Immunisation in the 21st century

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The past

The 20th century has seen the introduction of numerous vaccines whose benefit to society can only be described as miraculous. Smallpox, which used to plague humanity and cause untold human suffering, has now been eliminated from the face of the earth. The polio virus, which resulted in the paralysis of millions of children and adults worldwide, is becoming a rarity in developed countries, with the last recorded case of indigenously acquired poliomyelitis occurring in the USA in 1979 [1]. *Haemophilus influenzae* type B (Hib), once the leading cause of bacterial meningitis (and touching the lives of many Australians), has now been relegated to the 'historical interest only' category. The many physicians, scientists, nurses and other medical professionals who have contributed to these success stories should feel great pride and satisfaction. What they should not feel, however, is complacent! While we have managed to control these diseases by immunisation, with the possible exception of smallpox, they could all come back to haunt us if immunisation levels fall.

As a result of effective antimicrobial therapy for bacteria and viruses, together with effective immunisation, the 20th century has seen a remarkable reduction in deaths from infectious diseases. Unfortunately, much of the immunisation research of the 1930s has since been dropped in favour of research on new antimicrobial agents. However, despite the expenditure of billions of dollars and millions of manhours on the development of such agents, the 1990s have seen the emergence of the first bacterium resistant to virtually all known antibiotics [2]. The 21st century, then, will almost certainly see the emergence of untreatable strains of common and potentially lethal pathogens such as *Streptococcus pneumoniae* (Figure 1). Indeed, multiply-resistant *Streptococcus pneumoniae* are becoming common worldwide and present real problems for the management of meningitis [3]. Immunisation holds the promise of preventing disease from resistant organisms and may also, in some circumstances, inhibit the spread of resistant organisms by reducing carriage.

The future

The vaccines of the 21st century are likely to be safer, more convenient and immunogenic, able to protect against a wider range of pathogens and, possibly, even less expensive! Some of the new vaccines released in Australia in the last decade, and those likely to be released within the next few years, will be discussed.

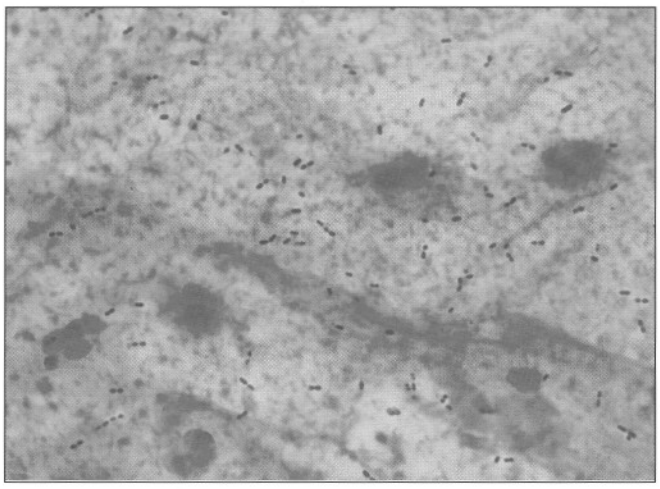
Conjugate vaccines

The polysaccharide capsules of pathogenic bacteria such as *Haemophilus influenzae* type B, *Streptococcus pneumoniae* and *Neisseria meningitidis* protect the organism against attack by the immune system. A specific antibody response by the host is the only way these bacteria can be effectively cleared from the body [4]. Unfortunately, since the naked polysaccharide antigen does not produce a response leading to long-term immune memory, the antibody response is not long-lasting (which means that the older-type vaccines must be readministered every few years). In addition, children under the age of 2 do not mount effective antibody responses to naked polysaccharide antigens. However, by combining (conjugating) the polysaccharide with a protein – to which adults and infants under the age of 2 are able to mount a long-lasting and effective immune response – the body is tricked into producing these good-quality immune responses to the polysaccharide antigen as well. This is the basis for the spectacularly successful *Haemophilus influenzae* type B vaccine. The good news is that, using the same principle, vaccines for *Streptococcus pneumoniae* and some sero-groups of *Neisseria meningitidis* are currently being developed and trialed around the world and may be available in Australia in the next few years [5].

