infectious Diseases	Milan Italy	7-10 May	www.eccmid-icc2011.org/
European Society for Paediatric Gastroenterology, Hepatology and Nutrition 44th Annual Meeting 2011 (ESPGHAN 2011)	Hilton Sorrento Palace Hotel, Via, Italy	25 - 28 May	www.espghan2011.org/home.aspx
ESPID: European Society for Paediatric Infectious Diseases	The Hague World Forum, The Hague, The Netherlands	7-11 June	www2.kenes.com/espid2011/Pages/Home.aspx
5th Europaediatrics Congress 2011	Austria Centre, Vienna, Austria	23 - 26 June	www.europaediatrics2011.org/
ICAAC: Interscience Conference on Antimicrobial Agents and Chemotherapy	Chicago, Illinois, USA	17-20 September	www.icaac.org/
European Respiratory Society Annual Congress 2011	Amsterdam, Netherlands	24 - 28 September	www.erscongress2011.org/
51st Annual Meeting of the European Society for Paediatric Research 2011 (ESPR 2011)	The Sage, Gateshead, Newcastle, United Kingdom	14 - 17 October	www2.kenes.com/espr2011/Pages/Home.aspx
WSPID: World Society for Paediatric Infectious Diseases	Melbourne Convention Exhibition Centre, Melbourne, Australia	16-19 November	www.wspid.com/home.asp

CPD Accreditation

Doctors can acquire CPD points with this newsletter by visiting www.paediatrician.co.za, www.mycpd.co.za, www.pandasa.co.za or www.criticalcare.org.za and completing an online form of 15 questions. Doctors whose articles are published in this newsletter will also automatically be awarded CPD points. Accreditation is available only for a limited time on the site. Should you have any queries regarding the accreditation, please contact E2 Solutions at: 011 888 9620 or 011 340 9100 or gertrude@e2.co.za

HIV and Pneumococcal Disease

Dr Marta C. Nunes, PhD and Prof Shabir A. Madhi,
Medical Research Council: Respiratory and Meningeal Pathogens Research Unit and Department of Science and Technology/National Resarch Foundation: Vaccine Preventable Diseases, University of the Witwatersrand

The incidence of invasive pneumococcal disease is greatest among children younger than 5 years of age, the elderly and other immunocompromised groups such as those with HIV and sickle-cell disease. Pneumococcal conjugate vaccines (PCV) have been licensed in several countries to prevent pneumococcal disease including meningitis, sepsis, pneumonia and acute otitis media. The burden of pneumococcal disease has been aggravated by the HIV-epidemic. In South Africa, the prevalence of HIV in children is less than 5%, however this small section of the community contribute to 60-70% of all invasive pneumococcal disease in children under 5 years of age.

Consequently, HIV-infected children are a high-risk group who need to be adequately targeted for the prevention of pneumococcal disease in settings such as South Africa. This article will briefly review aspects of the burden of pneumococcal disease in these children and the prevention thereof with pneumococcal conjugate vaccines.

Streptococcus pneumoniae and HIV-infection

Streptococcus pneumoniae (the pneumococcus) is a major cause of human disease ranging from mild syndromes like otitis media and common upper respiratory tract infections, to severe invasive diseases. Invasive pneumococcal disease (IPD) includes bloodstream infections, bacteraemic pneumonia and meningitis. The WHO estimates that child deaths caused by pneumococcus range from 700,000 to 1 million every year worldwide.[1] Currently it is considered that pneumococcus is the most common cause of vaccine-preventable death in children aged less than 5 years.[2] Pneumonia, especially pneumococcal pneumonia, is one of the major causes of childhood mortality in developing countries, and of adult mortality worldwide.[3] Pneumococci are asymptomatic colonisers of the human nasopharynx and upper respiratory tract, their prevalence of colonisation decreases with the age of the host.[4] It is accepted that nasopharyngeal and/or oropharyngeal colonisation by invasive pneumococcal serotypes precedes pneumococcal disease.[4,5] The existence of 92 immunologically distinct serotypes, differing in the chemical composition of the respective polysaccharide capsule complicates simple epidemiological descriptions. In general, the variation in invasiveness among strains was associated more with the identity of the capsular serotype, rather than with a specific genotype.[6]

Human immunodeficiency virus (HIV) infection, with or without progression to acquired immunodeficiency syndrome (AIDS), significantly increases the risk of invasive disease due to pneumococcus.[7-9] HIV-infected persons are 10 to 324 times more susceptible to pneumococcal infections than the general population and recurrent episodes are more common (for review see reference #10). Furthermore, serious bacterial infections occur throughout all stages of HIV disease.[7] The increased susceptibility of HIV-infected individuals to pneumococcal disease in part relates to impairment of both cell-mediated and humoral arms of the immune system. Other mechanisms such as decreased levels of secretory IgA, reduced IgA-dependent and complement-independent phagocystosis of bacteria by mononuclear cells and lower levels of IgG2 causing deficient response to polysaccharide stimulation, are also defective during HIV infection.[11] Another factor might be an increased rate or density of pneumococcal colonisation in HIV-infected individuals.[12,13] HIV-infected individuals are more likely to be persistent pneumococcal carriers than non-infected controls.[13,14] Several studies also report that HIV-infected adults tend to be colonised by pneumococcal serotypes more commonly colonising children and/or serotypes that more frequently show resistance to penicillin and other antibiotics.[15,16]

IPD burden in HIV-infected children

Immaturity of the immune system to adequately responding to polysaccharide antigens during the first two years of life results in enhanced susceptibility to bacterial infections by encapsulated bacteria during this period. This risk of developing IPD is ongoing beyond two years of age in HIV-infected children because of HIV-induced T-cell and B-cell dysfunction.[17] In a recent report on the global estimates of morbidity and mortality from diseases caused by peumococcus, O'Brien and colleagues estimated that 91,300 of the 826,000 childhood deaths occurring from pneumococcal disease in 2000 occurred in HIV-infected children.[18]

