Pertussis vaccines: past, present and future in Australia

Proceedings of a workshop held at the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, Royal Alexandra Hospital for Children and University of Sydney, Westmead, New South Wales, 9 August 1997.

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Abstract

In August 1997, a workshop was convened by the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases to consider current issues in the use of pertussis vaccines and implications for the Australian immunisation schedule. Topics covered included the history, efficacy and reactogenicity of whole-cell and acellular vaccines and vaccine schedules. Acellular pertussis vaccine is preferred by the National Health and Medical Research Council for the primary course as well as the 18 month and 4-5 year old childhood doses. At the time of the workshop, a 3-component acellular vaccine (DTPa) had been approved (licensed) in Australia for all doses in the childhood schedule. It was the first vaccine subject to a cost-effectiveness evaluation under the new vaccine funding arrangements. Issues considered in the evaluation of the cost-effectiveness of the vaccine were discussed. These included comparative efficacy, adverse events and compliance, and the question of community as well as individual benefit from the use of the vaccine. *Comm Dis Intell* 1998;22:125-132

Introduction

Despite the long term availability of an effective vaccine, low vaccination coverage has contributed to the regular outbreaks of Pertussis in Australia over the past 4 years.[1] The recent availability of an acellular pertussis vaccine, and the potential availability of combination vaccines, are expected to lead to improved immunisation coverage. However, the introduction of such vaccines into the Standard Vaccination Schedule requires consideration of a wide range of issues including efficacy, side effect profiles and cost effectiveness. To develop a better understanding of these issues, a two day workshop was convened in August 1997 by the National Centre

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for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS). The Centre was established by the Commonwealth Department of Health and Family Services in August 1997 to carry out research to inform policy and planning for immunisation services in Australia.

The meeting brought together a group of Australian experts in infectious diseases, microbiology, immunology and public health to discuss pertussis with Professor James Cherry, a recognised international authority on pertussis and pertussis vaccines. The workshop examined current issues in the use of whole cell and acellular vaccines and implications for the Australian immunisation schedule. Issues relating to the economic evaluation of vaccines were also considered.

Part I - Whole cell and acellular vaccines; the current scene

History

Whole cell vaccines

An overview of whole-cell pertussis vaccine (Pw) in Australia was given by Professor Ian Gust. The first commercial whole-cell vaccines in Australia were made by the then Commonwealth Serum Laboratories (now CSL Limited) in about 1920, but were not used widely until the 1940s. At this time pertussis, diphtheria and tetanus vaccines still had to be given as separate injections, and debate began about whether it was possible to combine antigens. By 1953 the first Australian-made Triple Antigen (DTPw) (diphtheria and tetanus toxoids with whole-cell pertussis) was produced.[2] Although there have been many changes in the surveillance of pertussis in Australia over the past 50 years, a more than tenfold reduction in the incidence of pertussis (from 500-750 per 100,000 to 25-30 per 100,000) and a more than hundredfold reduction in deaths (from 4,000 in the period 1926-1945 to 21 in the period 1976-1995) have occurred during the whole-cell vaccine era. This is impressive evidence of the effectiveness of whole-cell vaccines in Australia.

Acellular vaccines

Professor James Cherry outlined the history of acellular pertussis vaccines (Pa). Japanese investigators accelerated the development of acellular pertussis vaccines in the 1970s. This followed an epidemic of pertussis that occurred after the cessation of whole-cell pertussis immunisation, in early 1971, because of concern about adverse effects.[3] Development of the acellular vaccines became possible once biologically active and extractable components of *Bordetella pertussis* were identified. One or more of the following five components are included in all vaccines developed to date:

- detoxified pertussis toxin (PT);
- the outer membrane protein pertactin (PRN); and
- three surface proteins - filamentous haemagglutinin (FHA) and two agglutinogens (AGGs).

The first acellular vaccines were strongly influenced by the notion that pertussis was a single toxin disease, like diphtheria, and could be prevented by use of a pertussis toxoid. This is incorrect, partly because *Bordetella parapertussis*, which does not produce pertussis toxin, causes an almost identical clinical picture.

The first licensed vaccines in Japan contained PT alone or together with FHA. These vaccines were used in the early trials in Sweden, where epidemic pertussis had also followed cessation of immunisation. The vaccines showed low protective efficacy in Sweden (54% for monocomponent and 67% for 2-component vaccine given as 2 doses after 9 months of age)[4] and were not licensed anywhere apart from Japan. In the United States of America, the National Institutes of Health coordinated phase I and II trials of 13 candidate acellular vaccines, selecting the most promising ones to enter randomised controlled trials in Europe.[5]

Efficacy

Whole-cell vaccines

A number of candidate vaccines were examined in trials conducted by the Medical Research Council in the United

Editor's column

We received both compliments and criticisms of our last issue of *CDI*, confirming that people do read and appreciate the journal even if they do not always agree with it. Please continue to send us your feedback as it is only by hearing from our readers that we can make the sorts of improvements that will keep *CDI* relevant and useful.

This issue of *CDI* features a report of the workshop on pertussis vaccines (p 125) convened by the National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases in August 1997. As well as providing a summary of the history of pertussis vaccines, the report highlights some of the complexities that face us in making decisions about which vaccines should be incorporated into the Standard Vaccination Schedule. These complexities will increase as the range of diseases for which vaccines are available expands and more combination vaccines come on to the market. The report also discusses some issues in the evaluation of the cost-effectiveness of vaccines used in population programs. Such evaluations are relatively new but likely to be of increasing importance in vaccine scheduling decisions. With the launch of the Measles Control Program this month, the article by *Burgess et al* on adverse events following measles immunisation (p 136) is both timely and reassuring. The slight increase in notifications of meningococcal disease noted in the Communicable Diseases Highlights on page 139 reminds us that we are entering the peak season for meningococcal disease. The short report by *Harvey* (p 134) reviews the 1997 meningococcal disease data and points to the need for increased vigilance to diagnose cases early and commence treatment promptly. There is nothing like claiming that something is a first to provoke correspondence to the Editor. Following reminders of two other reports of infant botulism, we have published (p 133) a clarification of the editorial comment that accompanied last issue's case report.

Table 1. International infant efficacy trials of pertussis vaccines[6,7,11]

Site	Manufacturer (of acellular vaccine)	Composition				Schedule (months)	Efficacy (95%CI) [1]			
		PT	FHA	PRN	FIM		DTPa		DTPw	
Germany	Con (USA)	x	x			2, 4, 6	96	(78-99)[2]	97	(79-100)
Germany	Wyeth	x	x	x	x	2, 4, 6, 15-18	82	(73-87)	91	(85-94)
Sweden	Con (Canada)	x	x	x	x	2, 4, 6	85	(81-89)	48	(37-58)[3]
Sweden	SKB	x	x			2, 4, 6	59	(51-66)	48	(37-58)[3]
Italy	CB	x	x	x		2, 4, 6	84	(76-90)	36	(14-52)[3]
Italy	SKB	x	x	x		2, 4, 6	84	(76-90)	36	(14-52)[3]
Sweden	NAV	x				3, 5, 12	71	(63-78) [2]	Not tested	
Germany	SKB	x	x	x		3, 4, 5	89	(77-95)	97	(83-100)
Africa	PM	x	x			2, 4, 6	86[2]		96	

1. Using WHO definition of 21 days or more cough.
2. These results are likely to be too high due to study methods and observer bias
3. Study used Connaught (Canada) whole-cell vaccine.

Con (USA) = Connaught (USA)
Con (Canada) = Connaught (Canada)
SKB = SmithKlineBeecham
NAV = North American Vaccine
CB = Chiron Biocine
PM = Pasteur Meriux
DTPa = Acellular Diphtheria - Tetanus - Pertussis vaccine
DTPw = Whole-cell Diphtheria - Tetanus - Pertussis vaccine

Kingdom in the 1950s. These trials established a correlation between clinical efficacy and the mouse protection test (Kendrick assay), which has been used ever since to monitor the potency of whole-cell vaccines. Australia has adopted the United Kingdoms' criterion of requiring 4 mouse protection international units (IU), but the United States of America has allowed vaccines to have as low as 2 IU. One of the outcomes of the recent comparative trials has been evidence that whole-cell vaccines may vary significantly in efficacy (Table 1).[6,7] It is suggested that whole-cell vaccines, such as the CSL vaccine, which pass the more stringent mouse protection test (4 IU) are likely to be more protective, but there are limited observational (household contact) data and no trial data estimating the efficacy of the Australian whole-cell vaccine.[2] In general, although waning immunity occurs over time with both, whole-cell vaccines protect better against disease than natural infection. A British study has estimated that waning of immunity is almost complete by 5 years after vaccination.[8] Some experts believe that if the vaccine contains all 3 agglutinogens (1,2,3) it is more likely to be protective against all 3 serotypes of the organism (type 1,2,3; type 1,2; and type 1,3).[2]

Acellular vaccines

In contrast to whole-cell vaccines, the Kendrick test does not correlate with efficacy for acellular vaccines, making large trials the only means of evaluating efficacy. Professor Cherry gave a detailed review of the seven large controlled trials now published, all but one in Europe, to evaluate the efficacy of the acellular vaccines (Table 1).[6,7,9] The results of the most recent study (Sweden II) were not published at the time of the meeting but were published subsequently.[10] Professor Cherry emphasised that differences in methodology and case definitions make comparisons between trials difficult.[6,11] In particular, the World Health Organization (WHO) case definition (21 days of cough) detects only typical whooping cough, which is more common in unvaccinated individuals. Using the WHO definition therefore inflates vaccine efficacy estimates compared with case definitions which include milder but still culture positive infections.[6] When mild cases are taken into account, the efficacy of acellular vaccines varies widely. Their efficacy broadly correlates with increasing numbers of components, from around 50% with 1 or 2 components to around 70% with at least 3 components, including PRN, and 80% or more with 5 component vaccines.[6,11] In the second Swedish trial, a 5-component acellular vaccine and the British whole-cell vaccine gave better protection against less severe disease (laboratory confirmed pertussis with or without cough, and whooping cough diagnosed by the child's parents) than a 3-component vaccine (not the 3-component vaccine currently approved in Australia).[10] All three vaccines tested in the second Swedish trial gave similar protection if the WHO case definition was used (laboratory confirmed with cough for 21 or more days).[10]

Reactogenicity

Whole-cell vaccines

Whole-cell vaccines contain inactivated *B. pertussis* organisms and a variable but significant amount of endotoxin, which is probably responsible for the relatively

Table 2. Side effects of Triple Antigen containing whole-cell pertussis vaccine (DTPw) in 591 Australian children[1]

Reaction	Percentage[2]
Systemic	
Fever ≥ 38°C[2]	16
Irritability	90
Crying - intermittent, inconsolable	40
Crying - persistent high-pitched	8
Vomiting	11
Hypotonic-hyporesponsive episode	0
Convulsions	0
Local	
Redness ≥ 2.4 cm	27
Induration ≥ 2.4 cm	30
Swelling	45
Tenderness	46

1. All children were given at least 2 doses of paracetamol around the time of each vaccination.
2. Mean after first three doses at 2, 4 and 6 months of age, to the nearest whole number.

high rate of fever, local reactions, pain and prolonged crying from whole-cell vaccines (Table 2).[12] Endotoxin cannot be exclusively responsible, as these effects also occur, at a lower rate, with DT vaccine. Attempts were made in Australia and elsewhere to eliminate endotoxin from whole cell pertussis vaccines, but this proved difficult and was superseded by development of acellular vaccines.