Multivalent vaccines

With the introduction of increasing numbers of vaccines into the routine childhood immunisation schedule, our children

Figure 1. Streptococcus pneumoniae.



are becoming the proverbial pin-cushions! Administering diphtheria/tetanus/pertussis (DTP), Hib and now hepatitis B vaccine may involve three injections at separate sites for each visit. The vaccine manufacturers have been very mindful of this and are conducting considerable research in the area of multivalent vaccines, where several different vaccines are combined in order to be given in the same syringe. While it may seem simple to combine all the vaccines in a single syringe and inject them, unfortunately this can result in poor immune responses to some vaccine components. Much time and effort has gone into studying formulations which combine a number of vaccines. Indeed, the next few years should see the release of a variety of multivalent vaccines which enable five or more vaccines to be given as a single injection (although, as with the current vaccines, multiple doses of combination vaccines will need to be given over several months).

Acellular vaccines

The principle of the acellular pertussis vaccine, recently released in Australia, is that rather than killing the entire bacterium and mixing it with an adjuvant (which enhances the immune response), only the important antigens (proteins) – those responsible for generating the protective immune response – are incorporated into the vaccine. In the case of the pertussis vaccine, these are pertussis toxin, filamentous haemagglutinin and pertactin [6]. Since many components of the whole-cell vaccine provide no protective immunity but can contribute to side-effects such as fever and redness at the injection site, the incidence of minor side-effects such as fever over 38°C may be reduced from approximately 40 per cent down to 5 per cent by removing these components [6]. This may lead to improved compliance.

New vaccines to protect against old diseases

Rotavirus, the most common cause of viral diarrhoea in children worldwide, frequently occurs in the winter months, although there are sporadic cases throughout the year. Several candidate rotavirus vaccines have been trialed around the world and some appear capable of reducing the incidence of severe rotavirus diarrhoea by 80 per cent [7]. Utilising animal strains of rotavirus (non-pathogenic to humans) to which the important protective antigens from human rotavirus strains have been added, they are live virus vaccines (similar to the oral polio virus vaccine), appear to be safe and will probably be released in Australia in the next 2 or 3 years. Rotavirus is a very common nosocomial pathogen and the prevention of hospital admissions of children with this disease will dramatically reduce its spread in hospitals, thereby decreasing the demand for isolation facilities.

Varicella virus, which causes chicken pox, has long been a major problem for infection control management in hospitals. Problematic and not infrequent scenarios in paediatric hospitals include those in which siblings, having visited a paediatric oncology patient, develop chicken pox within 2 days of the visit, or the medical student working in the labour ward erupts in chicken-pox vesicles. Already in some countries it has been suggested that a live, attenuated vaccine (the OKA strain – not yet approved for marketing in Australia) become part of the routine immunisation schedule for children [8]. Other indications for varicella immunisation include non-immune health-care workers in paediatric hospitals and those caring for immunocompromised patients. Non-immune relatives of immunosuppressed patients would also be good candidates for the vaccine.

The Vaccine Impact Surveillance Network

The Vaccine Impact Surveillance Network in Western Australia is a network of infectious disease physicians, medical microbiologists, infection control practitioners, public health physicians, general practitioners and other medical professionals who collaborate in the collection of data on diseases either currently vaccine-preventable or that will be in the near future. One of the great hindrances to the early introduction of new vaccines in this country has been the paucity of active surveillance systems to provide accurate Australian data on the incidence and demography of diseases, strain types and the cost to the community of these diseases. In the absence of such information, governments are reluctant to introduce

new vaccines. Infection control practitioners who regularly monitor admissions for, and nosocomial transmissions of, potentially vaccine-preventable diseases such as rotavirus and respiratory syncytial virus are in an ideal situation to help collect this vital data. Therefore, anyone interested in contributing to the collection of such data is invited to contact the author.

Conclusion

With the increasing incidence of multiply resistant bacteria, the 21st century will be challenging for the infection control practitioner, and one of the main defences against some such organisms will be active immunisation. Fortunately, with a number of good candidate vaccines on the horizon, major tragedy may be averted. Infection control practitioners could certainly play a vital role in the collection of data on vaccine-preventable diseases in the future and facilitate the early introduction of these new vaccines.

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