Different studies from the United States and Africa, at the time of limited or no antiretroviral treatment of HIV-infected children, reported that the incidence of IPD in HIV-infected children ranged between 183 and 18,500 episodes per 100,000 person years. This corresponded to a 9- to 43-fold increased risk of IPD in HIV-infected compared with HIV-uninfected children.[9,19, 20] In addition HIV-infected infants,had an 8-fold greater risk of recurrent episodes of IPD.[21]

Case-fatality rates from IPD among HIV-infected and HIV-uninfected children were reported to be fairly similar, ranging from 0 to 23% and 0 to 15%, respectively.[9,19,22,23] However mortality in HIV-infected children with advanced HIV disease was reported to be higher than that in children with moderate AIDS.[9] One study, prior to the use of H. influenzae type b vaccine in South Africa, reported that Streptococcus pneumoniae was the most common cause of meningitis in HIV-infected children, compared to HIV-uninfected children, among whom H. influenza type b was the most common pathogen.[22]

Effect of vaccination

The paediatric serogroups (serogroups: 6,9,14,19,23) are more prevalent in HIV-infected children than HIV-uninfected children.[9] Regional studies performed before the licensing of the pneumococcal conjugate vaccines (PCV) into the childhood immunisation programme showed that in the United States, 85 to 93% of invasive isolates from HIV-infected children were included in the 7-valent PCV.[19] A vaccine which in addition to the serotypes included in a 7-valent formulation of PCV (i.e 4, 6B, 9V, 14, 18C, 19F and 23F) also includes serotypes 1 and 5 could potentially provide protection against 83 to 91% of serotypes causing invasive disease among HIV-infected children in South Africa.[9,24]

A clinical PCV efficacy trial in South Africa measured vaccine efficacy in HIV-infected children in the absence of antiretroviral therapy.[24] Overall, the vaccine provided a 65% protection against vaccine-serotype invasive disease in HIV-infected children. Although this point estimate of efficacy was lower than that achieved in HIV-uninfected children (83%), vaccination of HIV-infected children nevertheless prevented an 18-fold greater

burden of IPD than in HIV-uninfected children. PCV immunisation was also associated with a 13% reduction in pneumonia and a 6% reduction in mortality in HIV-infected children but these reductions were nonsignificant.

The overall burden of all-cause pneumonia prevented in HIV-infected children was 9-fold greater than that prevented in HIV-uninfected children. In HIV-uninfected children a significant 20% reduction in pneumonia was observed.[24] A five-year follow-up study reported a greater decline in the vaccine efficacy in HIV-infected children in the absence of antiretroviral treatment, for vaccine-serotype IPD (39%) compared with HIV-uninfected children (78%).[25] Furthermore a greater decay in antibody concentration was detected in the follow-up study in HIV-infected compared to HIV-uninfected children and the immune response to a booster dose of vaccine was lower in HIV-infected infants.[26] A more recent study has however reported that the quantitative and qualitative antibody responses to PCV are similar in HIV-infected infants on antiretroviral treatment compared to HIV-uninfected children.[27] This indicates that vaccine efficacy will be much improved and possibly more durable in HIV-infected children on antiretroviral treatment.

Impact of HAART on pneumococcal disease

The introduction of highly active antiretroviral therapy (HAART) has substantially improved the prognosis of HIV-infected patients. Highly active antiretroviral therapy has changed the history of HIV infection, with a noteworthy decline in the incidence of different HIV-related opportunistic infections as well as the overall mortality even before total immune reconstitution.[28, 29] Immune reconstitution involves a slow and gradual process of recovery of naive and memory cells. This is considered to occur after 12-24 months of effective antiretroviral therapy. The decreased risk of opportunistic infections has been associated with an increase in the CD4-T lymphocyte count following initiation of HAART.[30]

Potent antiretroviral therapy might improve immunological status enough to provide non-specific protection against pneumococcal infections. In industrialised countries, epidemiological studies in children and adults have identified a reduction in the incidence of pneumococcal infections,[31] invasive pneumococcal disease[32-34] and substantial reduction in hospital admissions for pneumonia[35] with the use of antiretroviral therapy. In particular a retrospective cohort study enrolling 260 HIV-infected children and adolescents in the United States, which involved 23 episodes of IPD, predominantly bacteremia without a focus, over a 17-year period suggested that the use of HAART was associated with an 84% reduction in the burden of IPD in HIV-infected children.[34] Even though this report did not include a comparator group of HIV-uninfected children, to exclude temporal changes in the burden of IPD as a possible reason for the decline observed in their cohort, adult studies have reported that after introduction of HAART, although decline in IPD rates were observed, the burden of IPD among HIV-infected individuals still remained substantially higher than among uninfected individuals.[33,36]

A recent report on the trends of incidence of IPD in South African children revealed an inverse temporal association between HAART coverage and the burden of IPD in HIV-infected children.[37] After HAART introduction in mid-2004 the burden of IPD decreased by 50.8% and the incidence of IPD-related mortality declined by 65.2% from 2003 to 2008 in HIV-infected children less than 18 years old. This decline was evident for pneumococcal bacteremia, pneumococcal pneumonia and pneumococcal meningitis. In addition, similar reductions were observed for serotypes included in the 7-valent PCV and non-vaccine serotypes. Nevertheless the burden of IPD remained unchanged in HIV-uninfected children over the study period. Despite the reduction of IPD in HIV-infected children over time, the risk of IPD remained 42-fold greater in HIV-infected than in HIV-uninfected children. This risk was, however, less than the 97-fold increased risk observed in HIV-infected children before HAART rollout.[37] In a setting with high HIV prevalence improved access to HAART and immunisation with PCV is essential.