Whole-cell pertussis vaccine is incorporated into the WHO's Expanded Programme on Immunization (EPI) and is now routine in most countries. However, in some countries the vaccine has been subject to adverse publicity, related to the relatively high rate of minor and moderate side effects and unsubstantiated statements about more serious ones.[13] The only estimates of severe reactions to the Australian vaccine come from a study of two earlier formulations of DTPw, where hypotonic-hyporesponsive episodes (HHE) occurred in 3 out of 1,075 infants.[14]

Acellular vaccines

The much lower incidence of the more common but less severe reactions (such as local swelling, pain and fever) with acellular vaccines was easily established early on. Data concerning uncommon but more severe reactions, such as fits and HHEs were more difficult to accumulate, but the combined results of a number of controlled trials now show that these are also significantly lower than with whole-cell vaccines and do not appear to be related to the number of components or to any one component.[6,9] In the United States of America two products were licensed in 1991 for the fourth and fifth infant doses. Surveillance after this licensure showed that post-vaccination seizures and hospitalisation were reduced by 60%–70% with the acellular product (DTPa).[9] However, none of the trials has been large enough to evaluate the rate of rare serious side effects such as anaphylaxis or encephalopathy in comparison with whole-cell vaccine. What has been established is that HHEs occasionally occur both with acellular pertussis vaccine and with combined diphtheria and tetanus vaccine (without the pertussis component) and that this occurs at about a rate of 1 in 10,000 doses compared to about 1 in 1,000 with the whole-cell vaccine.[6,9] Professor Cherry pointed out that comparing absolute rates of HHEs between trials (different case definitions) and communities (higher rates of reporting in more versus less advantaged) is difficult, but relative comparisons should be valid.

Licensing of acellular vaccines

Status in Australia

One 3-component vaccine (Infanrix, SmithKline Beecham) had been approved for marketing (licensed) in Australia at the time of the meeting. A 5-component vaccine (Tripacel, CSL Vaccines, manufactured by Connaught Laboratories, Canada) has since been licensed. Both vaccines are approved for use for primary and booster doses. In November 1996, the National Health and Medical Research Council recommended that acellular vaccine should be preferred for the booster doses at ages 18 months and 4-5 years.[15] On the advice of its Pertussis Working Party, the National Health and Medical Research Council recommended in June 1997 that acellular vaccines should be preferred for the infant schedule also.

Status in the United Kingdom

Acellular vaccines have not been licensed in the United Kingdom. Here pertussis has been controlled using 3 doses of the British whole-cell vaccine (made by Evans Medeva), administered at 2, 3 and 4 months of age. At present, no boosters are given although preschool boosters with an acellular vaccine are being considered. The incidence of side effects in the infant schedule is low.[10,16]

Acellular pertussis vaccines in adults

Dr Tim Heath reviewed the accumulating literature on the importance of adults in the maintenance of pertussis transmission in the community, much of it emanating from Professor Cherry's research groups in California and Germany.[17] Although it was once thought that clinical whooping cough was followed by life-long immunity, there is evidence that immunity from infection wanes, possibly more than that from immunisation. Very young infants, who are most at risk from serious complications, frequently have contracted pertussis from an adult contact. Acellular pertussis vaccines offer for the first time the possibility of including a pertussis booster with the already recommended tetanus and diphtheria boosters for adults. Trials investigating this are under way in the United States of America and in Australia.

Combination vaccine trials in Australia

Combinations containing whole-cell pertussis vaccine

Associate Professor Terry Nolan discussed the status of multivalent vaccines containing Pw. The motivation for producing such vaccines is the increasing number of antigens being incorporated into the primary schedule. Single injections are likely to be more acceptable to both parents (improving compliance and timeliness) and providers (reduction in material and delivery costs). However, immunological responses to antigens presented in combination cannot be assumed to be equivalent and, in general, responses to Hib in combination have been lower. These problems seem close to resolution now.

Although a number of countries have licensed whole-cell combinations, with either Hib vaccine or hepatitis B and inactivated polio vaccine, Australia is probably unique among industrialised countries in developing a pentavalent combination using a reformulated whole-cell vaccine. Trials of this vaccine, containing DTPw as base, the PRP-OMP♦ Hib vaccine and recombinant hepatitis B in a liquid formulation (produced by CSL Vaccines), have been conducted in Melbourne during the past 5 years. In a controlled trial of this pentavalent vaccine, reactogenicity and immunogenicity has been assessed in about 845 babies after the first 3 doses, and in a smaller number after the fourth dose.[18,19] In contrast to the acellular vaccine combinations, after 3 doses at 2, 4 and 6 months, Hib antibody responses were significantly higher with the whole-cell combination than singly, but there was a lower hepatitis B surface antibody response. The implications of this are uncertain, but preliminary results suggest that hepatitis B responses may be satisfactory with either the

♦ PRP-OMP vaccine (PedvaxHIB) is a conjugated vaccine in which polyribitol ribosyl phosphate (PRP), the purified capsular polysaccharide of Haemophilus influenzae type b, is conjugated to a carrier protein, the meningococcal outer membrane protein (OMP).

addition of monovalent hepatitis B at birth for all babies or the inclusion of hepatitis B vaccine in the combination given at 18 months of age.

Combinations containing acellular pertussis vaccine

Professor Don Roberton discussed multivalent vaccines containing Pa. Comprehensive assessment of combination vaccines has a number of prerequisites as outlined by Edwards and Decker,[20] including blinded and standardised serological assays. To date, most studies of combinations including Hib and acellular pertussis vaccines show reduced Hib responses. Most results are available only in abstract form, but a Finnish study showing significantly reduced Hib responses when given in combination with DTPa and inactivated polio vaccine, has been published.[21] It is not clear why this is occurring, although the most likely explanation is that some adsorption of the PRP antigen is occurring in the combination. The reactogenicity and immunogenicity of a pentavalent vaccine containing acellular pertussis (using the 3-component product currently approved in Australia and manufactured in Europe), diphtheria, tetanus, Hib and hepatitis B is under study in 360 infants in Adelaide and Sydney. The formulation of the Hib component of this vaccine has been changed to overcome adsorption, if present. Enrolment is completed; follow up and evaluation will be completed during 1998. Another group of full-term and preterm infants, immunised with DTPw according to the current schedule, will be evaluated for boosting by the combination vaccine at 18 months.

Pertussis vaccine schedules

Throughout the world various schedules are used. In the United States of America the primary schedule doses are given at 2, 4 and 6 months and most of the European trials have used this schedule. In June 1990, the United Kingdom introduced a 2, 3, 4 months of age schedule with whole-cell vaccine, replacing a 3, 5, 10 months of age schedule. A series of small comparative trials over a number of years has examined the immunogenicity and reactogenicity under the two schedules, using a number of acellular vaccines and the Evans-Medeva whole-cell vaccine. The results of these trials have been summarised recently.[16] These data were reviewed in detail at the workshop by A/Professor Nolan.

Local erythema and swelling were strikingly reduced under the 2, 3, 4 month schedule, for both Pw (22% to 4%) and Pa (11-21% to 1-5%). Fever greater than a cutoff figure (which differed among studies) was not reduced under the 2, 3, 4 month schedule (11% versus 12%) but was much less common with the acellular vaccines (1-5%). When serological responses under the two schedules were evaluated, there was a significantly reduced geometric mean titre to detoxified pertussis toxin after the third dose with the accelerated schedule, but responses to other antigens were unchanged.

Discussion about the United Kingdoms' experience encompassed a number of issues:

- optimum uptake is the key to control, irrespective of which schedule is used;
- the implications of the known lower antibody responses with earlier immunisation;
- the incidence of fever reported for Pw under both schedules was much lower than expected from experience elsewhere, and similar to that seen with diphtheria-tetanus vaccines;
- will the organism continue to circulate in older children without boosters?
- would this schedule improve uptake in Australia and what would the comparative reactogenicity be under Australian conditions?

Panel discussion on pertussis vaccine schedules in Australia

The discussion was led by Professor Richard Doherty, Professor Don Roberton, Associate Professor David Isaacs, Dr John Carnie and Professor James Cherry.

Multiple injections versus reactogenicity

Professor Cherry was asked to comment on the situation in the United States of America, where, because of compensation legislation, the cost of Pw is much closer to Pa than in Australia. In the United States of America, a Hib/DTPw combination (Tetramune, Wyeth-Lederle) has been available for some time and hepatitis B and inactivated polio vaccine, each given by injection, are now also routinely recommended for infants; a total of 3 injections. Some parents are opting for their children to have the Hib/DTPw combination rather than Hib and DTPa separately, or oral polio vaccine rather than inactivated polio, because of the lesser number of injections, despite the higher potential for side effects with the DTPw. Costs of acellular vaccines and inactivated polio are a significant factor, particularly in health maintenance organisations (HMOs). No data on the prevalence of these approaches were available.

A comparable scenario exists in Australia with the whole-cell multivalent combination likely to be approved some time before acellular combinations. This raises the question of the need to choose between the reactogenicity associated with combinations containing whole-cell vaccine and increased number of injections if the acellular vaccine is chosen. A study commissioned by the Commonwealth Department of Health three years ago (unpublished), indicated that some parents were reluctant to accept multiple injections. No data on attitudes to this issue in representative Australian populations were available at the time of the workshop.

The place of acellular pertussis vaccines in the immunisation schedule

After a discussion about the place of Pa in the immunisation schedule the consensus was that a change to a 2, 3, 4 month schedule was not appropriate in Australia at this time, because of the potential for confusion and the over-riding need to improve compliance with the current schedule.

Professor Gust expressed concern that the economic analysis of acellular versus whole-cell vaccine (see Part II) had not taken sufficient account of the then unpublished results of the Sweden II trial, which suggested superior efficacy for the whole-cell vaccine used in the United Kingdom and a 5-component acellular vaccine over a 3-component vaccine (not the 3-component vaccine currently approved in Australia). On the basis of assumed equivalent efficacy of the Australian and United Kingdom DTPw and the fourfold greater cost of acellular vaccines, he proposed that acellular vaccines should be used only

for the 18-month and 5-year booster doses. Whole-cell vaccine should continue as the routine vaccine for the infant schedule, with acellular vaccine used only for infants with adverse reactions.

