

IMAC response to “Just a Little Prick*” by Peter and Hilary Butler

Summary

This work by Hilary and Peter Butler is a summary of Hilary’s personal study and interpretation of orthodox complementary and alternative medical literature, media stories and various expert opinions concerning vaccination interspersed with a variety of personal accounts of adverse events following immunisation. The authors argue that vaccinations are ineffective and unsafe. They also make allegations of health professional, government and industry cover-up and conspiracy-for-profit.

Hilary and Peter Butler also conclude that the impact of mass vaccination programmes on control of infectious disease is overrated. In this work, they are strong advocates for the role of gut flora, mammalian milk and theories of endotoxaemia in the modulation of the immune system, and the use of nutritional supplementation for the treatment and prevention of infectious illnesses. A premise of the book is that the low probability of contracting a vaccine-preventable disease and the risks of vaccination render mass immunisation programmes both unnecessary and dangerous.

The authors make a wide variety of claims, and a full discussion and response to them are beyond the scope of this critique. IMAC’s position on this work includes points of agreement and disagreement.

Points of agreement with the authors are the following:

- 1) Nutrition, hygiene, sanitation and socio-economic disparities play an important role in both the spread and control of infectious diseases and are an integral part of health interventions to control infectious disease within populations and among individuals.
- 2) Breastfeeding reduces the incidence and impact of some infectious diseases in infants and should be actively promoted.
- 3) There is some evidence to suggest environmental factors such as sleep deprivation, psychological state and environmental toxins may affect immune response to both natural infection, and, in some cases, to vaccination. (Current evidence does not, however, indicate that vaccination is unsafe or ineffective in such situations, or that, as the authors imply, vaccinations are causative mechanisms for infectious disease).
- 4) In the light of current evidence, mass BCG vaccination is untenable as a strategy for the prevention and control of tuberculosis in New Zealand. (However, we would disagree that selective BCG immunisation is unjustified on the basis of current evidence).

IMAC finds the following claims that are put forward to be unsubstantiated by current evidence from orthodox medical literature (addressed in subsequent sections):

- 1) Pertussis vaccination is ineffective and unsafe.
- 2) Meningococcal vaccination is unnecessary because *N. meningitidis* is carried asymptotically in most people.
- 3) Hepatitis B immunisation is dangerous, unnecessary, and is the cause of a number of idiopathic illnesses.
- 4) Influenza immunisation is ineffective and unsafe.
- 5) MMR vaccination is unsafe and measles infection is harmless.
- 6) Varicella is harmless.
- 7) Oral polio vaccine is ineffective in preventing the transmission of polio.
- 8) Diphtheria immunisation is ineffective.
- 9) Vaccines contain toxic compounds, including aluminium, thiomersal, and viruses.
- 10) Vaccination may pre-dispose to *E. coli* endotoxaemia.
- 11) Nutritional therapy, including high-dose vitamin therapy, prevents infection.

- 12) Advice obtained from IMAC is biased because IMAC receives funding from pharmaceutical companies that manufacture vaccines.

In summary, while the authors raise some valid points, IMAC's interpretation of the available evidence from orthodox medical literature does not support many of the arguments used by the authors to reach their conclusions, and are, in our opinion, misleading. IMAC also wishes to clarify our sources of funding and re-emphasise our independence from commercial conflicts of interest.

Throughout the article, links to personal accounts of vaccine-preventable diseases are also provided.

* Butler P, Butler H, Just a Little Prick, RRMT, Auckland, 2006

Nutrition, sanitation, industrial pollution, socioeconomic factors, psychosocial state and infectious disease control

A comprehensive review of the interaction of these factors on the immune system and the spread of infectious diseases is beyond the scope of this critique. In her chapter entitled, "What causes sickness" Hilary Butler rightly points out that a variety of host-environment interactions influence an individual's immune response to infection. She then cites various examples to supposedly demonstrate why vaccination is therefore not as "necessary" as she perceives the Ministry of Health and the medical profession state it to be. Citing an article from New Zealand Woman's Weekly on centenarians in ex-Soviet Georgia to draw together the threads of material she has presented in the chapter, Hilary Butler lauds these individuals as "an example of eating right, living right, loving right to make our genes work right." The fact that they inherited good genes to start with is overlooked.