References:

1. Pneumococcal conjugate vaccine for childhood immunisation--WHO position paper. Wkly Epidemiol Rec 2007;82(12):93-104.
2. CDC. Invasive pneumococcal disease in children 5 years after conjugate vaccine introduction-eight states, 1998-2005. MMWR 2008;57(06):144-8.
3. Williams BG, Gouws E, Boschi-Pinto C, Bryce J, Dye C. Estimates of world-wide distribution of child deaths from acute respiratory infections. Lancet Infect Dis 2002;2(1):25-32.
4. Gray BM, Converse GM, 3rd, Dillon HC, Jr. Epidemiologic studies of Streptococcus pneumoniae in infants: acquisition, carriage, and infection during the first 24 months of life. J Infect Dis 1980;142(6):923-33.
5. Bogaert D, De Groot R, Hermans PW. Streptococcus pneumoniae colonisation: the key to pneumococcal disease. Lancet Infect Dis 2004;4(3):144-54.
6. Brueggemann AB, Griffiths DT, Meats E, Peto T, Crook DW, Spratt BG. Clonal relationships between invasive and carriage Streptococcus pneumoniae and serotype- and clone-specific differences in invasive disease potential. J Infect Dis 2003;187(9):1424-32.
7. Gilks CF, Ojoo SA, Ojoo JC, Brindle RJ, Paul J, Batchelor BI, et al. Invasive pneumococcal disease in a cohort of predominantly HIV-1 infected female sex-workers in Nairobi, Kenya. Lancet 1996 16;347(9003):718-23.
8. Jordano Q, Falco V, Almirante B, Planes AM, del Valle O, Ribera E, et al. Invasive pneumococcal disease in patients infected with HIV: still a threat in the era of highly active antiretroviral therapy. Clin Infect Dis 2004;38(11):1623-8.
9. Madhi SA, Petersen K, Madhi A, Wasas A, Klugman KP. Impact of human immunodeficiency virus type 1 on the disease spectrum of Streptococcus pneumoniae in South African children. Pediatr Infect Dis J 2000;19(12):1141-7.
10. Bliss SJ, O'Brien KL, Janoff EN, Cotton MF, Musoke P, Coovadia H, et al. The evidence for using conjugate vaccines to protect HIV-infected children against pneumococcal disease. Lancet Infect Dis 2008;8(1):67-80.
11. Janoff EN, Breiman RF, Daley CL, Hopewell PC. Pneumococcal disease during HIV infection. Epidemiologic, clinical, and immunologic perspectives. Ann Intern Med 1992;117(4):314-24.
12. Cardoso VC, Cervi MC, Cintra OA, Salathiel AS, Gomes AC. Nasopharyngeal colonisation with Streptococcus pneumoniae in children infected with human immunodeficiency virus. J Pediatr (Rio J) 2006;82(1):51-7.
13. Gill CJ, Mwanakasale V, Fox MP, Chilengi R, Tembo M, Nsofwa M, et al. Impact of human immunodeficiency virus infection on Streptococcus pneumoniae colonisation and seroepidemiology among Zambian women. J Infect Dis 2008;197(7):1000-5.
14. Rodriguez-Barradas MC, Tharapel RA, Groover JE, Giron KP, Lacke CE, Houston ED, et al. Colonisation by Streptococcus pneumoniae among human immunodeficiency virus-infected adults: prevalence of antibiotic resistance, impact of immunisation, and characterization by polymerase chain reaction with BOX primers of isolates from persistent S. pneumoniae carriers. J Infect Dis 1997;175(3):590-7.
15. Crewe-Brown HH, Karstaedt AS, Saunders GL, Khoosal M, Jones N, Wasas A, et al. Streptococcus pneumoniae blood culture isolates from patients with and without human immunodeficiency virus infection: alterations in penicillin susceptibilities and in serogroups or serotypes. Clin Infect Dis 1997;25(5):1165-72.
16. Nicoletti C, Brandileone MC, Guerra ML, Levin AS. Prevalence, serotypes, and risk factors for pneumococcal carriage among HIV-infected adults. Diagn Microbiol Infect Dis 2007;57(3):259-65.
17. Kapogiannis BG, Soe MM, Nesheim SR, Sullivan KM, Abrams E, Farley J, et al. Trends in bacteremia in the pre- and post-highly active antiretroviral therapy era among HIV-infected children in the US Perinatal AIDS Collaborative Transmission Study (1986-2004). Pediatrics 2008;121(5):e1229-39.
18. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet 2009 12;374(9693):893-902.
19. Andiman WA, Mezger J, Shapiro E. Invasive bacterial infections in children born to women infected with human immunodeficiency virus type 1. J Pediatr 1994;124(6):846-52.
20. Jones N, Huebner R, Khoosal M, Crewe-Brown H, Klugman K. The impact of HIV on Streptococcus pneumoniae bacteraemia in a South African population. Aids 1998;12(16):2177-84.
21. Gesner M, Desiderio D, Kim M, Kaul A, Lawrence R, Chandwani S, et al. Streptococcus pneumoniae in human immunodeficiency virus type 1-infected children. Pediatr Infect Dis J 1994 Aug;13(8):697-703.
22. Madhi SA, Madhi A, Petersen K, Khoosal M, Klugman KP. Impact of human immunodeficiency virus type 1 infection on the epidemiology and outcome of bacterial meningitis in South African children. Int J Infect Dis 2001;5(3):119-25.
23. McGregor D, Barton M, Thomas S, Christie CD. Invasive pneumococcal disease in Jamaican children. Ann Trop Paediatr 2004 Mar;24(1):33-40.
24. Klugman KP, Madhi SA, Huebner RE, Kohberger R, Mbelle N, Pierce N. A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. N Engl J Med 2003;349(14):1341-8.
25. Madhi SA, Adrian P, Kuwanda L, Jassat W, Jones S, Little T, et al. Long-term immunogenicity and efficacy of a 9-valent conjugate pneumococcal vaccine in human immunodeficient virus infected and non-infected children in the absence of a booster dose of vaccine. Vaccine 2007;25(13):2451-7.
26. Madhi SA, Klugman KP, Kuwanda L, Cutland C, Kayhty H, Adrian P. Quantitative and qualitative anamnestic immune responses to pneumococcal conjugate vaccine in HIV-infected and HIV-uninfected children 5 years after vaccination. J Infect Dis 2009;199(8):1168-76.
27. Madhi SA, Adrian P, Cotton MF, McIntyre JA, Jean-Philippe P, Meadows S, et al. Effect of HIV infection status and anti-retroviral treatment on quantitative and qualitative antibody responses to pneumococcal conjugate vaccine in infants. J Infect Dis ;202(3):355-61.
28. Gona P, Van Dyke RB, Williams PL, Dankner WM, Chernoff MC, Nachman SA, et al. Incidence of opportunistic and other infections in HIV-infected children in the HAART era. Jama 2006;296(3):292-300.
29. Palella FJ, Jr., Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med 1998;338(13):853-60.
30. Pakker NG, Kroon ED, Roos MT, Otto SA, Hall D, Wit FW, et al. Immune restoration does not invariably occur following long-term HIV-1 suppression during antiretroviral therapy. INCAS Study Group. Aids 1999;13(2):203-12.
31. Dworkin MS, Ward JW, Hanson DL, Jones JL, Kaplan JE. Pneumococcal disease among human immunodeficiency virus-infected persons: incidence, risk factors, and impact of vaccination. Clin Infect Dis 2001;32(5):794-800.
32. Grau I, Pallares R, Tubau F, Schulze MH, Llopis F, Podzamczer D, et al. Epidemiologic changes in bacteremic pneumococcal disease in patients with human immunodeficiency virus in the era of highly active antiretroviral therapy. Arch Intern Med 2005;165(13):1533-40.
33. Heffernan RT, Barrett NL, Gallagher KM, Hadler JL, Harrison LH, Reingold AL, et al. Declining incidence of invasive Streptococcus pneumoniae infections among persons with AIDS in an era of highly active antiretroviral therapy, 1995-2000. J Infect Dis 2005;191(12):2038-45.
34. Steenhoff AP, Wood SM, Rutstein RM, Wahl A, McGowan KL, Shah SS. Invasive pneumococcal disease among human immunodeficiency virus-infected children, 1989-2006. Pediatr Infect Dis J 2008;27(10):886-91.
35. Viani RM, Araneta MR, Deville JG, Spector SA. Decrease in hospitalization and mortality rates among children with perinatally acquired HIV type 1 infection receiving highly active antiretroviral therapy. Clin Infect Dis 2004;39(5):725-31.
36. Nuorti JP, Butler JC, Gelling L, Kool JL, Reingold AL, Vugia DJ. Epidemiologic relation between HIV and invasive pneumococcal disease in San Francisco County, California. Ann Intern Med 2000;132(3):182-90.
37. Nunes MC, von Gottberg A, de Gouveia L, Cohen C, Moore DP, Klugman KP, et al. The impact of antiretroviral treatment on the burden of invasive pneumococcal disease in South African children: a time series analysis. AIDS 2010.