In the ensuing discussion, no overall consensus was reached. Some speakers stated that they disagreed with the Pertussis Working Party's conclusion that acellular vaccine should be preferred to whole-cell vaccine for infants, arguing that the vaccines should be equally preferred for the first three doses. Others expressed the view that the Working Party's recommendations should be adopted, and that it would be impractical to restrict the use of acellular vaccine in infants, once it became available for older children.

Professor Cherry considered that a possible difference of 10% in efficacy between acellular and whole-cell vaccines, even if substantiated, was not important if 5 doses were being given, as in the schedules for Australia and the United States of America. The major factor in recommending acellular vaccines in North America was public beliefs about adverse reactions.

Part II - Economic evaluation of acellular pertussis vaccine in Australia

Since the beginning of financial year 1997-1998, decisions on Commonwealth Government funding of new vaccines, recommended by the NHMRC for inclusion in the standard vaccination schedule, may incorporate an evaluation of the cost-effectiveness of the new vaccine by the Pharmaceutical Benefits Advisory Committee (PBAC). The currently approved 3-component DTPa (Infanrix) was the first vaccine evaluated by the PBAC under these new arrangements.♦♦

Dr Suzanne Hill, Discipline of Clinical Pharmacology, University of Newcastle, was on the team which independently appraised the economic analysis of Infanrix for the PBAC. She outlined the nature of the PBAC process in general and highlighted issues involved in the economic evaluation of vaccines.

Access to drugs and vaccines in Australia

Two processes contribute to making drugs and vaccines accessible in Australia:

- the marketing approval (licensing) process, through the Therapeutic Goods Administration (TGA), which considers the quality, safety and efficacy of pharmaceutical products; and
- the process for subsidising the cost of drugs through inclusion on the national Pharmaceutical Benefits Scheme (PBS), for which the data required are comparative efficacy and comparative cost-effectiveness.

The PBS was established in 1953 and has been a remarkably robust political policy, the aim of which is to provide access to essential drugs. Drugs are evaluated for listing on the PBS by the PBAC, which is a powerful advisory committee; the Minister cannot make a decision to list a drug unless the PBAC has recommended that (s)he do so.

Requirement for the PBAC to consider comparative cost-effectiveness

An amendment to the *National Health Act* in 1989 established the requirement for the PBAC to consider comparative cost-effectiveness in making recommendations to the Minister. The PBAC guidelines for comparative cost-effectiveness, first developed in 1990-1991, are now in their second edition and consist of two major parts:

- establishing the relative clinical benefit of any new product, and
- evaluating that benefit.

This is a very clinical and epidemiological approach, and has been one of the points of contention about the guidelines. It is somewhat different to the approach to economic evaluation adopted in Canada and in some of the health maintenance organisations (HMOs) in the United States of America, where the emphasis has been much more on an economic model rather than starting with assessment of the relative clinical benefit.

In looking at clinical benefit, the first question is choice of comparator. The company is asked to conduct a mini-systematic review to identify the best data that are available to support its drug's performance against this comparator. The Committee has expressed a definite preference for randomised controlled trials, where the trial arms compare the two treatments directly, if at all possible. Companies are asked to estimate the relative effect size, and they have two options - equivalence to the comparator or a claim for superiority. The company is then asked to conduct what has become known as a 'trial-based economic evaluation', where it provides an estimate of the costs and benefits around the outcome that is measured in the trial. In the evaluation of benefit it is asked to adopt a societal perspective. It is then asked to provide an estimate of the incremental cost-effectiveness ratio, that is, the incremental cost per outcome. Finally, companies estimate the total financial implications to both the PBS and the government of the potential listing of the drug.

To date the Committee has considered over 350 applications, and it is clear that establishing equivalence to a comparator is easier than establishing superiority. Decisions are not based solely on the cost-effectiveness ratio; a number of other factors are considered, including the total financial implications. If it is estimated that the cost to the Commonwealth of a new drug may be more than $10 million, the Cabinet, as well as the Minister, must take the decision to approve the listing. The Committee is required to take into account the perception of clinical or community need for a drug, the question of equity of access, and what might be called 'the rule of rescue', where the assessment tends to err on the side of positive rather than negative assessment.

Cost-effectiveness evaluation for vaccines

Vaccines have been required to be approved for marketing through the TGA, but have not generally been subject to evaluation of comparative efficacy and cost-effectiveness, either because they were PBS listed for individual use prior to the introduction of current guidelines or because funding for population use (as for NHMRC schedule vaccines) has

♦♦ Evaluations for funding vaccines in the NHMRC Standard Vaccination Schedule are undertaken by the PBAC as an expert advisory body to the Department of Health and Family Services. They are separate from the PBS listing process and do not result in recommendation for PBS listing.

been provided under separate processes. Infanrix was the first vaccine subjected to an economic evaluation and presented a number of new issues to the PBAC.

Although vaccines are used for prophylaxis rather than treatment, they are not alone in that, drugs for osteoporosis and hypertension, for example, are also prophylactic. Probably of more difficulty for evaluating vaccines is the question of community as well as individual benefit, which is not usually part of a drug evaluation.

Issues in evaluating cost-effectiveness of vaccines

One of the immediate issues for the first evaluation of a vaccine by the PBAC was the availability of comparative efficacy data. The obvious comparator was the CSL Triple Antigen (DTPw). For Infanrix, the assessment of comparative efficacy was relatively straightforward because of the existence of good quality randomised trial data with clearly defined outcomes such as protective efficacy and side effects.

Other issues were:

- compliance with vaccine schedules and what actually drives it; and
- data to support the assumption that adverse effects are the major factor in determining compliance.

A key assumption was that a decrease in side effects would lead to an increase in vaccination rates, translating into an improvement in coverage and completion rates, a change to which the model was extremely sensitive. An added difficulty in assessing this assumption was the relative impact of other initiatives to increase immunisation rates, such as financial incentives for parents and providers, the new Australian Childhood Immunisation Register and mandatory review of vaccination status at school entry.

The estimates presented for Infanrix (under $3,000 per infection averted, and under $25,000 per life year gained) can be considered in the context of previous decisions about other drugs. A league table of estimated cost per quality adjusted life year (QALY) for various drugs presented to the PBS since 1990 suggests that estimates of $20,000–$30,000 per QALY are acceptable and estimates of more than $100,000 are unacceptable. The estimates for Infanrix were well within the boundaries considered by PBAC when evaluating drugs.

Because of the concern about the assumption of increased coverage and the sensitivity of the overall model to that assumption, the intermediate outcome of cost per averted side effect was considered in the evaluation. The effect of the vaccine in the community on other parts of the immunisation process were also considered.

Finally we come to the 'willingness to pay' factor. It is clear that some people have been willing to pay quite a lot for this vaccine, which raises the difficult issue of the need to trade off the costs of a vaccine, for example, against the costs of something else.

The evaluation process is part of a consistent move to evidence-based decisions. For pharmaceuticals, the clinical evidence is often much better than for other health technology interventions. For pertussis vaccine the data were complex. The important question of how the impact of the introduction of acellular vaccines will be evaluated must be considered immediately.

Economic evaluation of Infanrix versus whole-cell vaccine

Ms Michelle Burke, health economist with SmithKline Beecham (SKB), led the team that conducted the economic analysis of the vaccine (Infanrix) which was submitted to the PBAC. She presented the methodology and summary findings of the economic analysis, but was unable to present detailed data because of commercial confidentiality issues.

The team working on the analysis developed a model with several key assumptions:

- the efficacy of Infanrix (DTPa) and the CSL whole-cell vaccine (DTPw) was equivalent;
- the better tolerability of Infanrix would result in improved coverage rates; and
- increased coverage would lead to fewer cases and deaths from pertussis.

The model developed was complex. It included changes over time in both the probability of infection, to account for cyclical epidemics, and coverage rates. It also included consideration of children of differing ages and immunisation histories. No empirical data were available for a number of variables in the model (for example, improvement in coverage from use of Infanrix) and values for these variables were derived from the consensus opinion of an expert panel. Sensitivity analysis was used to examine the changes that occurred in the model estimates when different values, within the plausible range of values, were substituted for the value selected as baseline for the model.

The model estimated that the cost per pertussis infection prevented was less than $3,000, and the cost per life year gained was less than $25,000. These estimates were sensitive to changes in the following three factors: baseline coverage rates, coverage with Infanrix, and the probability of pertussis infection. Where less favourable estimates were obtained with sensitivity analysis, estimated costs did not increase to unacceptable levels.

As submissions on cost-effectiveness for the PBAC are protected under secrecy provisions of the *National Health Act*, Dr Hill congratulated SKB on their willingness to have their data discussed.

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Speakers

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Editorial note

Since the workshop, Commonwealth funding has been made available to all States and Territories for DTPa vaccine to be provided free for the booster doses at 18 months and 4-5 years of age and for primary course doses in infants who have had reactions to DTPw. The South Australian and Northern Territory Governments have made additional funds available to provide DTPa vaccine free for all primary course and booster doses for children who live in their jurisdictions.

The funding of vaccines is a complex issue and requires consideration of the context in which they are recommended for use. Where vaccines are recommended for limited use on the basis of individual medical need, it is appropriate that they be evaluated by the PBAC for funding under the PBS. Where vaccines have been recommended by the NHMRC for inclusion on the Standard Vaccination Schedule, funding through the PBS is not the most cost effective mechanism. Using PBAC processes for the evaluation of vaccines enables evidence-based decisions to be made in determining the funding of these vaccines through alternative mechanisms.

For a number of reasons, several alternative mechanisms have developed and vaccine funding currently occurs through three separate streams. To ensure that future vaccine funding arrangements are simpler and more transparent, the Commonwealth Government recently announced that, from the 1999-2000 financial year, all childhood vaccines will be funded through one stream under the Public Health Outcome Funding Agreements (http:www.health.gov.au/pubs/budget98/fact/hfact1.htm)**.** Also announced in the Budget was an increased threshold for Ministerial approval of essential vaccine funding. This will ensure that, as new vaccines become available through advances in vaccine technology, there will be timely provision of funds to purchase them.

Pertussis: the way it was

The following is a graphic reminder of why we need to immunise our children against pertussis. To many public health workers it also demonstrates that 'the more things change, the more they stay the same'.

From: Hamilton DG. Whooping cough immunization. MJA 1979; 2:651. ©Copyright 1979. *The Medical Journal of Australia* - reproduced with permission.