Evidence from orthodox medical literature would agree that there are a number of host and environmental factors that influence infectious disease mortality and morbidity. Changes in standard of living, including provision of sewerage, limit the spread of infections via the faecal-oral route. For example, rates of childhood exposure to hepatitis A virus are lower in countries with developed economies than in countries with developing economies, as can be demonstrated by the epidemiologic changes in parts of Brazil as hygiene improved(1). (Ironically, vaccination against polio may now be more "necessary" since a greater proportion of the adult population will not have been infected with polio during childhood and are therefore at increased risk of paralytic polio if they contract polio as an adult.)

Some vaccine-preventable diseases, however, continue to circulate despite improvements in living conditions. For example, measles and pertussis are highly infectious and persist despite the reduction of household overcrowding. US data from 1900 until 1974 demonstrates increased rate of decline in pertussis mortality as a result of pertussis vaccination. Had the rate of decline continued as it had between 1900 and 1939 when pertussis vaccination was not undertaken in the US, there would have been approximately 8000 deaths between 1970-1974 compared to the 52 that actually occurred (2).

Changes in the standard of living have undoubtedly reduced the incidence of, and complications from, infectious diseases, but it would be difficult to conclude from current evidence that these improvements alone are responsible for the dramatic reduction in infectious disease rates. Despite the relatively well developed infrastructure in New Zealand (housing, sewerage, etc.) measles has not been eliminated and epidemics still regularly occur(3). Mathematical modeling from a mass immunisation campaign in New Zealand suggests that mass vaccination prevented 90-95% of cases (3).

Hilary Butler rightly uses a number of examples to demonstrate the importance of adequate nutrition in the reduction of morbidity and mortality due to infection, for example vitamin A deficiency and measles. The authors also mention in passing the possible health benefits of probiotics. The Australian College of Paediatrics also supports the use of vitamin A supplementation in New Zealand and Australian infants hospitalized with measles **when there is pre-existing marginal nutrition or vitamin A deficiency in the patient or their community**, as well as for older patients with certain medical conditions(4). Again, Butler rightly states that deficiencies of micronutrients, including selenium and vitamin C, may predispose to infection. What the authors neglect to mention is that the current evidence demonstrates alteration of immune system parameters due to micronutrient deficiency for the most part *in the context of protein-energy malnutrition* (5, 6). It would be difficult from current evidence to generalise this to individuals within countries with developed economies such as New Zealand, where protein-energy malnutrition is rare. The recent childhood nutrition study shows such deficiencies in New Zealand children is rare(97).

Similarly, a review of the evidence for probiotics indicates some efficacy in the prevention of viral diarrhoeal illnesses and antibiotic-associated diarrhoea. However, the authors also state that "clinical testing has focused mostly on immune cell levels and not on actual incidence of

the disease...Thus it is difficult to extrapolate results from immune function studies to the expected effects on human health”(7).

Hilary Butler also states that “it has long been proven that bad nutrition and environmental toxicities can be the cause of a malfunctioning immune system”. Exactly what does orthodox medical literature say on this topic? Studies of the effects of particulate air pollution on children and infants do demonstrate adverse effects on lung function and bronchial reactivity(8). This certainly predisposes such individuals to complications due to respiratory tract infections from compromise to non-specific immune defenses in the lung, similar to the way Chronic Obstructive Pulmonary Disease (COPD) patients are more susceptible to complications from influenza. This does not necessarily preclude the individual developing a specific immune response to an infective agent (much as a person with COPD can develop protective antibodies to influenza virus after natural infection or vaccination).

Animal studies, human cell studies and some case reports do associate heavy metals(9), volatile industrial compounds(10), pesticides(11) and environmental oestrogens(12) with changes in immune system functioning. However, on the basis of current evidence it is unclear whether such “immunotoxicity” actually increases susceptibility to infectious diseases. How this data might apply to possible environmental exposures in a New Zealand context remains unclear. At present, all that can be said is there is some rationale for reducing exposure to these chemicals (which is in agreement with the views of the authors), but whether they predispose populations or individuals to infections remains controversial.