Antimicrobial Stewardship

Prof Theunis Avenant, Department of Paediatrics
Kalafong Hospital and University of Pretoria

The increasing emergence of multi-resistant pathogens, as illustrated by the widely reported pan-drug-resistant organisms or "superbugs", may see us return to an era before antibiotics were available. Inappropriate antibiotic use has largely contributed to this problem.

It is unlikely that we will see any major progress in the development of new classes of antibiotics in the next decade. When this eventually happens, resistance will almost certainly appear shortly after the introduction of such new classes of drugs. We thus have to make sure that the currently available antimicrobials are used in the best way. Healthcare workers will not only have to revisit the way in which antibiotics are used, but will actively have to change ingrained habits.

Two strategies are needed to prevent and control antimicrobial resistance:

- Infection control measures
- The optimisation of antibiotic use.

The latter is often referred to as "antibiotic stewardship".

The term "stewardship" is used widely and equates to the assumption of responsibility for something. Antibiotic stewardship aims at ensuring the proper use of antibiotics to provide the best patient outcomes, lessening the risk of adverse effects (including antibiotic resistance) and promoting cost effectiveness.

Institutional Antibiotic Stewardship

Programmes

The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America have published comprehensive guidelines for developing institutional programmes to enhance antibiotic stewardship.[1] These guidelines focus on hospital practice, as it is not clear which interventions will be responsible for improvement in a clinic setting.

Two core strategies are proposed:

1. Prospective audit with intervention and feedback
2. Formulary restriction and pre-authorisation.

These core strategies should be supplemented by additional elements listed below, based on local practice patterns and resources.

Drug resistant organisms are currently widely recognised and highlighted as a major threat to our existence. This opportunity should be used to garner wide support for the concept of antimicrobial stewardship.

Core strategies

1. Prospective audit with intervention and feedback.
   Audit of antibiotic use followed by education and suggestions on antibiotic use, has been shown in several studies, to reduce the inappropriate use of antibiotics, resulting in decreased antimicrobial expenditure. A decrease in the rate of infection with multidrug resistant organisms has also been demonstrated. Unfortunately this strategy requires a large personnel commitment.

2. Formulary restriction and pre-authorisation.
   The most effective method of controlling antibiotic use is antimicrobial restriction. This can be achieved in one of two ways. The first is limitation through a hospital formulary. The second method requires pre-authorisation and motivation. These measures may lead to large reductions in antibiotic use and cost. In studies the outcomes of these policies unfortunately have not shown consistent results. It is important to make sure that decisions on restriction are made by appropriate management teams. A ban on the use of specific agents may also lead to it being replaced by a different, but not necessarily harmless, antibiotic. An example is the replacement of cephalosporin use with imipenem use in a study by Rahal.[2] The result was a 69% increase in the incidence of imipenem-resistant *Pseudomonas aeruginosa* infections.

Perceived loss of autonomy by colleagues may lead this strategy to fail. Authorisation and discussion of the choice of antibiotics with experts, nevertheless clearly has a beneficial effect.

Additional elements

Education

Education remains one of the essential parts of any programme aimed at influencing prescribing habits and increasing acceptance of stewardship strategies. Unfortunately, unless this is accompanied by active interventions such as order forms and prospective audit, it is not really effective in changing prescribing practices of doctors.