The telephone rang and the voice at the other end said; "Come down to my office, Hamilton." It was Dr Ratcliff, the very capable but severe and somewhat aloof superintendent of the Children's Hospital. The tone of his voice boded no good for his medical registrar, the first the hospital had had and still somewhat on trial. I presented myself, and on his desk was the early edition of *The Sun* newspaper open at a page where a large headline screamed: "Doctor attacks hospital and Health Department."

That was 1940. In those days whooping cough was a very grave disease of young children. In the previous 50 years in New South Wales it had killed more children under five than diphtheria. After gastroenteritis it was the greatest infectious killer of infants. That year it destroyed 85 infants in our hospital, out of 293 admitted. A whole 30-bed ward was filled for months with these poor little ones. Most of those admitted were young. The older ones were not in great danger and stayed at home, going on for seemingly endless weeks with their distressing spasms of breath-robbing cough ending in a vomit or choking whoop. Very many of the infants stopped breathing in their spasms and their colour blackened till a nurse rushed to revive them with oxygen. There were no antibiotics to treat them, pneumonia often developed and they lay there in their little cots, emaciated and weak, wracked by their coughing spasms, losing their nutrition by the vomiting or the very breath of life by the respiratory spasm that their cough brought on.

In the midst of this we received reports of trials in America of immunization using a new vaccine that gave 75% protection to children who were known to be exposed to pertussis after the immunization. The medical staff formed a small committee — of Dr Lindsay Day, Dr Donald Vickery and me — to seek ways to get this immunization established in Australia. The Commonwealth Serum Laboratories agreed to make the new vaccine and to circularize all doctors about its use. *The Medical Journal of Australia* cooperated eagerly and published valuable information. We approached the Director of Health in New South Wales with proposals for an immunization campaign. He replied that his Department was putting all its effort into persuading the community to accept diphtheria immunization that gave much better protection. If at the same time they advocated something that gave only 75% protection it would destroy the public's faith in immunization. When we asked could the Hospital conduct its own campaign, we were told a hospital was to treat illness, not prevent it.

When a newspaper reporter rang me early one morning and said he had heard I was interested in whooping cough immunization I described the gravity of the illness and the American experiences, and naively told him what the Director of Health had told us. It was my first lesson in Press relations. I was very unpopular, but it made whooping cough good copy for a few days and other members of the staff were able to make valuable statements anonymously to the Press. The war delayed things, but by 1950 immunization was widespread and deaths from pertussis fell to a trickle of one or two a year.

Dr Donald Hamilton, a well known Sydney paediatrician, was a talented clinician, memorable teacher and raconteur, and a serious artist. After retiring from the consultant staff of the Royal Alexandra Hospital for Children in the 1970s he wrote "Hand in hand" - the history of the Hospital's first 100 years. Dr Hamilton died at the age of 87 on 29 June 1998 as this issue of CDI went to press.

Infant botulism - clarification

In the last issue we reported on a case of infant botulism which was notified directly to *CDI* as a case report. The case was not reported in the National Notifiable Diseases Surveillance System as the case definition for that system is specifically for foodborne botulism.[1] *CDI* is aware of two other reported cases of infant botulism in the past 6 years. The first case, a 2 month old male infant from South Australia, occurred in October 1995, and was reported to the specialised surveillance system for acute flaccid paralysis (AFP) managed by the Australian Paediatric Surveillance Unit.[2] The second case, reported in June 1997, was a 5 month old male infant from Western Australia (Adams C, Watson A, Health Department of Western Australia, personal communication).

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Meningococcal disease in Australia: 1997 and beyond

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In 1997, the death of a young western Australian woman made meningococcal disease a media issue. The publication of horror stories of babies losing limbs created panic and the sense of an epidemic out of control. As we move into the peak period for occurrence of meningococcal disease in 1998, it is timely to review the 1997 data from the National Notifiable Diseases Surveillance System (NNDSS) and to remind readers of the importance of early diagnosis and treatment in the management of meningococcal disease.

Increased rate in 1997

Preliminary figures for 1997♦ indicate that there have been 496 notifications to the NNDSS of meningococcal infection with onset dates during 1997. This corresponds to a rate of 2.7 notifications per 100,000. This rate is slightly higher than the rates for the previous five years, which have ranged from 1.7 per 100,000 in 1992 to 2.3 per 100,000 in 1996.[1] This is consistent with the trends in other industrialised countries.[2]

Cases occurred in all States and Territories. The Australian Capital Territory reported 9 (2% of total cases), New South Wales 222 (45%), Northern Territory 15 (3%), Queensland 72 (14%), South Australia 22 (4%), Tasmania 9 (2%), Victoria 100 (20%) and Western Australia 47 (10%).

Disease is not epidemic

The pattern of disease remained sporadic with occasional clusters of cases, which is typical of the pattern in developed countries. Unpublished data from the Australian Meningococcal Surveillance Program (AMSP) indicate that the predominant serogroup overall continued to be serogroup B (Prof J. Tapsall, personal communication). Of the 343 isolates of meningococci examined by the AMSP in 1997, there were 219 (64%) serogroup B, 108 (32%) serogroup C, and the remaining 4% included serogroups Y, Z and W135. New South Wales had a higher proportion of serogroup C isolates than other jurisdictions and a number of clusters of cases were linked to two specific strains. These will be described more fully in a future issue of *CDI*.[3]

Seasonal pattern

The usual seasonal pattern occurred with 65% of cases occurring in the six month period between the beginning of June and the end of November. The peak month of onset was August with 63 cases. This was lower than the peak monthly number of cases (73) in 1996, which occurred in July. However, the peak period was slightly longer in 1997 than in 1996 (Figure 1).

Age distribution

The male female ratio was 1.0:1. As in previous years, the age distribution of cases was bimodal with the highest rates in the 0-4 year age group (14.9 notifications per 100,000) and a second peak in the 15-19 year age group (6.6 notifications per 100,000) and the 20-24 year age group (3.5 notifications per 100,000) (Figure 2). Of the 193 cases in children aged under 5 years, 72 (37%) were in

Figure 1. Notifications of meningococcal disease, 1994 to 1998, by month of onset

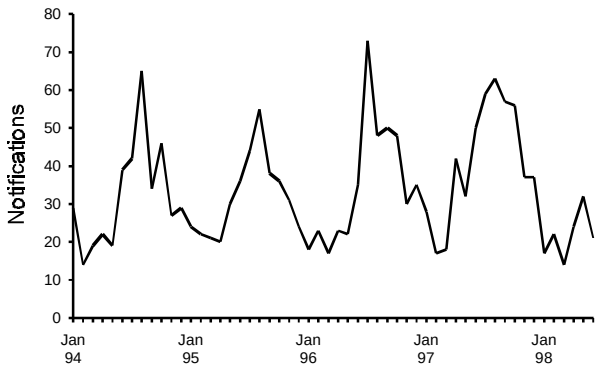
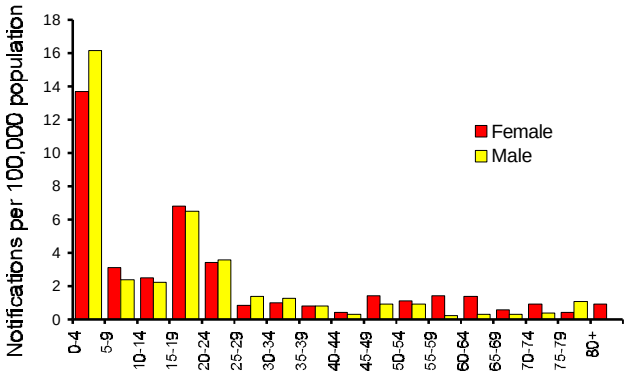


Figure 2. Notification rate of meningococcal disease, 1997, by age group and sex



♦ Data for 1997 are still being finalised and will be published in *CDI* later this year as part of the Annual Report of the National Notifiable Diseases Surveillance System.

Meningococcal disease

Symptoms

- Fever
- Headache
- Stiff neck
- Nausea
- Weakness and drowsiness
- Rash

Doctors

- Maintain a high index of suspicion for cases.
- Notify suspected cases to relevant public health authority by phone.
- Treat suspected cases immediately with antibiotics, preferably intravenously.
- Try to obtain blood culture prior to treatment BUT
- **DO NOT DELAY THE ADMINISTRATION OF ANTIBIOTICS**

Community

- Recognise symptoms.
- Seek medical attention immediately.
- Be persistent in seeking medical attention if symptoms are not improving as expected.

Public health authorities.

- Collaborate with treating doctor to identify close contacts of cases and administer chemoprophylaxis to protect exposed individuals.
- Consider immunisation for specific situations according to NHMRC Guidelines.

infants under the age of 1 year. This corresponds to a rate of 28.5 notifications per 100,000, the highest of any age group.

Preparing for the 1998 peak season of meningococcal disease

Although meningococcal disease is not a common disease in Australia, it can result in permanent disability and in 5-10% of cases ends in death.[4] The cornerstone for controlling this disease is early diagnosis and prompt treatment on suspicion of the disease. The community need to be made aware of the symptoms of meningococcal disease and encouraged to seek medical attention promptly.

Meningococcal disease can be very difficult to diagnose as many of the early symptoms are similar to other, milder infectious diseases. Patients should not hesitate to seek further medical assessment if anyone, particularly a young child, is not recovering as expected from such an illness. Doctors, especially general and emergency medicine practitioners, need to start treatment on suspicion of the disease and not wait for confirmation of the diagnosis. All cases should be notified by phone to the relevant public health authority to enable prompt public health action to control the spread of the disease.

Several States and Territories have already publicised the coming season through press releases and the development of educational materials. This will assist in educating the community about the need for vigilance and the actions they can take. However, educating the patient is of limited value if the medical practitioners they consult are not sufficiently aware of the disease and the actions they should take.

To assist practitioners, the National Health and Medical Research Council has published guidelines for the control of meningococcal disease.[5] These can be purchased through the Australian Government Publishing Service♦♦ or accessed via the Internet at:

Http://www.health.gov.au/hfs/nhmrc/advice/nhmrc2.

They are essential reading for both clinicians and public health workers.

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♦♦ AGPS - phone orders 132 447

The Measles Control Campaign and immunisation adverse events

Margaret A Burgess[1], Timothy C Heath[1], Peter B McIntyre[1]

The Measles Control Campaign

The Commonwealth Department of Health and Family Services has announced that the 'Measles Control Campaign' will be launched on 9 July 1998. Between August and November 1998, in a school-based program, all children in primary schools throughout Australia will be offered an additional dose of measles-mumps-rubella (MMR) vaccine, irrespective of their prior vaccination history. Parents of preschool-aged children who do not have a MMR vaccination recorded on the Australian Childhood Immunisation Register (ACIR) will receive a letter from the Register urging them to have their child vaccinated, and parents of high school students will be similarly advised to ensure that their children have had at least two doses of MMR.

