Festschrift for Professor Margaret Burgess AO

Compiled by: Julia ML Brotherton on behalf of the staff of the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases and the presenting speakers.

Abstract

In honour of the retirement of our director Margaret Burgess, National Centre for Immunisation Research and Surveillance (NCIRS) held a Festschrift on 5th to 6th February 2004. The themes of the event were Vaccines for the 21st Century and Congenital and Neonatal Infections. International guests attended the Festschrift, as well as over 180 colleagues and co-workers from across Australia. A summary of the presentations over these two fascinating days is provided herein. *Commun Dis Intell* 2004;28:349–355.

Day One Presentations

Session 1: The Children's Hospital at Westmead Grand Rounds
Chair: Professor Kim Oates

Congenital rubella in Australia 1941 to 2004: Professor Margaret Burgess

Margaret described the important role researchers in Australia, and especially those from the Royal Alexandra Hospital for Children, have played in the story of rubella in pregnancy. In 1941, Norman Gregg, an ophthalmic surgeon at the hospital, was the first to report an association between children born with cataracts and a history of rubella in the mother during the early part of the pregnancy. Later, Australian researchers Swan (1943) and Lancaster (1951) reported that deafness in children was associated with rubella infection during pregnancy. The long-term outlook of children with congenital rubella has also been explored by Australian researchers in three reviews (in 1966, 1991 and 2001) of Gregg's patients born in 1941. The 50 patients were found to have an increased risk of diabetes, thyroid disorders and early menopause compared with the Australian population of the same age, and several had glaucoma and hypertension. Despite this, they were well adjusted socially.

Margaret also highlighted the impact of vaccination in Australia. Rubella vaccine was licensed in Australia in 1970 and was first used in a targeted school-girl vaccination program. Now the vaccine is given to children at one and four years of age and immunity is high in children and women of child-bearing age. However there remains a cohort of young adult males who are still susceptible and Asian born pregnant women presently have a 5–10 times higher risk of being seronegative compared with Australian born women. Vaccination has led to a remarkable reduction in rubella, but two cases of congenital rubella in 2003 (the first locally acquired cases since 1997) remind us that we need to remain vigilant.

Rubella — the global picture: Professor Felicity Cutts

Professor Cutts began her presentation by discussing the global burden of rubella and congenital rubella syndrome (CRS). In 2001, 123 countries (57%) performed surveillance for rubella and 51 (24%) had a surveillance system in place for CRS. However surveillance, especially for CRS and during non-outbreak periods, is very insensitive, so serosurveys have been performed in some countries to obtain better estimates of the burden. Estimates of the prevalence of CRS from these serosurveys range from 0.7 (in parts of Europe) to 1.75 (in parts of the Americas) per 1,000 live births. The serosurveys also provided estimates of the level of vaccination coverage required in each country to achieve herd immunity (e.g. 85–91% in Ethiopia).

Rubella vaccination has been reported to be cost-effective in Latin American and Caribbean countries, as well as in developed countries. However, Professor Cutts cautioned that this does not mean infant vaccination should be introduced in all countries. Infant vaccination shifts the average age of infection upwards and may increase the risk of infection in women of child-bearing age (and the risk of CRS) so it should only be introduced if sufficient coverage can be achieved. The required level of coverage depends on the intensity of rubella transmission and is about 80 per cent in developed

* Full paper is available from the National Centre for Immunisation Research and Surveillance, The Children's Hospital at Westmead, Locked Bag 4001, Westmead NSW 2145.

countries. If the required level can not be reached with an infant program, then selective vaccination of adolescent and adult females will also reduce the risk of CRS, but will take longer to have an impact and will not affect the transmission of rubella. For rapid elimination of CRS, routine infant vaccination is supplemented by vaccination of susceptible adult women (e.g. post-partum vaccination). To eliminate rubella transmission, most industrialised countries now offer a second opportunity for rubella vaccination to school-aged children, while Latin America is pioneering the use of large-scale mass vaccination campaigns of adult men and women. For example, an outbreak of rubella that resulted in 46 documented cases of CRS (0.5/1,000 live births) occurred in Costa Rica in 2000, after almost 30 years of routine infant rubella vaccination. Following the mass campaign in which 95 per cent of men and women aged 15–39 years were vaccinated, the last case of rubella was reported in August 2001.