Clinical practice guidelines

A multitude of guidelines to improve patient care are produced nowadays. It is however not always easy to measure their impact. Local microbiology and resistance patterns should always be considered when developing guidelines. When implemented correctly they will lead to improved use of antibiotics and thus result in decreased cost and decreased development of resistance.

Antimicrobial cycling

The scheduled substitution of a specific antibiotic or antibiotic class for a period of time is called "cycling". The best known examples are the substitution of gentamicin with amikacin and the cycling of anti-pseudomonal drugs. It has however been shown that the reintroduction of the original drug leads to rapid re-emergence of resistance. There is currently insufficient evidence to recommend the use of antibiotic cycling as a means to prevent or reduce resistance. Further studies may give guidance on how this should be implemented, if at all.

Antimicrobial order forms

In several studies, the use of antibiotic order forms has lead to a decrease in pharmacy costs. The main drivers behind this seem to be the need to define the length of treatment and justifying the use or continued use of the drugs. Care must however be exercised that inappropriate discontinuation of therapy does not result from an automatic stop order, that is often a part of such a programme.

Combination therapy

Empirical broad spectrum therapy for the initial treatment of serious infections remains important in preventing inadequate cover and the subsequent increased mortality. However, in most cases, encountered in everyday hospital practice, the use of combination therapy is unnecessary. Little evidence exists to support combining antibiotics to prevent resistance. Exceptions are conditions such as HIV and tuberculosis where mutational resistance will develop when using single drug therapy.

Streamlining or de-escalation of therapy

As mentioned above, initial combination therapy may be necessary until the results of cultures are known. At this stage antimicrobial therapy should be de-escalated or streamlined to more targeted therapy. This will decrease antimicrobial exposure and contain cost.

Dose optimisation

Individual patient characteristics should be taken into account when optimising dosing. Other aspects that need attention are the causative organism, site of infection and pharmacodynamic and pharmacokinetic characteristics of the drug. In practice this translates to measures such as prolonged infusions of beta lactam antibiotics and extended interval dosing of aminoglycosides.

Parenteral to oral conversion

Most patients with serious infections will be treated with intravenous antibiotics on admission. As clinical improvement occurs a switch to oral antibiotics need to be considered. Advantages of a strategy like this are:

- Reduced length of hospital stay
- Reduced health care costs
- Decreased complications associated with intravenous access.

A study of children treated for lower respiratory tract infections showed a reduction of 52% in costs when a systematic plan of parenteral to oral conversion was followed.[3]

The use of newer antibiotics, such as linezolid, with increased oral bioavailability may aid in this strategy. Caution must however be exercised, as the development of antimicrobial resistance and increased antibiotic cost may cancel the positive effects of an early switch to oral antibiotics.

Efforts to establish antimicrobial stewardship programmes are likely to be futile without the support and collaboration of the hospital administration and medical staff leadership.

Antibiotic stewardship teams

Multidisciplinary teams are necessary to implement antibiotic stewardship in hospitals. They should include an infectious diseases physician/paediatrician, clinical pharmacist, clinical microbiologist and infection control specialist. Collaboration with the infection control- and therapeutics committee is essential.

The paucity of infectious disease specialists, infection control personnel and clinically trained pharmacists, which are often seen as major stumbling blocks in establishing stewardship teams, is not an insurmountable problem in our country due to the fact that most of our physicians and paediatricians are well experienced in the management of infectious diseases. Furthermore we have excellent group of microbiologists to aid us in this endeavour.

Efforts to establish antimicrobial stewardship programmes on the other hand are likely to be futile without the support and collaboration of the hospital administration and medical staff leadership. Administrative support should additionally be provided to track the use of antibiotics. Ongoing monitoring and reporting of antimicrobial resistance patterns to the team is vital.

As multidrug resistant organisms are not limited to either the public health- or private healthcare setting, close cooperation is necessary for antibiotic stewardship to succeed in the country as a whole. An initiative like the Best Care…Always! (BCA) campaign is already making a difference in highlighting the concept of antibiotic stewardship and coordinating efforts between different role players.

Conclusion

Drug resistant organisms are currently widely recognised and highlighted as a major threat to our existence. This opportunity should be used to garner wide support for the concept of antimicrobial stewardship.

Antibiotic stewardship programmes have been shown to decrease the use of antibiotics up to 36%.[4] Apart from reducing the development of resistance it may lead to a substantial savings to hospitals, both in drug costs and secondary expenses.

As hospitals are the main drivers of the development of drug resistant organisms, they carry the responsibility for proper stewardship. Commitment to implement stewardship programmes must come from the leading administrators, both in the public and private health care sectors.

Not making the best use of the currently available antimicrobials may see us enter a post-antibiotic era where bacteria again reign supreme.

References

1. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis 2007;15:159-77.
2. Rahal JJ, Urban C, Horn D, et al. Class restriction of cephalosporin use to control total cephalosporin resistance in nosocomial Klebsiella. JAMA 1998;280:1233-1237.
3. Al-Eidan FA, McElnay JC, Scott MG, et al. Sequential antimicrobial therapy: treatment of severe lower respiratory tract infections in children. J Antimicrob Chemother 1999;44(5):709-15.
4. Patel D, Lawson W, Guglielmo BJ. Antimicrobial stewardship programs: interventions and associated outcomes. Expert Rev Anti Infect Ther 2008;6(2):209-22.

The importance of informed consent in the light of recent legislative developments

Elsabe Klinck
Consultant, EK Consulting, Johannesburg

Introduction

Informed consent is often regarded as an "old" ethical rule. It has also become entrenched in South African law as part of the common law position. Informed consent has, however, obtained importance beyond it just being the "right thing" to do, as recent laws place more emphasis on the reasons why informed consent is a necessity in the provision of healthcare in South Africa. Two such laws are the Children's Act of 2005, and the 2008 Consumer Protection Act (CPA).

Laws and ethical rules previously known to healthcare professionals

The main legal provisions in relation to informed consent can be found in the National Health Act of 2003. It provides for -

- what should form part of the informed consent process;
- who should consent;
- what happens if a person cannot consent to treatment; and
- circumstances under which one can dispense with the requirement of informed consent.