The primary school program is expected to reach more than 90% of the almost 2 million Australian children aged 5 to 12 years, in a period of less than 6 months. It can be predicted to result in an increased number of reports of suspected adverse reactions to the vaccine. Systems are currently being coordinated between the Commonwealth and State and Territory Health Departments to keep a careful tally of these reports and to make sure that they are appropriately followed up. This is necessary to keep the community fully informed, and to make sure that it is clear that this short-term increase in side effects is outweighed by improved disease control.

Adverse events associated with MMR vaccination

Published studies mostly relate to vaccination of young children or adults with no prior immunity. In the Australian re-vaccination program the rates will be lower, as the majority of school children will be immune to one or more of the vaccine components.

The incidence of reactions following primary MMR vaccination of preschool-aged children has been documented in a randomised controlled trial; reactions likely to be attributable to the vaccine included rash (2%), fever (6%), conjunctivitis (2%) and drowsiness or irritability (2-4%).[1] The risk of a febrile convulsion following vaccination in this age group is 1 in 3,000.[2] The United States Institute of Medicine carefully reviewed data on serious adverse events related to measles and rubella vaccines and concluded that anaphylaxis occurred rarely (there were only two well documented cases in the literature), thrombocytopenia occurred at a rate of 1 in 30,000 to 1 in 40,000, and that death could be caused by measles vaccine virus in immunocompromised children.[3-5] The Institute of Medicine's review also confirmed that rubella vaccine could cause acute arthritis or arthropathy in post-pubertal women (13-15%), but vaccine-associated arthropathy is mostly transient and natural rubella has a much higher rate of this complication (52%).[6-9]

Although the Institute of Medicine reported that the data were inadequate for accepting or rejecting an association between measles vaccine and encephalitis or encephalopathy,[3] a recent report continues to suggest a rare association.[10] It is estimated that encephalitis may occur in 1 in 1 million recipients of measles vaccine and 1 in 3 million recipients of the mumps vaccine strain (Jeryl-Lynn) available in Australia.[11]

Adverse events not associated with MMR vaccine

There are adequate data to refute the recent suggestions that MMR vaccine is associated with autism, inflammatory bowel disease and asthma.[12,13]

Contraindications and false contraindications to MMR vaccine

Asthma, allergy to egg, and mild intercurrent illness are not contraindications to MMR vaccine.[11,14]

Children who have had a previous serious allergic reaction to the vaccine should be referred for advice about risks of further vaccination. Children who are immunosuppressed due to medication or underlying disease (except asymptomatic HIV infection) should *not* be vaccinated.[11]

Experience in the United Kingdom

In England, commencing in November 1994, over 7 million school children aged 5 to 16 years received an additional dose of measles-rubella vaccine, in a program similar to, but shorter (4 to 6 weeks) than, the Australian one.[15-17]

Before the program commenced, doctors were reminded about the importance of reporting all suspected adverse reactions immediately to the Medicines Control Agency (MCA) which is similar to the Australian Drug Reaction Advisory Committee. During the program, data collected by the MCA were reviewed daily by a medical assessor and electronically transmitted to the vaccination teams. This ensured that the adverse events were under continuous review and long-term follow-up was conducted.

A total of 2,735 adverse reactions were reported in 1,202 children by the end of October 1995; a reporting rate of one affected child for approximately 6,700 immunisations. Most reports related to minor reactions, many of which were unlikely to have been due to the immunisation. There were no deaths. Serious reactions could be classified into two groups; those occurring around the time of the immunisation and those occurring later.

Early onset reactions

Symptoms and signs of anaphylaxis or allergic reactions (for example, bronchospasm) within 24 hours of vaccination were reported in 1 in 65,000 (123 reports). Fifty-two per cent of these children received adrenaline

and some were admitted briefly to hospital, but there were no serious sequelae.

There was also a small group of children who had syncopal episodes which precipitated brief convulsions at the time of, or shortly after, immunisation. This is a common occurrence in mass vaccination programs; nurses are familiar with its management and the children recover promptly and completely. Canadian workers have found that in school-based programs fainting accompanied by pallor is sometimes mistaken for anaphylaxis and is therefore likely to be over-reported.[18]

Neurological reactions

There were 91 reports of neurological reactions including 61 convulsions (37 of which are mentioned above). Reported rates of encephalitis or encephalopathy (11 cases), Guillain-Barre syndrome (3 cases) and meningitis (2 cases) were no higher than the background rates of those conditions. For example, epidemiological data suggest that 1 to 7 cases of Guillain-Barre syndrome would be expected in the United Kingdom over a 4-week period in this age group in the absence of an immunisation program. Attending medical officers were asked for details of serological and cerebrospinal fluid (CSF) findings in these cases, but these were not always available. Only one of the 11 children with encephalitis or encephalopathy failed to recover completely. This boy had a slight residual hemiparesis and his serology confirmed that he had been immune to measles prior to the vaccination.

Arthropathy and other reactions

There were six reports of arthritis, but only one with onset within 14-21 days after vaccination, the usual time of onset of rubella vaccine provoked arthritis. In addition, there were 41 reports of arthropathy; most were unlikely to have been caused by the vaccine because the time of onset was not within 14-21 days from vaccination. Other suspected reactions reported included erythema multiforme (9), herpes zoster (7), Henoch-Schönlein purpura (5) and thrombocytopenia (2). Of these, only erythema multiforme and thrombocytopenia were biologically plausible associations.

Implications for the Australian Measles Control Campaign

Experience in the United Kingdom has shown that, with appropriate systems for vaccination and surveillance in place, a large school-based campaign can be carried out effectively and without incident. The medical profession, the media and the community need to be fully informed about every detail, including the fact that the vaccine is *not* prepared in fetal cells (it is prepared in a continuous cell line which in 1961 originated from fetal fibroblasts).

The importance of the program is in preventing the outbreak of measles predicted to occur in the next year or two, and its associated deaths and disability. This has to be balanced against an expected temporary increase in reports of adverse events following vaccination.

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Editorial note

Reporting on adverse events following immunisation for the national Measles Control Campaign

For the period of the national Measles Control Campaign, the following reporting mechanisms for Adverse Events Following Immunisation (AEFI) will be in place:

- Immediate AEFI will be reported by the teams of nurses conducting the school-based vaccination clinics on a daily basis to the State and Territory Measles Coordinators.
- General Practitioners will be asked to report all AEFI by phone to the State and Territory Measles Coordinators. A description of conditions to be reported will be

provided to all GP's prior to the commencement of the campaign.

- All serious AEFI will be notified by State and Territory Measles Coordinators to the National Manager, Measles Control Campaign by phone and a written report provided as soon as possible after the event.
- Reports of AEFI will be forwarded to the national surveillance scheme (Serious Adverse Events Following Vaccination Surveillance Scheme) and the Australian Drug Reaction Advisory Committee (ADRAC).

Follow-up of AEFI will be undertaken by States and Territories according to normal procedures.

The NCIRS was established by the National Centre for Disease Control, Commonwealth Department of Health and Family Services. The Centre analyses, interprets, and evaluates national surveillance data on immunisation coverage and vaccine preventable diseases. NCIRS also identifies research priorities, and initiates and coordinates research on immunisation issues and the epidemiology of vaccine preventable diseases in Australia.

Bulletin Board

The Australian Health Outcomes Collaboration

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30th Annual Conference
Celebrating Public Health: Decades of Development, Decades of Opportunity
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The Australian Institute of Environmental Health

25th National Conference
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The Public Health Association of Australia Inc.,

6th National Conference on Immunisation
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The Australasian Society for HIV Medicine

19th Annual Conference
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Contributions to the Bulletin Board are invited from those organisations with forthcoming events relevant to communicable disease control.

Communicable Diseases Surveillance

Highlights

Communicable Diseases Surveillance consists of data from various sources. The National Notifiable Diseases Surveillance System (NNDSS) is conducted under the auspices of the Communicable Diseases Network Australia New Zealand. The CDI Virology and Serology Laboratory Reporting Scheme (LabVISE) is a sentinel surveillance scheme. The Australian Sentinel Practice Research Network (ASPREN) is a general practitioner-based sentinel surveillance scheme. In this report, data from the NNDSS are referred to as 'notifications' or 'cases', whereas those from ASPREN are referred to as 'consultations' or 'encounters' while data from the LabVISE scheme are referred to as 'laboratory reports'.

Reporting period 27 May to 23 June 1998

Vaccine preventable diseases

The number of notifications for *Haemophilus influenzae* type b, measles, mumps and rubella remains low in comparison with previous years.

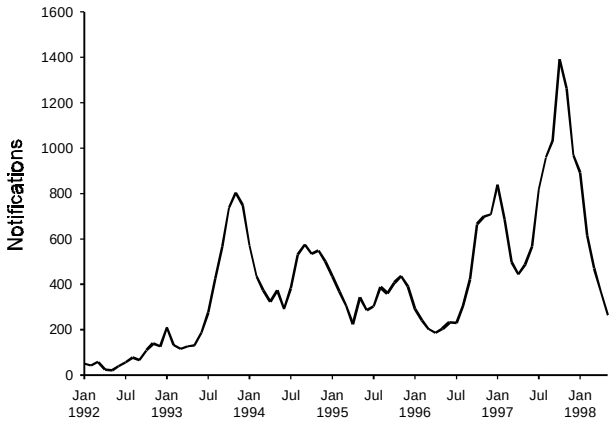
Pertussis notifications for this reporting period and for the year to date are lower than for the comparable periods of 1997 (Figure 1). The number of notifications for pertussis with onset in May 1998 is lower than in previous months of this year. This contrasts with the situation in each of the of the previous five years where numbers have increased after April. Nearly half of all pertussis notifications with onset in 1998 were in the age groups 0 to 4 years (13%), 5 to 9 years (18%) and 10 to 14 years (16%). The male to female ratio was 1.13:1.

Arboviruses

A further 12 notifications of dengue have been recorded for the current reporting period, bringing the total reported in 1998 to 288. The outbreak in Far North Queensland appears to have subsided.

The numbers of new notifications for Barmah Forest virus infection and Ross River virus infection have also continued to decline over the last two months as expected for the time of year.

Figure 1. Notifications of pertussis, 1992 to 1998, by month of onset



Hepatitis A

The peak in activity recorded earlier in the year now seems to be over.