Vaccines in the 21st Century: Professor Stanley Plotkin

Emeritus Professor Stanley Plotkin reflected on the history of vaccination and outlined his perception of six revolutions in vaccine development. The first revolution described was the development of attenuated vaccines made in the laboratory: animal viruses as vaccines (vaccinia), physical attenuation (rabies, anthrax), and passage in animals or *in vitro* (yellow fever, bacille Calmette-Guerin.) The second revolution was the discovery that inactivated organisms or sub-units of organisms could function as vaccines, leading to vaccines based upon polysaccharide capsules, proteins or toxoids. After World War II, the development of vaccines through the passage of organisms in cell culture *in vitro*, produced the third revolution. The fourth revolution was the development of molecular biology, which has resulted in a new array of strategies for vaccine development starting from information on the microbial genome (DNA, cDNA, or RNA.) Examples of such strategies are recombinant protein production, prime boost using DNA and/or vectors and reverse genetics. The fifth revolution has been the development of methods to induce cell mediated immune responses, such as through the use of live microbes, live vectors, alphavirus replicons, DNA, lipopeptides and Th1 adjuvants. Professor Plotkin believes that the sixth revolution in vaccination will relate to the development of new strategies in vaccine delivery. Non-parenteral methods of vaccination being investigated include intranasal (influenza), aerosol (measles/rubella), transcutaneous, oral (e.g. transgenic plants) and rectal (sexually transmitted infections).

Professor Plotkin also provided updates on several vaccines in advanced states of development including live influenza, rotavirus, measles-mumps-rubella-varicella, meningococcal conjugate against groups A/C/W-135/Y, meningococcal group B outer membrane protein and human papillomavirus vaccines. Particular challenges and trends in vaccination in 2004 described by Professor Plotkin included the need for new combination paediatric and adult vaccines, the rise of adolescent vaccines, and in new vaccination targets such as for hospitalised patients, for pregnant women, against bioterrorism threats and against chronic infections. The main threats to vaccination in the 21st Century were identified as cost, supply, safety and anti-vaccinationism. Professor Plotkin reflected that we are in the golden age of vaccine development, in which it is feasible to produce any antigen we want for use in a vaccine, but that we currently lack sufficient knowledge of pathogenesis and immunology to choose the best antigens and methods of vaccination.

Session Two: The Australian Contribution to Vaccine Research
Chair: Professor Sir Gustav Nossal

Historical background: Professor Sir Gustav Nossal

Professor Sir Gustav Nossal outlined the history of vaccine development in Australia from World War I to the present. Over that period, a number of scientists working at notable institutions, such as the Commonwealth Serum Laboratories (CSL) and the Walter and Eliza Hall Institute (WEHI), made important achievements in vaccine technology and delivery. Early collaborations between CSL and WEHI, under their respective directors Penfold and Kellaway, resulted in Australia-wide availability of passive immunisation for snake and spider bites through the provision of antivenene. A strong collaboration on influenza work saw the popularisation and improvement of Goodpasture's technique for growing viruses in hen's eggs. In the middle of last century the Commonwealth Serum Laboratories were in charge of vaccine production. This included providing Salk vaccine (inactivated polio vaccine) for the nation and, working with Burnett during World War I, live attenuated intranasal influenza vaccine was given to 20,000 army recruits. Another major contribution of CSL was providing antiD for the active immunisation of Rhesus negative women.

Advances in animal vaccine development in Australia have been made by CSIRO's Animal Health Division, especially through the work of Lionel Bull e.g. bovine pleuropneumonia vaccine. Progress in the development of human vaccines advanced by scientists around Australia has included vaccines for cholera, tuberculosis, Q fever, human papillomavirus, *Helicobacter pylori* and malaria. These contributions will not go unrewarded in the ongoing effort to reduce the burden of these diseases.

Vaccine trials in Australia: Professor Terry Nolan

Professor Terry Nolan outlined the recent history of vaccine trials in Australia from the 1980s until the present. A range of governmental initiatives in the 1980s paved the way for increased trials and a broad range of vaccines were successfully trialed. Australia is an attractive site for industry sponsored trials because it is seen as good value economically, has a rigorous regulatory environment, accepted internationally, access to a large population in the Southern hemisphere with alternate seasonal cycles, good recruitment capabilities and high quality researchers. Recent threats to future trials were outlined, including complicated and lengthy ethics procedures, competitive recruitment between countries, and funding restrictions. The successful creation of the Indigenous trial network, although expensive to set up, is an excellent initiative with an exciting future. The road ahead promises new vaccines trialed by enthusiastic and dedicated researchers.