Section 6 of the NHA requires of "every health care provider" to inform a patient of:

- His/her health status;
- The range of diagnostic procedures and treatment options "generally available" to the patient;
- The benefits, risks, costs and consequences generally associated with each option; and
- The patient's right to refuse health services and the implications of such a refusal.

Where more than one healthcare professional is involved in the provision of healthcare to a particular patient, all the healthcare professionals should ensure that the aspect(s) of the healthcare provision they are involved in, are dealt with in terms of the above provision. Where a healthcare facility, such as a hospital, takes care of the general nursing requirements relating to the patient, an anaesthetist would be involved in an operation and a surgeon in an operation, each is separately legally responsible for obtaining informed consent for the various aspects of (a) admittance into- and care in the hospital, (b) anaesthetics, and (c) the specific operation.

As far as the person's health status is concerned, the NHA recognise the principle of "therapeutic privilege", i.e. circumstances where it is not in the patient's best interest to disclose his/her health status. This provision should, however, be exercised only in limited types of circumstances, and after advice has been obtained from an ethics committee. It should also be noted that the Promotion of Access to Information Act of 2000 (PAIA) does not permit the withholding of information from a patient should the patient request such information. The PAIA allows for the patient, who is requesting information that might be detrimental to him/her, to nominate a healthcare professional to whom the sensitive information is to be disclosed, and the nominated healthcare professional shall then disclose the information to the patient.

The "benefits, risks and costs" of all "generally available" treatment options should be discussed with the patient. The more complex the patient's condition, the more detail may be required in this regard.

The "benefits, risks and costs" of all "generally available" treatment options should be discussed with the patient. The more complex the patient's condition, the more detail may be required in this regard. Under "costs", healthcare professionals should also address the issue of medical scheme cover, if the patient is a medical scheme patient. Attention should be given to the fact that the patient may face a co-payment, or even full payment to the health service providers.

Under "risks" it is generally understood that the commonly known risks relating to healthcare provision should be disclosed to, and accepted by, the patient, and then also any risk of life or limb, as well as the probability of such events occurring – the need for this is even higher in the light of the Consumer Protection Act (CPA) discussed below. Attention should be paid to "ordinary" effects of a particular treatment (e.g. disorientation, pain, etc) and complications that could occur.

There is no requirement that the consent be in writing, however, the more invasive and drastic the treatment, the more important written consent becomes. It is also advised that the patient receive a copy of the consent and all the information shared with him/her during the consent process.

Where a patient is unable to give consent, consent may be provided by –

- A person mandated by the user in writing to grant consent on his or her behalf; or
- A person authorised to give such consent in terms of any law (such as the Children's Act) or court order (such as the person appointed by the court as the curator of a mentally ill person).

If none of the above situations exist, consent can be given by the spouse or partner of the user or, in the absence of such spouse or partner, a parent, grandparent, an adult child or a brother or a sister of the patient, in the specific order as listed in the NHA.

In some cases a law may compel that treatment be provided, or testing be done (such as in the case of alleged rapists).

Treatment may also be provided without consent if a failure to treat the patient, or group of people which includes the patient, will result in a serious risk to public health, e.g. in highly infectious pandemics. In emergency situations treatment may also be provided without consent if any delay in the provision of the health service might result in "death or irreversible damage to his or her health", provided that the patient has not expressly, impliedly or by conduct refused that service.

Where persons other than the patient consents, such person is to be provided with the same information, and all the steps set out above, have to be followed, for such consent to be valid.

Latest laws on informed consent and related matters

Children's Act

Regulations to the Children's Act of 2005 were published in April 2010. These regulations brought into operation the consent of children to healthcare provision.

Children must have access to information relating to -

- Health promotion;
- The prevention and treatment of ill-health and disease, sexuality and reproduction;
- Their health status; and
- The causes and treatment of their health status.

The information must be relevant and in a format accessible to children with due consideration of the needs of disabled children. Moreover, the law requires that the child must always be consulted, even if s/he is not the one providing the consent in the end, bearing in mind the child's level of maturity.

Children from 12 years and older can independently consent to medical treatment. The child must, however, be of such maturity and mental capacity that s/he understands the risks, benefits, social and other implications of the medical treatment. No form is prescribed for this consent, but the medical practitioner should make a declaration to this effect on the consent form s/he uses and/or in his/her notes in the child's file. Although a child consented on his or her own, the child should also be informed of the costs of treatment, if any. As the parents or guardian are legally liable to carry such costs, the fact that a child has been to a healthcare practitioner may not be totally confidential. If the child is a dependent on a medical scheme, s/he should understand that statements are regularly sent to the principal member, and the parent or guardian may find out about the visit to a healthcare professional in that way.

The parent, guardian or care-giver of a child who is below the age of 12, or a child over the age of 12 and up to 18, and who is not sufficiently mature to understand the risks, benefits and other implications of the treatment, should still consent on behalf of the child. If the child is over the age of 12, she/he can also consent to the medical treatment of his or her own child.

Children of 12 and older, who are mature and show an understanding of the various risks, benefits and complications, can consent to an operation. The law does not define "surgical operation" and professional groupings may agree on where the line is to be drawn between "medical treatment" and "operations". But in consenting to an operation, a mature 12-year old must be assisted by a parent or guardian in doing so. A caregiver cannot consent and cannot assist children in cases of operations.

Children of 12 and older, who are mature and show an understanding of the various risks, benefits and complications, can consent to an operation.

There is a prescribed form which must be used in all cases of operations on children who are between 12 and 18. The form contains:

- Details of the child, the medical practitioner who will be performing the operation and the parent or guardian assisting the child.
- A declaration by the medical practitioner on the nature of the surgical problem, that the operation is the most suitable operation, the risks, benefits of- and alternatives to the surgery, and the social and other implications – all discussed with the child in a manner that the child understood.
- A declaration by the practitioner that the child has been given an opportunity to ask questions, and that the child is sufficiently mature and has the mental capacity to understand the benefits, risks and implications.