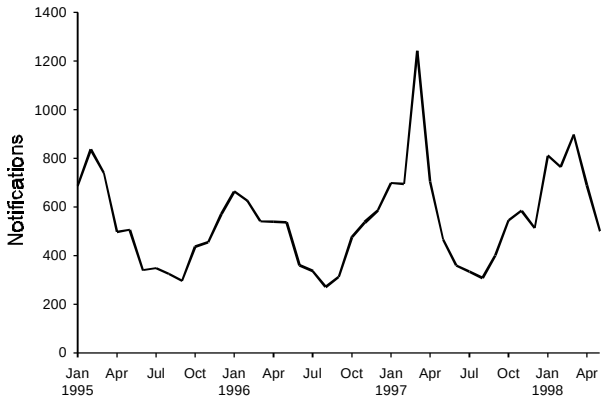
Meningococcal infection

A slight increase has been observed in notifications of meningococcal infection during the last two months. Increased numbers of cases are usually recorded in Australia during the months of Winter and Spring (see report on page 134).

Salmonella

The increase in the number of notifications recorded early in 1998 is similar to the seasonal pattern recorded in previous years (Figure 2). The number of cases has declined in recent months.

Figure 2. Notifications of salmonella, 1995 to 1998, by month of onset



Respiratory syncytial virus

The number of laboratory reports of respiratory syncytial virus rose slightly in May but remained low for the time of year (Figure 3). For the current reporting period 50% of reports were for infants under the age of 1 year and a total of 88% for the under 5 years age group.

Figure 3. Laboratory reports of respiratory syncytial virus, 1996 to 1998, by month of specimen collection

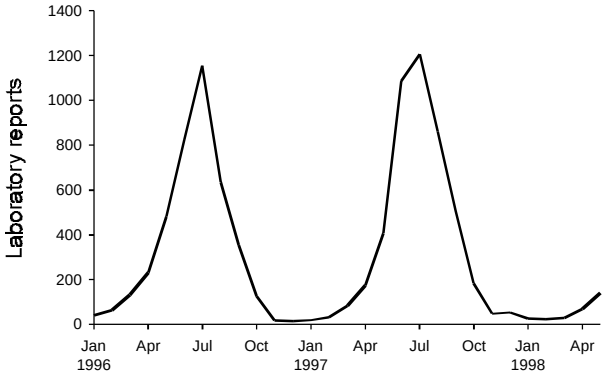
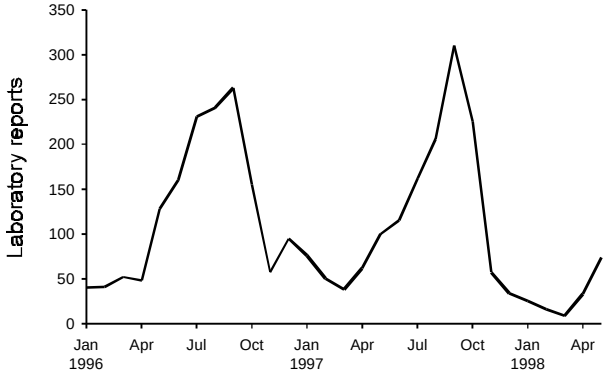


Figure 4. Laboratory reports of rotavirus, 1996 to 1998, by month of specimen collection



Rotavirus

The LabVISE scheme has recorded a recent rise in the number of reports of rotavirus in recent months (Figure 4). Numbers are average for the time of year. Most reports in this four week period (88%) were for children under the age of 5 years.

Tables

There were 5,736 notifications to the National Notifiable Diseases Surveillance System (NNDSS) for the four week period, 27 May to 23 June 1998 (Tables 1 and 2). The numbers of reports for selected diseases have been compared with historical data for corresponding periods in the previous three years (Figure 5).

There were 1,565 reports received by the *CDI* Virology and Serology Laboratory Reporting Scheme (LabVISE) the four week period, 21 May to 17 June 1998 (Tables 3 and 4).

The Australian Sentinel Practice Research Network (ASPREN) data for weeks 21 to 24 ending 21 June 1998 are included in this issue of *CDI* (Table 5).

Table 1. Notifications of diseases preventable by vaccines recommended by the NHMRC for routine childhood immunisation, received by State and Territory health authorities in the period 27 May to 23 June 1998

Disease[1,2]	ACT	NSW*	NT	Qld	SA	Tas	Vic	WA	This period 1998	This period 1997	Year to date 1998*	Year to date 1997
Diphtheria	0	0	0	0	0	0	0	0	0	0	0	0
H. influenzae type b infection	0	0	0	0	0	0	2	1	3	3	16	23
Measles	4	4	0	1	0	0	7	7	23	62	223	243
Mumps	0	1	1	1	0	0	2	2	7	15	80	99
Pertussis	3	66	1	72	14	5	41	12	214	490	3,158	3,548
Rubella[3]	4	2	1	32	0	0	12	5	56	86	359	711
Tetanus	0	1	0	0	0	0	1	0	2	2	2	6

NN. Not Notifiable

1. No notification of poliomyelitis has been received since 1986.
2. Totals comprise data from all States and Territories. Cumulative figures are subject to retrospective revision, so there may be discrepancies between the number of new notifications and the increment in the cumulative figure from the previous period.
3. Includes congenital rubella.

* Data from NSW are incomplete for this reporting period, as one Public Health Unit was unable to provide data

Table 2. Notifications of diseases received by State and Territory health authorities in the period 27 May to 23 June 1998 (diseases preventable by routine childhood immunisation are presented in Table 1)

Disease[1,2,3]	ACT	NSW*	NT	Qld	SA	Tas	Vic	WA	This period 1998	This period 1997	Year to date 1998[4, *]	Year to date 1997
Arbovirus infection (NEC)[5]	0	0	1	4	0	0	2	0	7	12	65	99
Barmah Forest virus infection	0	2	0	22	0	0	0	1	25	49	336	465
Brucellosis	0	0	0	0	0	0	0	0	0	1	19	16
Campylobacteriosis[4,6]	18	-	15	300	62	16	20	99	530	920	3,817	5,560
Chancroid	0	0	0	0	0	0	0	0	0	0	1	1
Chlamydial infection (NEC)[7]	23	NN	40	307	42	16	104	175	707	756	5,077	4,557
Cholera	0	0	00	0	0	0	0	0	0	0	3	1
Dengue	0	3	0	9	0	0	0	0	12	2	288	190
Donovanosis	0	NN	3	1	NN	0	0	0	4	4	20	16
Gonococcal infection[8]	4	34	63	81	11	0	31	83	307	434	2,531	2,235
Hepatitis A	7	42	3	79	4	0	5	7	147	249	1,495	1,766
Hepatitis B incident[4]	0	0	0	3	0	0	7	0	10	16	87	125
Hepatitis C incident[9]	0	0	0	-	0	4	-	-	4	10	48	37
Hepatitis C unspecified[4]	24	NN	20	228	NN	26	8	97	403	787	2,684	4,647
Hepatitis (NEC)	0	0	0	0	0	0	0	NN	0	2	4	13
Hydatid infection	0	0	0	0	0	0	0	0	0	5	17	19
Legionellosis	0	3	0	2	0	1	1	4	11	19	121	90
Leprosy	0	0	0	0	0	0	0	0	0	0	2	7
Leptospirosis	0	0	0	6	0	0	0	1	7	17	81	66
Listeriosis	0	0	0	0	0	0	3	0	3	3	28	45
Malaria	2	3	5	130	1	0	1	1	143	59	365	408
Meningococcal infection	0	7	2	8	1	2	7	5	32	36	133	165
Ornithosis	0	NN	0	0	0	0	3	0	3	2	18	34
Q Fever	0	7	0	20	0	0	3	0	30	56	246	297
Ross River virus infection	1	10	6	124	0	0	0	2	143	569	2,203	5,968
Salmonellosis (NEC)	7	28	34	170	31	7	73	46	396	395	4,138	4,225
Shigellosis[6]	0	-	6	10	2	0	5	8	31	69	336	461
Syphilis[10]	2	22	16	19	0	1	0	3	63	106	587	632
Tuberculosis	2	11	2	13	0	1	8	1	38	78	391	503
Typhoid[11]	0	0	0	0	0	0	0	1	1	6	41	47
Yersiniosis (NEC)[6]	0	-	0	14	1	0	4	0	19	16	144	148

1. For HIV and AIDS, see Tables 7 and 8.
2. Totals comprise data from all States and Territories. Cumulative figures are subject to retrospective revision so there may be discrepancies between the number of new notifications and the increment in the cumulative figure from the previous period.
3. No notifications have been received during 1998 for the following rare diseases: botulism (foodborne), lymphogranuloma venereum, plague, rabies, yellow fever, or other viral haemorrhagic fevers.
4. Data from Victoria for 1998 are incomplete.
5. NT: includes Barmah Forest virus.
6. Not reported for NSW because it is only notifiable as 'foodborne disease' or 'gastroenteritis in an institution'.
7. WA: genital only
8. NT, Qld, SA and Vic: includes gonococcal neonatal ophthalmia.
9. Qld, Vic and WA incident cases of Hepatitis C are not separately reported.
10. Includes congenital syphilis
11. NSW, Qld, Vic: includes paratyphoid.

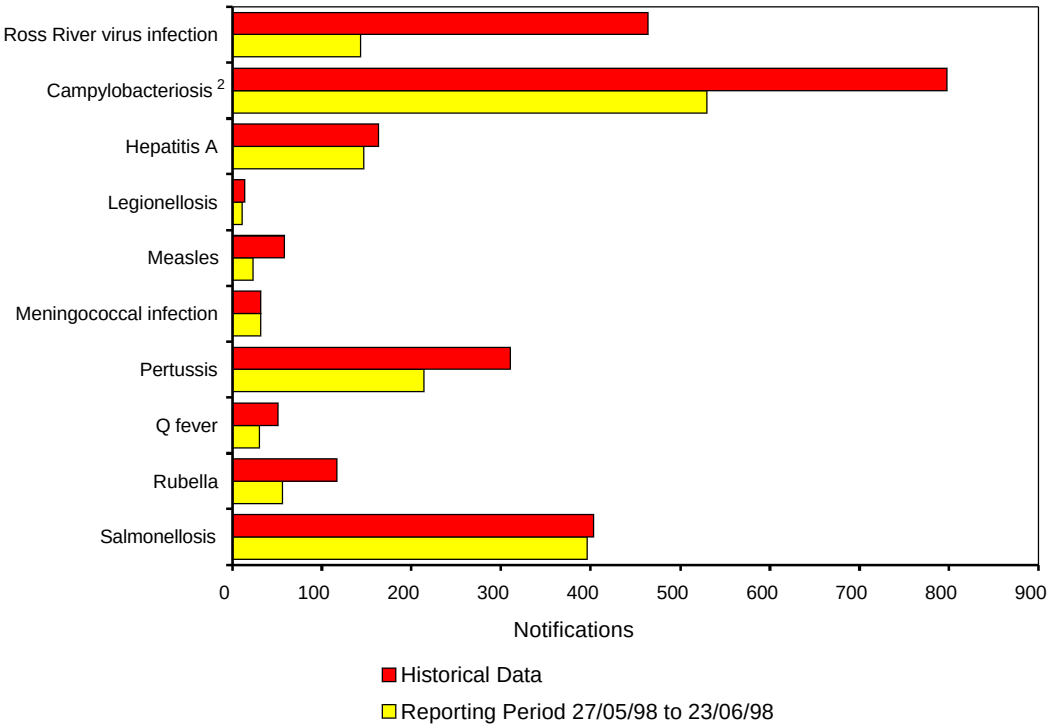
NN Not Notifiable.