Collaborative Research Centre for Vaccine Technology: Professor Anne Kelso

The Collaborative Research Centre (CRC) for Vaccine Technology was established in 1993 with the aim of maximising the economic and social benefits of publicly funded vaccine research and design through collaboration between researchers, government and industry. In the past decade, the CRC has taken many novel ideas and transformed them into potential commercially successful products and along the way considerably enhanced the numbers of commercially aware PhD students and research managers in Australia. Highlighted concepts included new platform technologies to combine multiple T cell epitopes and methods to enhance immunogenicity. The CRC's vaccine targets include malaria (2 potential candidates), Epstein-Barr virus, cytomegalovirus (CMV) and Group A *Streptococcus* and a highly publicised animal immunocastration vaccine. Different pathways to protect and develop resulting CRC intellectual property were outlined including the creation of a start up company, VacTXPty Ltd. Finally, Professor Kelso noted that the CRC for Vaccine Technology will wind down in June 2006, leaving a lasting legacy of durable networks and will be replaced by the CRC for Immunological Principles.

The contribution of Professor Margaret Burgess: Professor Kim Oates, Associate Professor Peter Shaw, Dr Mary Bergin, Associate Professor Peter McIntyre

Professor Kim Oates summarised the early years of Professor Margaret Burgess' professional life. Margaret attended Fort Street Girls' High School, Sydney and was school captain in 1954. She completed her Bachelor degree in Medicine and Surgery in 1961 (University of Sydney), being awarded the Dagma Berne Prize for first place among women candidates and Distinction and first place in Surgery. She trained in Paediatrics and became a Fellow of the Royal Australasian College of Physicians in 1972. Between 1965 and 1984, she worked as a Research Fellow (1965–1970) at the Children's Medical Research Foundation, Royal Alexandra Hospital for Children, Sydney and then as a Norman Gregg Senior Research Fellow (1970–1984), also at the Children's Medical Research Foundation. She gained a MD in 1971 (University of Sydney). Her major work was on the epidemiology of congenital malformations and their relation to infection in pregnancy, particularly congenital rubella. Later on, her research focussed on vaccine preventable diseases. In the early 1970s her team of researchers carried out the first clinical trials of rubella vaccines in Australia.

Associate Professor Peter Shaw and Dr Mary Bergin then summarised Margaret's involvement with the Oncology Department at Royal Alexandra Hospital for Children (RHAC), Sydney. From 1972 until 1995, her work was shared between clinical work in the Oncology Department and research into vaccine preventable diseases. Margaret was appointed Senior Staff Physician at Royal Alexandra Hospital for Children in 1984. Her colleagues from Oncology remember her not only as a rigorous scientific researcher, but also as an accomplished clinician and an invaluable mentor. She contributed to a number of research projects, including the documentation of a high prevalence of growth failure and growth hormone deficiency in children who had been treated for acute lymphoblastic leukaemia, and the morbidity and mortality associated with varicella-zoster infection in the Oncology Unit.

In 1995, she became the Director of the Centre for Immunisation Research (CIR at the University of Sydney and RAHC). In 1997, under her leadership, the Centre was successful in securing the Commonwealth's tender to become the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS).

Associate Professor Peter McIntyre wrapped up the session with an impressive list of Margaret's achievements as Director of CIR/NCIRS. Early work by the Centre included the demonstration of the successful use of measles and mumps vaccines in Australian children aged as young as 12 months and the conduct of a very large hepatitis B serological study of 3,000 Sydney schoolchildren. Recent research has focused on barriers to immunisation uptake in Australia, the epidemiology of varicella-zoster, rotavirus, measles and pertussis, and trials of new vaccines including multivalent vaccines for children and pertussis vaccines for adults.