Similar conclusions can be reached about psychosocial factors and immunity. Sleep deprivation has been shown to induce changes in cell-mediated immunity, and in animal studies, chronic sleep deprivation predisposes to increased risk of adverse outcomes in septicemia. Again, the implications of these changes in humans are unclear(13,14). Psychological stress can exert neurohormonal effects on macrophage and neutrophil function and many components of the immune response to an infectious insult(15). Psychosocial factors may also alter the magnitude and time-course of the antibody response to vaccination (16,17). However, none of the evidence from psychoneuroimmunology at present would indicate that infectious disease incidence can be reduced by alleviating psychosocial stressors alone.

In summary, it is clear therefore that a number of factors affect immune response to infectious organisms, and can have marked effects on infectious disease morbidity and mortality. Therefore orthodox medical opinion would support the use of socio-environmental and lifestyle modification for the prevention and control of infectious diseases. It must be noted, however, that the above phenomena are risk rather than causative factors for infectious disease and that strategies to address the above factors do not in themselves provide individuals with specific immunity to certain infectious agents or prevent the circulation of an organism within a community. Vaccination has the potential, and in some cases has demonstrated the ability, to offer both.

Breastfeeding

Breastfeeding is a well-established preventative intervention for providing infants with protection against a variety of infectious diseases including diarrhoeal illnesses, respiratory tract infections, otitis media, urinary tract infection, neonatal septicemia and necrotizing enterocolitis(18). Breastfeeding may also provide passive immunity to vaccine preventable diseases such as *Haemophilus influenzae* type B(19) and measles(20). Hilary Butler rightly points out that factors in breast milk may enhance the immune response to both vaccination and natural infection.

Two important concepts about breastfeeding which the authors do not clearly state must be emphasized. Firstly, the immunity acquired by breastfeeding is a passive transfer of antibody (provided the mother has developed antibodies and they are secreted in the breast milk) that demonstrates a tendency to decay more rapidly relative to the active immune response

created by natural infection or a primary course of infant immunisation(3). Secondly, there is no evidence to suggest that vaccination in formula-fed or partially breastfed infants is unsafe or less effective. Primate studies and trial data from an oral rotavirus vaccine currently being evaluated do not suggest significant differences in antibody response to vaccination(21). Formula feeding itself is not a contraindication to any vaccination currently licensed in New Zealand(3). Current insights into the immunoprotective effects of breastfeeding suggest that infants under 6 months of age who are not predominantly breastfed are more prone to infection, and therefore as a population may derive more short-term benefit from immunisation when compared to their exclusively breastfed counterparts.

BCG Vaccination

The authors are correct to point out that the issue of BCG vaccine efficacy is controversial and that BCG possibly has no effect on the incidence of tuberculosis other than in neonates – see below(3). Considering the risks and benefits of BCG vaccination, the authors are correct to point out that mass BCG vaccination is not currently justified in the New Zealand context, and this is the position of the Ministry of Health(3). There is evidence from meta-analysis that BCG vaccination has a role in the protection of neonates from serious extrapulmonary complications of tuberculosis(22).

There is also some evidence that BCG immunisation prevents leprosy(23). There is therefore some justification for the practice of selective BCG vaccination in New Zealand as the disease is sometimes imported into this country. To write off such research as the medical profession conducting a “last-ditch stand to retrieve something from the mess of misinformation” as the authors have done is an unfair criticism. The current situation should be portrayed as willingness by the medical profession to re-examine and modify practice in the light of new evidence.

Tuberculosis – Pauline’s Story: <http://www.immune.org.nz/?t=704>

Pertussis vaccination effectiveness

Hilary Butler argues that pertussis vaccination is ineffective as “most cases occur in fully vaccinated children”, and that the “medical profession will have to admit that the pertussis vaccine never prevented spread of whooping cough”. Confusingly, she also contradicts herself later in the same chapter by implying that since the institution of mass pertussis vaccination, there are fewer children being infected or re-infected with pertussis: “Before vaccines a person got one significant clinical attack of pertussis between the ages of 3 and 11. There may have been regular minor infections through the later years that looked like bronchitis, but long-term immunity was reinforced by regular exposure to circulating bacteria. With increasingly unpredictable gaps between natural exposure, it is now commonplace overseas for adolescents and adults to get the actual clinical disease several times.” It would seem then, that Butler admits pertussis vaccination has had at least some effect on reducing pertussis transmission in the community.