NEC Not Elsewhere Classified

\- Elsewhere Classified.

* Data from NSW are incomplete for this reporting period, as one Public Health Unit was unable to provide data

Figure 5. Selected National Notifiable Diseases Surveillance System reports*, and historical data[1]



1. The historical data are the averages of the number of notifications in the corresponding 4 week periods of the last 3 years and the 2 week periods immediately preceding and following those.
2. Data from Victoria for 1998 are incomplete.

* Data from NSW are incomplete for this reporting period, as one Public Health Unit was unable to provide data.

Table 3. Virology and serology laboratory reports by State or Territory[1] for the reporting period 21 May to 17 June 1998, and total reports for the year

	State or Territory[1]								Total this period	Total reported in *CDI* in 1998
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA		
Measles, mumps, rubella										
Measles virus					1				1	36
Mumps virus		1						3	4	17
Rubella virus							1		1	62
Hepatitis viruses										
Hepatitis A virus		3	2		5		1	11	22	232
Arboviruses										
Ross River virus			1		2			10	13	521
Dengue not typed							1		1	20
Kunjin virus								1	1	4
Flavivirus (unspecified)							5		5	42
Adenoviruses										
Adenovirus type 1					4				4	13
Adenovirus type 3					3				3	20
Adenovirus type 6					4				4	5
Adenovirus type 7					2				2	13
Adenovirus type 40								1	1	4
Adenovirus not typed/pending		11			33			3	47	355

Table 3. Virology and serology laboratory reports by State or Territory[1] for the reporting period 21 May to 17 June 1998, and total reports for the year (continued)

	State or Territory[1]								Total this period	Total reported in *CDI* in 1998
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA		
Herpes viruses										
Cytomegalovirus		5			8	1	6	8	29	384
Varicella-zoster virus		11			16	1	9	24	61	634
Epstein-Barr virus	1	18	5		53		10	31	118	890
Other DNA viruses										
Parvovirus					8		10	2	20	87
Picorna virus family										
Echovirus type 4		1							1	2
Echovirus type 11		7							7	23
Echovirus type 17		1							1	1
Echovirus type 22		2					1		3	5
Poliovirus type 2 (uncharacterised)		1							1	2
Rhinovirus (all types)		13			1			14	30	218
Enterovirus not typed/pending		10				1		31	42	239
Ortho/paramyxoviruses										
Influenza A virus		96			105		2	75	278	508
Influenza B virus		2			12				14	89
Parainfluenza virus type 1		8			20			17	45	195
Parainfluenza virus type 2					1			2	3	23
Parainfluenza virus type 3								6	6	195
Parainfluenza virus typing pending						2			2	4
Respiratory syncytial virus		116			26			54	197	513
Other RNA viruses										
Rotavirus		6		2	9	5		60	82	232
Astrovirus							1		1	9
Norwalk agent							4		4	25
Other										
Chlamydia trachomatis not typed		18	125		50	6		160	359	2,115
Chlamydia psittaci							5		5	23
Chlamydia species		9							9	32
Mycoplasma pneumoniae		11	1		26		43	4	85	724
Coxiella burnetii (Q fever)					2		3	2	7	59
Bordetella pertussis							26	13	39	687
Legionella pneumophila					1				1	5
Legionella longbeachae					2			4	6	25
TOTAL	1	350	134	2	394	16	128	536	1,565	9,292

1. State or Territory of postcode, if reported, otherwise State or Territory of reporting laboratory.

Table 4. Virology and serology laboratory reports by contributing laboratories for the reporting period 21 May to 17 June 1998

State or Territory	Laboratory	Reports
New South Wales	Institute of Clinical Pathology & Medical Research, Westmead	176
	New Children's Hosiptal, Westmead	43
	Royal Prince Alfred Hospital, Camperdown	41
	South West Area Pathology Service, Liverpool	97
South Australia	Institute of Medical and Veterinary Science, Adelaide	394
Tasmania	Northern Tasmanian Pathology Service, Launceston	2
	Royal Hobart Hospital, Hobart	13
Victoria	Royal Children's Hospital, Melbourne	71
	Victorian Infectious Diseases Reference Laboratory, Fairfield	56
Western Australia	PathCentre Virology, Perth	310
	Princess Margaret Hospital, Perth	132
	Western Diagnostic Pathology	230
TOTAL		1,565

Table 5. Australian Sentinel Practice Research Network reports, weeks 21 to 24, 1998

Week number	21		22		23		24	
Week ending on	31 May 1998		7 June 1998		14 June 1998		21 June 1998	
Doctors reporting	49		50		50		47	
Total encounters	6,852		6,865		6,085		6,140	
Condition	Reports	Rate per 1,000 encounters	Reports	Rate per 1,000 encounters	Reports	Rate per 1,000 encounters	Reports	Rate per 1,000 encounters
Influenza	44	6.4	51	7.4	64	10.5	80	13.0
Rubella	3	0.4	0	0.0	1	0.2	0	0.0
Measles	1	0.1	1	0.1	0	0.0	0	0.0
Chickenpox	11	1.6	9	1.3	9	1.5	17	2.8
Pertussis	0	0.0	1	0.1	1	0.2	1	0.2
HIV testing (patient initiated)	14	2.0	9	1.3	17	2.8	14	2.3
HIV testing (doctor initiated)	5	0.7	2	0.3	6	1.0	7	1.1
Td (ADT) vaccine	33	4.8	43	6.3	27	4.4	30	4.9
Pertussis vaccination	43	6.3	36	5.2	35	5.8	27	4.4
Reaction to pertussis vaccine	2	0.3	1	0.1	0	0.0	1	0.2
Ross River virus infection	1	0.1	0	0.0	1	0.2	1	0.2
Gastroenteritis	71	10.4	76	11.1	72	11.8	51	8.3

The NNDSS is conducted under the auspices of the Communicable Diseases Network Australia New Zealand. The system coordinates the national surveillance of more than 40 communicable diseases or disease groups endorsed by the National Health and Medical Research Council (NHMRC). Notifications of these diseases are made to State and Territory health authorities under the provisions of their respective public health legislations. De-identified core unit data are supplied fortnightly for collation, analysis and dissemination. For further information, see CDI 1998;22:4-5.

LabVISE is a sentinel reporting scheme. Twenty-one laboratories contribute data on the laboratory identification of viruses and other organisms. Data are collated and published in Communicable Diseases Intelligence every four weeks. These data should be interpreted with caution as the number and type of reports received is subject to a number of biases. For further information, see CDI 1998;22:8.

ASPREN currently comprises about 100 general practitioners from throughout the country. Up to 9,000 consultations are reported each week, with special attention to 12 conditions chosen for sentinel surveillance. CDI reports the consultation rates for all of these. For further information, including case definitions, see CDI 1998;22:5-6.

Additional Reports

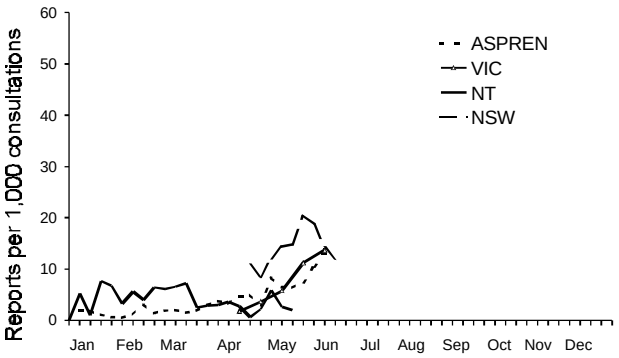
National Influenza Surveillance, 1998

Three types of data are included in National Influenza Surveillance, 1998. These are sentinel general practitioner surveillance conducted by the Australian Sentinel Practice Research Network, Department of Human Services (Victoria), Department of Health (New South Wales) and the Tropical Influenza Surveillance Scheme, Territory Health (Northern Territory); laboratory surveillance data from the Communicable Diseases Intelligence Virology and Serology Laboratory Reporting Scheme, LabVISE, and the World Health Organization Collaborating Centre for Influenza Reference and Research; and absenteeism surveillance conducted by Australia Post. For further information about these schemes, see CDI 1998; 22:83.

Sentinel General Practitioner Surveillance

Consultation rates for influenza-like illness recorded by the ASPREN and Victorian Schemes have been almost twice that of the previous reporting period. New South Wales has had the highest weekly consultation rates for the last month with 20.5 per 1,000 consultations reported for the first week of June (Figure 6). These rates are comparable to those observed for the same period in 1997.

Figure 6. Sentinel general practitioner influenza consultation rates, 1998, by scheme and week



Laboratory Surveillance

There has been a total of 499 laboratory reports of influenza for the year to date. Of these, 437 (87%) were influenza A and 62 (13%) influenza B (Figure 7). The cumulative number of influenza A laboratory reports for the year to date exceeds those for all years since 1993 for the same period. This may reflect an increase in laboratory testing rather than a real increase in the incidence of disease, as a similar rise in reports is not evident in the sentinel practice (ASPREN) data. Ninety-six reports (21%) were for children less than 4 years of age and all but one of these was for influenza A (Figure 8). In the ASPREN scheme children in the same age group accounted for only 5% of all influenza-like illness reports.

The reports of influenza B for the year to date have been approximately one quarter of those for the same period in 1997.