In 1998, Margaret became Professor of Paediatrics and Preventive Medicine at the University of Sydney. She was awarded an Order of Australia in 2003 for services to public health in Australia and overseas, particularly through the provision of policy advice to government and research into vaccine preventable diseases. She has been a member of various committees and working parties at the state, national and international levels such as the Australian Technical Advisory Group on Immunisation, Department of Health and Ageing and National Health and Medical Research Council and the Strategic Advisory Group of Experts to the Department of Vaccines and Biologicals, World Health Organization (WHO) (1999–2002). She is a patron of the NSW Deaf Children's Association. Margaret has authored at least 185 peer-reviewed articles and numerous books and book chapters. Peter finished with a poem particularly well suited to 'our' Margaret – 'To Margaret' by Charles Lamb (1775–1834).

To Margaret

Margaret, in happy hour
Christen'd from that humble flower
Which we a daisy call!
May thy pretty name-sake be
In all things a type of thee,
And image to thee in all.

Like *it* you show a modest face,
An unpretending native grace;
The tulip, and the pink,
The china and the damask rose,
And every flaunting flower that blows,
In the comparing shrink.

Of lowly fields you think no scorn,
Yet gayest gardens would adorn,
And grace, wherever set,
Home-seated in your lovely bower,
Or wedded - a transplanted flower-
I bless you, Margaret!

Charles Lamb (1775–1834)

Day two presentations: Vaccines for the prevention of congenital and neonatal infections

Session One: Developmental immunology and vaccines
Chair: Dr Alyson Kakakios

Clinical principles: Associate Professor Susan Prescott (School of Paediatrics and Child Health, University of Western Australia)*

Professor Prescott outlined the general concepts behind the immunological immaturity seen in the perinatal period, how the humoral and cellular immune system develops in the post natal period and how microbial products can modify the immune system's development. Interestingly there may be very good, as yet incompletely understood reasons, for the newborn's dampened and skewed immune response in 'letting the immune system off the leash slowly'. Current research looking at whether this is an intrinsic immaturity or active regulation and what factors are in play were highlighted. In addition, Associate Professor Prescott discussed different vaccination strategies to overcome this early hyporesponsiveness including using bacterial antigens and the potential concerns and limitations of these strategies. In the future improved understanding of the influence of perinatal exposures will assist in the development of vaccines aimed at allergic diseases, autoimmune diseases and malignancies.

Immunologic principles: Professor Patrick Holt (Institute for Child Health Research)

Professor Holt's presentation elaborated on some of the problems highlighted by the previous presenter. Evidence showing important immunological maturation between 12 to 18 months of age and some of the possible reasons to account for it were discussed, including genetic differences and environmental factors. Data yet to be published were presented showing that delayed immune maturation correlated with a family history of atopy. Professor Holt noted that perinatal immunology is a developing and exciting field and each new answer leads to new questions important for future vaccine initiatives.

Developmental immunology and vaccines in premature infants: Professor Don Roberton*

Professor Roberton presented a range of studies which showed that premature infants have lower antibody responses to many, but not all, immunisation antigens. For some of these antigens, the depressed response persists well into childhood. However, few studies have been performed to look at functional antibodies in this vulnerable group of children. One of the strategies to address this problem might be to combine immunisation of infants with boosting the immunity of pregnant women. This has been shown with Hib-PRPT vaccine to result in increased antibodies in breast milk. He concluded that clinical trials of vaccine efficacy in premature infants were needed, but highlighted the logistic difficulties associated with doing such trials. Based on current knowledge, the recommendation for premature infants is to vaccinate at chronological age, except for hepatitis B vaccine, which should be delayed until 30 days or discharge from hospital.

Session Two: Vaccines for neonatal viral infections
Chair: Prof David Isaacs

Human cytomegalovirus: Professor Stanley Plotkin

Professor Plotkin presented data showing that approximately one per cent of live births are affected by congenital CMV infection, of which about 20 per cent die or have long term sequelae. Congenital CMV is the leading infectious cause of neurological damage in infants. An effective CMV vaccine would not only prevent congenital infection but also the problem of CMV infection in transplant recipients. CMV vaccines currently in development include a live attenuated virus, a live attenuated/virulent recombinant virus and protein subunit vaccines consisting of glycoproteins or other proteins known to be important in immune responses. Several of the CMV vaccines have entered phase I or phase II trials. They have been shown to be safe and effective in inducing neutralising antibodies and cell-mediated immunity. One of the major hurdles to be overcome in phase III trials is recruitment of enough women to demonstrate protection from congenital infection in their babies.