The child signs a section on the form for s/he declares that the consent has been given freely, and that s/he risks, benefits and consequences of the operation and the parent(s)/guardian signs that s/he/they have duly assisted the child in providing the consent to the operation.

There is a separate prescribed form for consent to operation by parent(s)/guardians of children below the age of 12, or where the child is above the age of 12, but is insufficiently mature. This is also the form to be used by child-parents (i.e. a child who is below the age of 18, but the parent of a child) and his/her parents, who have to assist such a child to provide the consent for the grandchild.

Consent to an HIV test can be provided by a child 12 years of age or older, irrespective of the child's maturity levels. If the child is under 12 years of age but is sufficiently mature enough to understand the risks, benefits, social and other implications of the test, then that child may consent by him or herself; or if the child is not mature enough then the parent, guardian or caregiver must provide assistance to the child to make a decision or provide the necessary consent on the child's behalf. The inclusion of caregivers means that children in homes and orphanages, for example, can be tested for HIV if they are below the age of 12 with the consent of the caregiver.

Contraceptives (other than condoms) may be provided to a child on request and without the consent of the parent or caregiver if:

- The child is at least 12 years old and
- Proper medical advice is given to the child
- A medical examination is carried out to determine whether any medical reasons prohibit the provision of a specific contraceptive.

It should be noted that "maturity" is not a legal requirement in accessing contraceptives – it may indeed often be the immature children at risk in these circumstances. A child obtaining condoms, contraceptives or contraceptive advice is entitled to confidentiality (as is indeed the case in all healthcare to which the child independently consents).

It should be noted that during the process of providing medical advice and a medical examination, a healthcare professional may come across facts that could lead him/her to believe that there may be abuse or neglect. In such cases, the provisions of section 101 and the regulations and forms on the mandatory reporting of abuse and neglect have to be followed.

It should be noted that none of the provisions mean that the parent or guardian may never know, or never be involved in the child seeking healthcare. If a child who can lawfully consent, is satisfied with a parent or guardian being present, s/he can accompany the child. But Practitioners should ask, and note, whether the child is comfortable with the parent, guardian or caregiver being present.

A girl 16 years of age or older may provide consent to virginity testing, and a prescribed form must be completed and kept by the practitioner for at least three years after the test. Each child must be tested individually and in private and all tests must be conducted in a hygienic manner. The law also requires the least invasive means of testing for virginity is used with due regard to the child's right to bodily integrity.

A boy of 16 may consent (on a prescribed form) to a circumcision, if duly assisted by a parent or guardian. Circumcisions for social or cultural purposes or religious purposes are recognised, and should be done by a practitioner familiar with the practices or from the religion concerned and who has been

Children from 12 years and older can independently consent to medical treatment, however, the child must be of such maturity and mental capacity that she/he understands the risks, benefits, social and other implications of the treatment.

properly trained to perform circumcisions. Religious circumcision of a male child under the age of 16 must be given by the parent or guardian of such a child, on the prescribed form. Boys below the age of 16 may also be circumcised for medical reasons. There has been some dispute as to what "medical reasons on the recommendation of a medical practitioner" constitute. For example, under the current government HIV Counselling and Testing (HCT) programme, circumcision is regarded as part of the HIV preventation programme. Could it then be regarded as "medical reasons" to circumcise a boy below the age of 16, in order to possibly prevent future HIV infection? In view of the boy's right to physical integrity and the other means, including deferral of the decision until the age of 16, the answer may be "no".

The CPA

The CPA comes into force on 1 April 2011. According to the CPA, all consumers (patients) have the right to receive all information, notices, forms (practice forms, informed consent forms, letters of demand, etc) and any other communication in plain language. The CPA refers to the use of vocabulary and sentences in this regard, and encourages the use of illustrations, examples and other aids to understanding.

The right to disclosure and information in the CPA entitles all patients to know the exact price of goods or services. The CPA requires the price to be indicated so that it could reasonably associated with specific services or goods. If a price estimate (quotation) is provided, the terms and conditions that could influence the end-price should be clearly set out.

To use physical force, coercion, undue influence, pressure, duress or harassment, unfair tactics, etc in trying to get a patient to accept services or treatment would violate the right to fair and honest dealings in the CPA. In medical ethics, informed consent is a freely provided and voluntary consent, i.e. it would be unlawful and unethical if based on any undue influence or pressure. The CPA requires of one to take cognisance of the consumer's (patient's) ignorance, illiteracy, disability, etc. This right places three legal duties on practitioners:

- Do not use exaggeration, innuendo or ambiguity.
- Do not fail to disclose a material fact relating to the patient's health status, treatment, etc.
- Correct any misunderstanding the patient may have in relation to, for example his/her condition, available treatments (e.g. on a supposed curative effect of supplements) or the need to follow certain health instructions.
- Consumers should also know when goods are substituted, but as far as medicines are concerned, this is in any event a requirement of the Medicines Act (that permits generic substitution only).

The right to fair and just terms and conditions in the CPA also influence informed consent practices. It requires that where the patient is about to accept a risk that is "unusual" (i.e. not a commonly understood risk), his/her attention must be drawn to that fact and s/he must sign an acknowledgement of that unusual risk. As far as medicines are concerned, this also means that one should not assume that the patient would read (or understand!) the package insert.

Waivers or indemnities should also be treated with circumspection, as it may be found to be unfair or unreasonable towards the consumer (patient).

Conclusion

It should be clear that informed consent processes have to become far more comprehensive than they were in the past. Healthcare professionals should give particular attention to the risks and warnings associated with healthcare service provision, and should make sure that the patient understands the risks associated with it. Care should also be taken that patient misperceptions be corrected.

Report of the European Respiratory Society Meeting Barcelona 2010 - a paediatrician's perspective.

Professor Refiloe Masekela
Paediatric Pulmonologist,
Steve Biko Academic Hospital, Pretoria

The European Respiratory Society (ERS) meeting 2010 took place in the Catalan city of Barcelona at the Gran Fira Barcelona. The highlight of this year's congress was celebrating The Year of the Lung and celebrating the 20th anniversary of the ERS. There was an excellent paediatric track in the meeting; which included a wide range of conditions from congenital anomalies, acquired lung diseases and infectious diseases. I have included here some of the highlights from the meeting.