The apparent confusion and misperception can be easily clarified by understanding a few aspects of both the natural history of pertussis and the characteristics of the vaccine.

Pertussis is highly infectious and is spread by respiratory droplets. A high proportion of non-immune contacts of an individual infected with pertussis are likely to acquire the disease. Infants have a tendency to develop severe disease, whereas in older children, adolescents and adults the disease is typically milder and often indistinguishable from other viral respiratory tract illnesses. Whooping is unusual in adults and uncommon in infants. Immunity is not life-long. Infection, and possibly reinfection with pertussis during adolescence and adulthood was common, even in the prevaccine era(24).

Optimal immune response to currently available pertussis vaccination has a protective efficacy of 84% after a 3-dose primary series is completed(25). Immunity from vaccination appears to be sustained for at least 6 years, but is thought to wane thereafter(26).

Two practical difficulties arise as a result of this current understanding. Firstly, to increase the likelihood of achieving protection against pertussis for infants requires a high rate of timely completion of the whole primary series (incompletely vaccinated children will have a probability of being immune to pertussis which is less than 84%). New Zealand has relatively low rates of completion of on-time immunisation against pertussis (3). Secondly, if the immune response to pertussis vaccination or infection decreases over time, immunity against pertussis developed as an infant is likely to wane in mid to late childhood in the absence of boosting from either vaccination or natural infection. In the absence of sustained immunity, older children, adolescents and adults are therefore likely to remain a reservoir of infection. This infection can be passed to other infants and susceptible individuals; either those unvaccinated, those partially vaccinated, the 16% of individuals who were fully vaccinated but did not acquire protection (100%-84%) and those who are no longer immune because of the waning antibody response to vaccination over time. It is therefore not surprising that epidemics continue to occur regularly in New Zealand(3). An Auckland study found that children who received their pertussis immunisations late were 4-6 times more likely to be admitted to hospital with the disease than those who received their immunisation on time(92).

Application of simple arithmetic will also demonstrate the presence of a relationship between vaccine effectiveness, immunisation coverage and infection. Taking the pertussis vaccination as an example and using an effectiveness figure of 85% for convenience, imagine a group of 100 children. If 60% of children are given a pertussis vaccine that is 85% effective, then:

- 51 of the hundred children will be immune (60 x 85%)
- 49 will be non-immune.
 - 40 who are not vaccinated
 - 9 because of vaccine failure.

Therefore 18% (9 out of 49) cases of pertussis could conceivably occur in fully vaccinated children. If the proportion of vaccinated children is changed to 90%, then:

- 76 of the 100 children will be immune (90 x 85%)
- 24 will be non-immune
 - 10 who are not vaccinated
 - 14 because of vaccine failure

Now, 58% (14/24) cases of pertussis could conceivably occur in fully vaccinated children. More of the population as a whole is immune to pertussis in the scenario with higher vaccination coverage, even though most cases occur in the vaccinated group. The logical conclusion that can be drawn from this analysis, is not that pertussis vaccination does not work, but that as vaccination rates increase a greater proportion of cases are seen in those fully vaccinated.

A combination of both high rates of on-time completion of the primary course of immunisation and regular booster doses of pertussis vaccination throughout childhood, in adolescence and possibly in adults is likely to be required to optimize pertussis control within a population, and this is the rationale for the current pertussis immunisation schedule and recommendations in New Zealand (3).

In summary, pertussis epidemics continue to occur not due to an ineffective vaccine, but because of ineffective uptake and use of the vaccine. The author's arguments against pertussis immunisation are akin to asthmatics who do not take their inhaled corticosteroids as prescribed and then decide that because their asthma symptom control does not improve, inhaled steroids do not work.

Pertussis vaccine safety

Interspersed throughout the book are a number of personal stories, including accounts from parents of their children dying from SIDS or developing various types of neurological injury.

Frequent mentions are made of how these conditions become apparent after the receipt of pertussis-containing vaccinations (and others too). Although not explicitly stated, the implication is that vaccination is responsible for a variety of reactions, and according to the author includes “hives, broncho-oedema, seizures, and encephalitis-type reactions.”