Vaccines against Neonatal Herpes: Dr Cheryl Jones*

Neonatal herpes occurs in about one in 25,000 births in Australia with a quarter of infected babies dying shortly after birth. The most common source of the infection is from the mother who develops primary genital herpes infection in the later stages of pregnancy, often acquired from an asymptomatic partner. The most effective way of preventing neonatal herpes would be to immunise women against genital herpes with a long lasting broadly immunogenic vaccine. This may be best achieved by immunisation during early adolescence. Candidate vaccines that have been tested in clinical trials include live attenuated strains, replication-defective strains and protein sub-unit vaccines. A recent international multicentre efficacy trial of recombinant HSV-2 glycoprotein D sub-unit vaccine combined with the adjuvant monophosphoryl lipid have shown it to be partially protective in women who were seronegative for both herpes symplex virus (HSV) strains against genital disease (approximately 74% effective) and infection (approximately 40% effective), but not in men, or in women who were seropositive for HSV type 1. Future goals in the development of an effective vaccine to prevent neonatal herpes include better understanding of the immunological correlates of protection.

Hepatitis B virus: Professor Felicity Cutts*

Professor Cutts described the worldwide epidemiology and natural history of hepatitis B infection (HBV), which is responsible for approximately 750,000 deaths per year due to the development of cirrhosis and hepatocellular carcinoma. In relation to perinatal transmission, 70–90 per cent of infants born to mothers with a high HBV viral load (eAg +ve) and less than 10 per cent of infants born to mothers with low viral load (eAg -ve) become chronic carriers. In utero transmission is infrequent (<2%) and there is no evidence of transmission of hepatitis B through breastmilk. In areas of high hepatitis B

endemicity (≥ 8% infected) perinatal and early childhood infections are common. Primary vaccination (3 doses) will result in protective antibody levels in at least 95 per cent of infants.

In 1987 WHO recommended that by 1997 universal hepatitis B vaccination programs should be implemented. Unfortunately, by 2003 not all countries had programs in place with cost a significant barrier. The necessity for implementing a birth dose, rather than an alternate schedule, is variable according to the epidemiology, with a birth dose being less necessary in Africa where a lower proportion of infections are acquired perinatally than in South-East Asia where a high proportion are acquired perinatally. There are examples of the successful implementation of birth dose programs in developing world settings (e.g. Lombok). As the vaccine is extremely heat stable innovative strategies are possible in developing settings. Professor Cutts concluded that hepatitis B vaccine is a very effective vaccine, which is almost as cost-effective as measles vaccine.

Developing a live respiratory syncytial virus vaccine: Dr E David McIntosh (for Dr Valerie Randolph and Dr Frank Malinoski)*

Respiratory syncytial virus (RSV) is the leading cause of serious bronchiolitis and pneumonia in infants and young children, causing an estimated 4,500 deaths a year in the United States of America and 90,000 hospitalisations. There have been various attempts to develop a safe and effective RSV vaccine for infants since 1966. Currently, candidate live attenuated vaccine strains given intranasally are undergoing clinical testing, with promising early results. The recombinant approach to development has yielded a number of candidates, containing various mutations and deletions. Sub-unit vaccines are also undergoing clinical trials: a purified fusion protein-2 vaccine has shown promising results when administered to pregnant women.

Rotavirus: Professor Graeme Barnes*

Rotavirus infection is a significant problem in developing countries, with many hospitalisations for the disease occurring in young infants aged under six months. This epidemiology clearly favours neonatal immunisation. Neonatal rotavirus infection (in the first days/weeks of life) occurs in two circumstances: with community strains or with adapted nursery strains (nosocomial, with only one in 30 cases being symptomatic.) Cohort studies have demonstrated that whilst early infection with nursery strains does not offer protection against subsequent infection with rotavirus, it does offer protection against developing disease. Vaccines based upon neonatal strains are currently in development.

Session Three: Vaccines for other neonatal infections
Chair: Professor Don Roberton

Neonatal immunisation for pneumococcal disease: Dr Peter Richmond*

The burden of pneumococcal disease in early childhood is particularly high in Aboriginal and Torres Strait Islander populations in Australia, and in developing countries, where *Streptococcus pneumoniae* is the most common cause of meningitis and septicaemia in children aged less than three months. Infection and carriage in the first three months of life are linked to higher risk of pneumococcal disease in childhood and adulthood. The development of immunological tolerance during neonatal infection may be the cause of this higher risk. While early vaccination may prevent early infection, not enough is currently known about the impact of earlier 7-valent pneumococcal conjugate vaccination on immunological memory, response to infection or other vaccines, serotype replacement or adverse events. An Australian-funded study is currently underway in Papua New Guinea, and another in Kenya, to compare the outcomes of commencing vaccination at birth, one month and two months of age.