Figure 7. Laboratory reports of influenza, 1998, by type and week of specimen collection

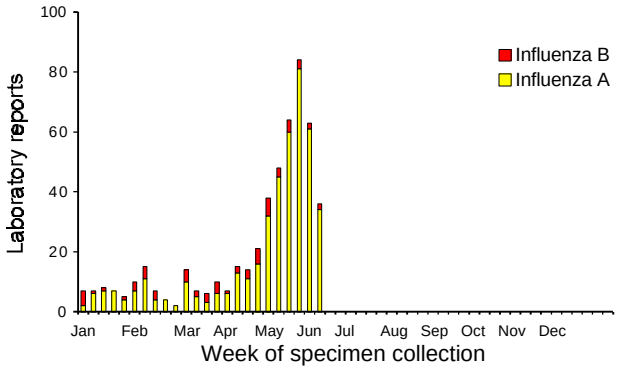
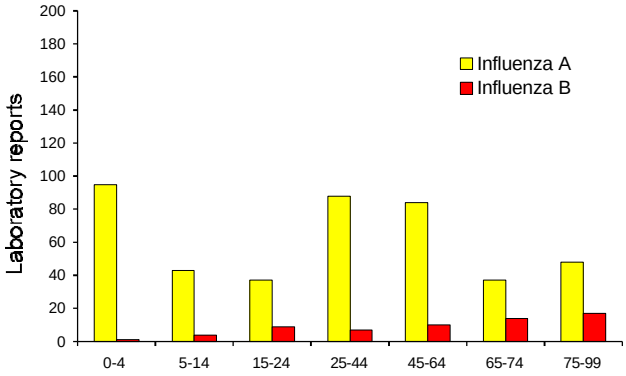


Figure 8. Laboratory reports of influenza, 1998, by type and age group



Absenteeism surveillance

Rates of absenteeism in Australia Post employees for three consecutive days of each week have been reported on a weekly basis since late April. No rise in weekly absenteeism rates have been reported for the year to date.

Sentinel Chicken Surveillance Programme

Sentinel chicken flocks are used to monitor flavivirus activity in Australia. The main viruses of concern are Murray Valley encephalitis (MVE) and Kunjin which cause the potentially fatal disease Australian encephalitis in humans. Currently 26 flocks are maintained in the north of Western Australia, seven in the Northern Territory, nine in

New South Wales and ten in Victoria. The flocks in Western Australia and the Northern Territory are tested year round but those in New South Wales and Victoria are tested only from November to March, during the main risk season.

Results are coordinated by the Arbovirus Laboratory in Perth and reported bimonthly. For more information see CDI 1998;22:7

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Sentinel chicken serology was carried out for 25 of the 28 flocks in Western Australia in April and May 1998. There were two seroconversions in the Wyndham flock in early April, one to MVE and one to Kunjin virus. There were four seroconversions to Kunjin virus in the Kununurra flock, two in April and two in May. One of the May seroconversions has not yet been confirmed. The young boy from a community near Wyndham who had encephalitis caused by MVE virus is still in hospital in Perth, and it now appears that he will be left with severe neurological complications.

Seven flocks of sentinel chickens from the Northern Territory were also tested in our laboratory in April and May 1998. There was one new seroconversion to Kunjin virus in the Katherine flock and one seroconversion to a flavivirus (probably not MVE or Kunjin virus) in the Tennant Creek flock in April. In addition, there were two seroconversions to Kunjin virus in the Gove chicken flock in May, but these have yet to be confirmed.

There were no seroconversions to flaviviruses in chickens tested from Victoria in April or May, and this programme has now finished for the season.

Serious Adverse Events Following Vaccination Surveillance Scheme

The Serious Adverse Events Following Vaccination Surveillance Scheme is a national surveillance scheme which monitors the serious adverse events that occur rarely following vaccination. More details of the scheme were published in CDI 1997:21;8.

Acceptance of a report does not imply a causal relationship between administration of the vaccine and the medical outcome, or that the report has been verified as to the accuracy of its contents.

It is estimated that 250,000 doses of vaccines are administered every month to Australian children under the age of six years.

Table 6. Adverse events following vaccination for the period 28 April to 1 July 1998

	Vaccines											
Event	DTP	DTP/Hib	DTP/OPV/Hib	DTP/OPV/Heb	DTP/OPV	DTP/OPV/Hib/ Heb	MMR	OPV/Hib/Other	Hep B	Other	Reporting States or Territories	Total reports for this period
Persistent screaming	28	2	40		2			1	2		ACT, NSW, NT, Qld, Vic,	75
Hypotonic/hyporesponsive episode	2	1	15	1							ACT, NSW ,SA	19
Temperature of 40.5°C or more	4	1	1								ACT, NSW	6
Convulsions	1	2	4		1	1					NSW	9
Anaphylaxis												
Shock												
Death			1								NSW	1
Other	3		6				1		1	1	ACT, NSW, NT, QLD, SA, Vic	12
TOTAL	38	6	67	1	3	1	1	1	3	1		122

Vaccines - Other includes: influenza, DTPa, CDT, OPV, pneumococcal, BCG, ADT and rabies immunoglobulin (HRIG)

Event - Other includes: lymphadenitis, local reactions, fever less than 40.5°, and non specific events such as vomiting

Results for the reporting period 28 April to 1 July 1998
There were 122 reports of serious adverse events following vaccination for this reporting period (Table 6). Onset dates were from 1995 to 1998, the majority (40%) being in 1998 and 39% in 1997. Reports were received from the Australian Capital Territory (10), New South Wales (59), the Northern Territory (3), Queensland (41), South Australia (5) and Victoria (4). No reports were received from Tasmania and Western Australia for this period. The majority of the reports received from New South Wales were from 1996 and 1997.

The most frequently reported events following vaccination were persistent screaming (75 cases, 61%) and hypotonic/hyporesponsive episodes (19 cases, 16%), followed by other events (12 cases, 10%). One death within 30 days of immunisation was reported from New South Wales. The baby was two months old, and the cause of death was determined to be Sudden Infant Death Syndrome (SIDS) by the coroner.

Nineteen of the 122 cases were hospitalised. There was incomplete information on follow-up of three cases while all of the other cases had recovered at the time of reporting. One hundred and sixteen adverse events (95%) were associated with Diptheria-Tetanus-Pertussis (DTP), vaccine either alone or in combination with other vaccines. Of these, 75 reports were associated with the first dose of DTP and 28 with the second dose.

HIV and AIDS Surveillance

National surveillance for HIV disease is coordinated by the National Centre in HIV Epidemiology and Clinical Research (NCHECR), in collaboration with State and Territory health authorities and the Commonwealth of Australia. Cases of HIV infection are notified to the National HIV Database on the first occasion of diagnosis in Australia, by either the diagnosing laboratory (ACT, New South Wales, Tasmania, Victoria) or by a combination of laboratory and doctor sources (Northern Territory, Queensland, South Australia, Western Australia). Cases of AIDS are notified through the State and Territory health authorities to the National AIDS Registry. Diagnoses of both HIV infection and AIDS are notified with the person's date of birth and name code, to minimise duplicate notifications while maintaining confidentiality.

Tabulations of diagnoses of HIV infection and AIDS are based on data available three months after the end of the reporting interval indicated, to allow for reporting delay and to incorporate newly available information. More detailed information on diagnoses of HIV infection and AIDS is published in the quarterly Australian HIV Surveillance Report, available from the National Centre in HIV Epidemiology and Clinical Research, 376 Victoria Street, Darlinghurst NSW 2010. Telephone: (02) 9332 4648 Facsimile: (02) 9332 1837.

HIV and AIDS diagnoses and deaths following AIDS reported for 1 to 31 January, as reported to 30 April 1998, are included in this issue of CDI (Tables 7 and 8).

Table 7. New diagnoses of HIV infection, new diagnoses of AIDS and deaths following AIDS occurring in the period 1 to 31 January 1998, by sex and State or Territory of diagnosis

										Totals for Australia			
		ACT	NSW	NT	Qld	SA	Tas	Vic	WA	This period 1998	This period 1997	Year to date 1998	Year to date 1997
HIV diagnoses	Female	0	0	0	1	0	0	0	0	1	11	1	11
	Male	0	36	0	10	1	0	8	2	57	77	57	77
	Sex not reported	0	1	0	0	0	0	0	0	1	1	1	1
	Total[1]	0	37	0	11	1	0	8	2	59	89	59	89
AIDS diagnoses	Female	0	0	0	1	0	0	0	0	1	2	1	2
	Male	0	5	0	2	0	0	0	2	9	40	9	40
	Total[1]	0	5	0	3	0	0	0	2	10	42	10	42
AIDS deaths	Female	0	0	0	0	0	0	0	0	0	2	0	2
	Male	0	3	0	1	1	1	0	0	6	28	6	28
	Total[1]	0	3	0	1	1	1	0	0	6	30	6	30

1. Persons whose sex was reported as transgender are included in the totals.

Table 8. Cumulative diagnoses of HIV infection, AIDS and deaths following AIDS since the introduction of HIV antibody testing to 31 January 1998, by sex and State or Territory

		ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Australia
HIV diagnoses	Female	20	538	7	120	51	4	191	82	1,013
	Male	178	10,204	93	1,772	621	75	3,682	840	17,465
	Sex not reported	0	258	0	0	0	0	28	1	287
	Total[1]	198	11,020	100	1,898	672	79	3,911	926	18,804
AIDS diagnoses	Female	7	157	0	44	19	2	62	23	314
	Male	80	4,330	30	753	318	41	1,516	336	7,404
	Total[1]	87	4,498	30	799	337	43	1,585	361	7,740
AIDS deaths	Female	2	112	0	28	14	2	43	15	216
	Male	52	3,034	23	524	215	27	1,198	241	5,314
	Total[1]	54	3,153	23	554	229	29	1,247	257	5,546

1. Persons whose sex was reported as transgender are included in the totals.

Corrections

Vol 22(5):91. **Table 9. Adverse events following vaccination for the period 16 December 1997 to 27 April 1998**. 'Total Death' should read 0, and 'Total Other' should read 25.

Vol 22(6):123. **Table 9. Percentage of children immunised at 1 year of age, preliminary results by disease and State for the birth cohort 1 July 1996 to 30 September 1996; assessment date 30 September 1997**. 'Total number of children Australia' should read 66,195.

Overseas briefs

Source: World Health Organization (WHO)

Enterovirus in Taiwan, China

Enterovirus 71 has been reported as the cause of the enterovirus outbreak in Taiwan, China. Autopsy revealed the presence of enterovirus 71 in the spinal cord and medulla of a fatal case. As of 17 June 1998, the outbreak had claimed 41 lives among infants and children. Health authorities estimate that up to 300,000 infants and children may have been infected with the virus throughout the island. An increased number of children have been hospitalised with aseptic meningitis or encephalitis. Of those hospitalised many had a febrile illness for 2 - 4 days before sudden deterioration and death within 12 - 24 hours.

As there is no vaccine for the virus, the health authorities recommend that parents keep their children away from public places and make sure they wash their hands often to reduce the risk of infection.

Cholera in United Republic of Tanzania

Following the breakdown of the main waterpipe in Dar es Salaam, Kinondoni district, a high number of cholera cases was reported in May. More than 1,000 cases occurred in a single week. Tanzania, where cholera is endemic, has been suffering from a major cholera outbreak since last year. In 1997, a total of 40,249 cases and 2,231 deaths were officially reported to the WHO. This year to 7 June, 11,512 cases and 321 deaths have been registered.

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Contributions

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