As well as taking into consideration trial data both during vaccine development and after licensure and use, there are processes in New Zealand (and many countries overseas) for the reporting and investigation of adverse events following immunisation(3). An adverse event following an immunisation may be caused by the vaccine or occur co-incidentally. For example, a fever that develops after immunisation may be a reaction to the vaccine or a consequence of a viral illness acquired around the time of vaccination. For an event to be associated with vaccination there must be a statistically significant increase in rates of the event in a vaccinated population compared to a comparable unvaccinated population. This has not been demonstrated for immunisation (including pertussis-containing vaccinations) and SIDS and several studies suggest that immunisation may protect against SIDS(26, 93-96).

The relationship of pertussis vaccination to brain damage is somewhat more controversial. An independent review of a large British study found that the evidence suggests an association between **whole cell** (which is no longer used in New Zealand) pertussis vaccination and acute encephalopathy. The reviewers noted that there was evidence showing that some children in the original British study who had suffered acute encephalopathy were found to have long-term neurological consequences whether they were from the vaccinated or unvaccinated group. The reviewers therefore concluded that the evidence may be consistent with a link between whole cell pertussis vaccination and chronic nervous system dysfunction “described by the [British study] in those children who experience a serious acute neurological illness within 7 days of DPT vaccination” (27). The NZ Immunisation Handbook(3) summarises the arguments against a link as understood by the current medical evidence, namely:

- Brain damage and forms of developmental delay become apparent in the first 1-2 years of life – the same time immunisations are scheduled.
- No specific type of brain damage has been linked to whole cell pertussis vaccination.
- Studies are cited which find no association with neurological illness.
- Studies on acellular pertussis vaccination (now the only form administered in New Zealand) show no association with neurological illness.

When considering the risks and benefits of immunisation, it is important for an individual, or in the case of a child, the caregiver, to have some way of gauging the risks of catching the illness and the risks associated with vaccination. Peter and Hilary Butler imply that encephalopathy from whooping cough is rare and therefore risking side effects from pertussis vaccination is unnecessary. To evaluate this argument, one must consider the prevalence of pertussis in New Zealand, the probability of developing complications from natural infection and compare this to the probability of developing complications from vaccination.

New Zealand data for infants under 1 year of age during the last epidemic suggests a disease rate of 327.5 per 100,000(3). Approximately 5% or 5000 per 100,000 of infants develop encephalopathy from the disease(28). Therefore, leaving it to chance alone, there is a 16 in 100,000 chance (5% x 327.5 per 100,000) of acquiring encephalopathy due to pertussis infection. The rate of acute encephalopathy from whole cell pertussis vaccination is at most 0.9 per 100,000 and for permanent brain damage 0.32 per 100,000(3) (and for acellular pertussis vaccines zero for both). Even when the data for whole cell pertussis vaccination is used, careful examination would show it is much “safer” (in terms of statistical probability) to vaccinate infants against pertussis rather than leave things to chance. Importantly - New Zealand uses acellular pertussis vaccine. **Acellular pertussis vaccination is not associated with permanent brain damage.**

Pertussis – Anna’s Story: <http://www.immune.org.nz/?t=696>

Meningococcal vaccination

Hilary Butler dismisses any need for meningococcal vaccination. “It’s not rocket science. But not even the media can do simple maths and ask why that, if the bacterium is so common, it does nothing to most people most of the time and suddenly descends like a relatively predictable axe on a few specific individuals.” The overall rate of meningococcal disease between 1991 and 2000 in New Zealand was 13.9 per 100,000, with a case fatality rate of 4%(29). Prevalence of meningococcal carriage is approximately 10%(30), however, the dynamics of carriage and the progression to disease are not well understood(31). Contrary to Hilary Butler’s assertions, on the basis of our current understanding of meningococcal disease, it is not possible to “predict” with accuracy who will acquire the organism (carriage), and which individuals who become carriers will develop meningococcal disease. Cases commonly occur in healthy individuals with none of the individual and socioeconomic risk factors that Butler alludes to. For example, New Zealand epidemiology demonstrates two peaks with increased disease rates in 15-19 year olds(29) (who carry a relatively low burden of ill health in general).