Is neonatal group B streptococcal disease vaccine preventable? Professor Lyn Gilbert*

Group B streptococcal disease emerged in the 1970s in Australia as the most common cause of neonatal sepsis and infectious stillbirth, probably through the emergence of a newly virulent serotype III. Since then, intrapartum antibiotic prophylaxis of pregnant women, identified through screening for carriage or clinical risk factors, has been effective in reducing the incidence of neonatal sepsis. Several vaccines have been developed over the years but none has progressed to phase III trials, because of the relatively low incidence of disease and reservations about vaccinating pregnant women. In future, improved methods are needed for identifying women at risk and virulent clones, to enable more targeted use of antibiotics or new generation vaccines.

Neonatal pertussis: Associate Professor Peter McIntyre*

Most cases of pertussis now occur in adolescents and adults. However, almost all deaths and 80 per cent of hospitalisations occur in those aged under three months. Three strategies have been considered to prevent neonatal disease—maternal, neonatal and parental immunisation. There is evidence to support the effectiveness of maternal immunisation and neonatal immunisation with DTPa. Immunisation of both parents is likely to be logistically more difficult and less cost effective. Analysis so far has shown a birth dose to be the most cost effective of the three options, but all are relatively expensive. However, it is likely that the currently available data underestimate the burden of disease, and therefore the cost-effectiveness of these strategies.

Immunisation for the prevention of neonatal tetanus: Professor Kim Mulholland

The incidence of neonatal tetanus is estimated by WHO to be approximately 200,000 cases per year. It occurs almost exclusively in developing countries in circumstances where most births are unassisted, and over 90 per cent of cases are fatal, due to lack of access to assisted ventilation. In 1989 the World Health Assembly adopted a resolution for the elimination of neonatal tetanus. Since then the incidence is estimated to have decreased by two-thirds. Current WHO policy is for a comprehensive strategy which includes the promotion of clean deliveries, disease surveillance and both childhood (3 doses of DTP in infancy and a booster 1 year later) and maternal immunisation. Tetanus vaccination coverage for the first three doses in infants and two doses in women has recently been estimated at around only 50 per cent in high-risk areas. A single-dose vaccine would significantly improve the prospects for elimination, but attempts to develop it have so far been unsuccessful, as boosting is needed. Work is progressing on a microcapsule delivery system for gradual vaccine release.

Tuberculosis: Professor Warwick Britton*

Bacille Calmette-Guerin vaccine has been used for the prevention of tuberculosis (TB) for over 50 years. It is most effective for the prevention of primary disease including miliary TB, but only 50 per cent effective against re-activation. It is therefore widely used for the prevention of serious disease in children in high prevalence countries, but has limited use in controlling TB incidence and is rarely used in adults. It has also been shown to have an adjuvant effect, boosting responses to the oral polio vaccine and hepatitis B vaccine, although the clinical significance of this is not clear. A recent study in Sydney found BCG to be effective in preventing asthma in children with a family history of atopic disease. Recent work focuses on the development of recombinant vaccines (against the sub-unit) and live attenuated vaccines. Future trials should be combined with HIV vaccine trials, given the importance of HIV-TB co-infection.

Conclusion

This colloquium allowed us to look back at the contributions many clinicians and researchers have made nationally and internationally to the development of vaccines and vaccination programs. In the near future infections such as measles and rubella will be little more than of historical interest in Australia. The colloquium also illustrated, sometimes in fascinating detail, the progress which is being made in basic research and in vaccine development by contemporary scientists. We heard about the wide range of organisms and diseases which have become or are likely to become amenable to prevention or treatment using vaccines.

We were left with several important challenges: how to appropriately evaluate and introduce some of the ‘old’ and many of the newer costly vaccines into developing countries, how to develop and deliver effective vaccines to neonates and how to work cooperatively in the early stages of vaccine research and development to make sure that the vaccines most needed globally (e.g. HIV) are fast tracked. The generous contribution of the international speakers to these discussions with our Australian experts helped all who attended to anticipate the likely future successes and disappointments.