Viral infections played a centre stage at the congress. Anne Malfroot presented her findings of a study on cystic fibrosis (CF) patients, where they found that out of 199 exacerbations, 64 were secondary to viral infections. The predominant viral pathogen in children under the age of 2 years was respiratory syncytial virus (RSV); whilst in those over the age of 18 years, Influenza virus predominated. 12.5% of exacerbations were due to Human Metapneumovirus. This later finding was slightly higher than the previously reported rate in the literature of <10%. These findings also were somewhat surprising as all the adult patients in their study had been vaccinated with the yearly influenza vaccine. This therefore calls in to question the immunogenecity of the influenza vaccine in CF patients. Keinerger et al presented data on CF and healthy control cells, showing that RSV/Rhinovirus (RV) infections stimulate all inflammatory cell lines, but that the IL-8 production in response to viral infections is less in CF cell lines when compared to healthy controls. This reduced IL-8 production was reflected in both bronchial and nasal cells. CF cells were also found to have deficient interferon beta production. This may explain why CF patients are at risk to have lower respiratory tract infections secondary to viral infections.

One of the hot topics sessions was titled 'bronchiolitis an old disease with many open questions'. The identified risk factors for severe bronchiolitis include bronchopulmonary dysplasia, environmental factors (including environmental tobacco smoke exposure), immunodeficiency (with prolonged viral shedding), age less than 6 weeks, chronic conditions (e.g. cardiac diseases) and male sex, were stressed. The role of the human Rhinovirus, which has more than 150 genotypes and 100 serotypes, was again cited as an important cause of bronchiolitis episodes in children. There was an interesting poster presentation by Schnibner from Australia on the use of high flow nasal cannula oxygen in children with bronchiolitis. They showed that giving high flow nasal oxygen at 2l/kg/min to children with bronchiolitis, reduced the need for intubation in these children from 37% to 7%. Subjects who responded with a reduction in heart rate as well as respiratory rate by 20% within 60 minutes had a clear benefit and required less intermittent positive pressure ventilation.

The beautiful Parc Guell by Gaudi was designed for Ernesto Guell is a popular tourist attraction in Barcelona.

Andrew Bush gave an interesting lecture on the early origins of COPD. The role of prenatal and early childhood factors which can result in COPD in later life were discussed. Exposure to nicotine in pregnancy can result in structural collagen distribution changes as well as affecting alveolar tethering. Some polymorphisms including ADAM 33 are also associated with abnormal foetal airway branching resulting in increased airways resistance. Epigenetics also plays an important role with a trans-generational increase in risk of asthma in children whose grandmothers have asthma. Bronchopulmonary dysplasia survivors also have increased air trapping and architectural abnormalities as adults. BPD survivors are known to have a markedly reduced FEV_1 as compared to controls at age 6-19 years placing them at higher risk for COPD. We were reminded once again that conditions acquired in the neonatal period can have an impact later on in life.

Felix Ratjen gave an overview of the highlights of cystic fibrosis research in 2010. He addressed the role of azithromycin in CF patients without pseudomonas infection/ colonisation. In a trial by Saiman et al, there was no difference between the placebo and active treatment group in terms of the primary endpoint of FEV_1. There was though, a 50% reduction in the number of exacerbations, as well as a 0.58kg increase in body weight, in the azithromycin treatment group (versus the placebo arm) at the end of 168 days. This new approach still requires further trials but offers hope for the future management of CF sufferers. With regards to eradication of *Pseudomonas aeruginosa*; the ELITE trial which compared inhaled tobramycin (TOBI) 28 versus 56 days found that one month treatment to be as good as two months. This has implications in reducing the medication burden for patients who are usually on multiple therapies. In terms of airway clearance, the osmotic agent mannitol has been found in a small study of 28 CF patients to cause an increase in FEV_1 in subjects. Further trials are needed to confirm these results.

CF patients are surviving longer in developed countries like Canada where the FEV_1 drops below 80% at an average age of 28 years. There is therefore a need for new biomarkers that can be used to detect early disease especially in young patients. These have to be reproducible and sensitive. The role of newer tests for use as outcome measures like the lung clearance index (LCI) and PET scanning were also discussed. In a study by Amin et al the role of LCI is detection of the treatment effect of hypertonic saline in mild CF subjects was explored and the LCI was found to show changes in treatment effect whilst no spirometric changes were detected. Amin et al also presented a study on PET/CT in children with CF with pulmonary exacerbations. The Suv_{max} and Suv_{mean} were measured before and after treatment. They found that the Suv_{max} was reduced post-treatment but that this was still higher than the baseline measurements.

This was a truly excellent congress. Hope to see you in Amsterdam 2011 for some cycling!

Broadest Coverage

of any Pneumococcal Conjugate Vaccine[1]

Pfizer Working together for a healthier world™

Pfizer Call Centre: 0860 Pfizer (734 937)
Website: www.Pfizer.co.za

Ref 1: Siber GR, Klugman KP, Mäkelä. Pneumococcal Vaccines: the impact of conjugate vaccine. Washington (DC): ASM Press; 2008. Chapter 10, Pneumococcal Serotype Epidemiology; p.143-146.

S2 **PREVENAR 13®. PREVENAR 13®** is a sterile solution of saccharides of the capsular antigen of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F individually conjugated to non-toxic diphtheria CRM_{197} protein and adsorbed on aluminium phosphate. Each 0,5 ml dose is formulated to contain 2.2 µg of each saccharide for serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F and 23F, and 4.4 µg of saccharide for serotype 6B, approximately 28 µg. Reg no.: 44/30.1/0002. **LICENCE HOLDER:** Pfizer Laboratories (Pty) Ltd. (Reg. No.:1954/00781/07). 85 Bute Lane , Sandton, 2196. Tel. No.: 0860 PFIZER (734937).

Please refer to detailed insert for full prescribing information.

75/PRV/12/10/PA