Contrary to the authors’ claims, MeNZB™ has not been associated with an increased death rate among vaccinated individuals after review by an independent safety monitoring board(32). Out of 3 million doses, only 9 episodes of anaphylaxis were noted (all were resolved without complications). The vaccine has not been associated with increased rates of chronic fatigue. Early data indicates that cases of the epidemic strain in the Northern region of New Zealand have fallen by 76% between 2003 and 2005(33). Common sense would therefore suggest that in the light of our current understanding, meningococcal vaccination is the best preventative strategy available at present.

The authors also unfairly accuse the medical profession of failing to address individual and socioeconomic risk factors for meningococcal disease. The Government’s infectious disease strategy for 2002-2006 includes a commitment to addressing such risk factors (34). As outlined in above sections, modifying individual and socioeconomic risk factors for infectious disease are also a cornerstone of good preventative medical care.

Meningococcal B disease: Donnea’s and Gemini’s stories.
<http://www.immune.org.nz/?t=702>

Hepatitis B vaccination

In her chapter entitled “Hepatitis B, a runaway publicity train”, Hilary Butler uses a variety of different sources to create the argument that hepatitis B vaccination is unnecessary, as a) the vaccine does not provide protection against hepatitis B infection; and b) the majority of the population was unlikely to acquire hepatitis B infection. Later in the book she attributes a number of idiopathic illnesses to hepatitis B vaccination; a view point that has no scientific support.

As with her arguments against pertussis vaccination, her claims appear compelling until the characteristics of both the natural history of the disease and the vaccination are understood.

Hepatitis B virus can be transmitted vertically (mother to neonate), or horizontally (person-to-person) through contact with infected body fluids (blood, semen, vaginal fluid, etc.). Three major patterns of infection are seen in Asia and the Western Pacific: vertical transmission at birth, infection acquired in childhood, or adolescent and adult transmission due to lifestyle practices(35). In the pre-vaccination era, transmission occurred commonly among school-aged children in New Zealand, although the exact mechanisms are unclear(3). It has been demonstrated that dried hepatitis B-infected blood can remain infectious for a week(36). Hepatitis B infections acquired in infancy and childhood have an increased risk of developing a chronic carrier state that is a major risk factor for cirrhosis and hepatocellular carcinoma

(liver cancer)(37). Contrary to Hilary Butler's claims, hepatitis B is an independent risk factor for cirrhosis and hepatocellular carcinoma. The effects of alcohol are additive, but not necessary, for the development of hepatocellular carcinoma (38).

The rationale for the practice of hepatitis B vaccination in New Zealand, therefore, is to reduce the risk of:

- Vertical transmission of the virus at birth from carrier mothers
- Horizontal transmission among children (particularly those of school age)
- Horizontal transmission among adolescents and adults due to lifestyle and occupational practices
- Spread from carriers to their household and sexual contacts.

Hilary Butler states that "The Health Department's view is that blood testing was expensive and not worthwhile because the vaccine the Government was buying was so cheap. In other words, they had little interest in finding carriers." This is quite the opposite of the actual intentions of the Hepatitis B screening programme, which aimed to find carriers (to whom the vaccination is of no use and in whom vaccinating creates a false sense of security), treat those infected and reduce the risk of their close contacts acquiring hepatitis B infection(39).

Examination of efficacy data on hepatitis B vaccination demonstrates that a primary course of vaccination when administered with hepatitis B immunoglobulin in neonates provides 80-97% protection against infection(40). Protective antibody levels are reached in 95% of New Zealand children, although vaccine response is lower in adulthood (approximately 70% in adults over 40 years). There is also some evidence for achieving a response in persistent non-responders through booster vaccinations, repeat primary courses or different methods of vaccine administration(41).

From this brief survey of the epidemiology of hepatitis B and the efficacy of the hepatitis B vaccine, the rationale behind the current strategy of universal infant immunisation and birth doses for infants of carrier mothers as well as selective immunisation of at risk groups, is obviously the optimal strategy to achieve control of hepatitis B in New Zealand.

Contrary Butler's claim, hepatitis B vaccination has not been linked to MS (42), chronic fatigue syndrome(43), diabetes(44), and suicide, AIDS, RSV or GBS (45). Rarely, hepatitis B vaccination may cause thrombocytopaenia which can be treated with corticosteroids and does not pre-dispose to thrombocytopaenia from other vaccinations(46). There are some case reports of a temporal relationship between hepatitis B vaccination and arthralgia (joint pain), however, a causal relationship between the two is not proven(47). Current evidence therefore supports the safety of hepatitis B vaccination.

Hepatitis B – Jennifer's Story: <http://www.immune.org.nz/?t=697>

Influenza vaccination

The authors are correct in stating the rare association between swine influenza vaccination (no longer used) and Guillain-Barre Syndrome (GBS)(48). The risks of GBS for the currently available influenza vaccination are in the order of 1 per million doses in individuals over the age of 45 years if such a relationship exists(49). New Zealand hospital data does not indicate an increase in hospital admission rates for GBS during the 1990s despite marked increases in influenza vaccine use(3).

The issue of influenza vaccination efficacy and how influenza vaccination programs should be implemented is not as simplistic as Hilary Butler portrays it to be in her chapter entitled "So does the flu vaccine work?". She states "it has never been the intention of the Influenza planners to aim for anything other than vaccinating everyone against influenza no matter what the efficacy isn't".

An important practical difficulty in influenza vaccination is the changing nature of strains. Effectiveness of the vaccine varies widely according to how much the circulating virus changes compared to the virus in the vaccine formulation. Vaccine effectiveness is maximal if the circulating virus strains and the vaccine strains are identical or similar, however, its efficacy may be nil if the circulating strains and the vaccine strains are vastly different. On the basis of current knowledge, it is not possible to predict with certainty which strains are likely to circulate in the community for the season. The other difficulty is that the vaccine's efficacy and effectiveness, including the benefits of influenza vaccination, are different for different population groups (50).

A brief summary on the current status of evidence for the use of influenza vaccination in the following population groups is as follows:

- A cost-effective measure for reducing absenteeism and production loss in healthy adult workers(51).
- Vaccination of health-care workers to reduce the risk transmission to patients at risk from serious complications related to influenza virus infection (52).
- Reduction in influenza-related hospital admissions and influenza-related mortality in elderly persons over the age of 65 years has been observed in observational studies and some randomized trials(53).
- Beneficial effects in some individuals with chronic disease:
 - Reduces acute exacerbations in COPD patients(54).
 - Reduces cardiovascular morbidity and all-cause mortality in patients with cardiovascular disease(55).
 - Reduces hospitalization in patients with diabetes during seasonal epidemics(56).
 - Increased survival in patients undergoing chemotherapy (with no increase in serious side effects)(57).
 - Adequate antibody response and possible protection against influenza in dialysis patients with chronic renal failure(58).
- Reduction in episodes of febrile respiratory illness and possibly influenza in healthy infants aged 6-24 months. Conflicting evidence for effectiveness against acute otitis media(59).
- Reduces the rate of laboratory-confirmed influenza and secondary acute otitis media in healthy school-aged children and may reduce transmission of influenza within the entire community(60).
- Reduces healthcare utilization in pregnant women due to influenza-like illness(61).
- No increase in asthma exacerbations after vaccination in asthmatics. Theoretical benefits of vaccinating individuals with severe asthma, including observational studies have not been conclusively established in clinical trials or meta-analyses(62).
- May reduce risk of stroke during the influenza season, including those individuals with TIA or previous stroke(63).
- The effects of influenza vaccination (if a suitable vaccine was available) during an influenza pandemic are not clear from the current orthodox medical literature(64).

From this brief overview of the current evidence, it is clear that influenza vaccination does have a variety of beneficial effects which differ for different population sub-groups. Hilary Butler's implied thesis that influenza vaccination does not work are therefore inaccurate. It is not surprising, however, that there is a lack of expert consensus on the most effective influenza vaccination strategy and that different countries have chosen different policies for influenza vaccination programs.

Influenza – Ida and Maude's stories: <http://www.immune.org.nz/?t=703>

Measles and MMR vaccination

Hilary Butler first presents data from a variety of sources to suggest that MMR vaccination was not necessary and that MMR campaigns in New Zealand did not prevent the 1997 measles epidemic. "Their predictions of a huge epidemic were grossly exaggerated, and

subsequent claims that the vaccination campaign prevented an epidemic of the scale they predicted are logically unsustainable.” She then argues that “nutrition and lifestyle dramatically change the equation of personal risk versus benefit for every individual and society as a whole”, implying that vaccination is unnecessary for healthy New Zealand children.

Hilary Butler’s use of figures from the 1991 New Zealand measles epidemic and the mass vaccination campaign in New Zealand to argue against measles vaccination in her chapter “Measles 1985-1998” are taken out of context, or data are not examined carefully. For example, the figure of “94.7% community immunity” ignores the subsequent analysis of school-aged children presented in the same paper which showed a lower rate of 85.5% protection against measles infection in the population under 20(64). Susceptible individuals in a population with low inter-epidemic natural measles transmission such as New Zealand will accumulate as a result of both non-vaccination and primary vaccine failure.

As measles vaccine uptake in New Zealand has increased, the interval between epidemics has continually increased, however there is a propensity for the age-distribution of cases to shift towards older, European children (contrary to the author’s arguments that measles is only an important disease in Maori and Pacific children)(3). There were 7 deaths and 10 cases of measles encephalitis in the 1991 measles epidemic(65). Mathematical modeling based on New Zealand data was used to correctly predict a measles epidemic in 1997(65, 66), and, based on calculations from the model, the MMR campaign initiated prevented at least 90% of cases(65).

Additional updates to the mathematical model demonstrated that by changing the MMR schedule such that the course was completed before school entry (as is the case with the current schedule) would further increase the interval between measles epidemics and possibly eliminate them altogether if measles immunisation coverage was sufficiently high(67). Butler also quotes a story of a family whose children were vaccinated who are said to have measles as an example of how measles vaccination does not work. It is important to note that in around 2% of cases MMR vaccine causes a mild rash and/or fever(68), which may be confused with measles.

Current evidence therefore, indicates that predictions of measles epidemics were not at all exaggerated and that measles immunisation has made a significant impact on rates of measles in New Zealand.

What of Hilary Butler’s arguments that, in general, measles is a harmless illness in children? While it is true that measles is generally a mild illness in healthy children, it would be important to note that over half of children who died from measles in the UK between 1970 and 1983 were previously healthy(69). A variety of clinical conditions also increases the risk of complications of measles (70), and therefore indicates the need to reduce transmission of measles within the community.

Hilary Butler then adds two personal accounts of children whose deterioration in health appears to be temporally related to MMR vaccine. The title of the chapter of the first account “collateral damage” implies that the vaccine is responsible for the health problems detailed in both children. In the first account, the child died of an acute encephalopathic illness. Although no cause for death is stated and the medical records are not presented, it must be noted that the addendum indicated a positive test for Coxsackie virus, known to cause viral encephalitis. In the second story, a mother recalls the onset of her son’s developmental delay which appears to have become apparent after MMR vaccination. In the absence of medical details of the case, it is difficult to comment on the role or otherwise of MMR vaccination as a causative factor in the illnesses suffered by these children.

Data from the US indicates a statistically significant association between encephalopathy and MMR vaccination at 8-9 days. There were 48 cases out of an estimated 75 million MMR doses, giving a rate of <1 per million doses(71), however a recent US study failed to find a

relationship between MMR and encephalopathy(72). If such a relationship exists, this compares quite favourably to a rate of encephalitis of 1 per 1000 or (1000 per million) in natural measles infection(73). The link between MMR and autistic spectrum disorders has been widely disproved (74, 75).

Measles – Foufou Susana’s Story: <http://www.immune.org.nz/?t=699>

Mumps – John’s Story: <http://www.immune.org.nz/?t=700>

Rubella – Beth’s Story: <http://www.immune.org.nz/?t=701>

Varicella

Peter Butler extols the benefits of “an all-embracing life-style – including chickenpox.” It is true that varicella infection is usually a mild and self-limiting illness in children, however, risk of severe disease and complications are greater in neonates, adolescents, adults and immunosuppressed individuals. Between 150 and 200 people are hospitalized each year in New Zealand with chickenpox. Complications of the infection can include cerebellar ataxia, pneumonia and super-infection with Group A streptococci. Pregnant women who acquire varicella infection are at increased risk of birthing a child with congenital varicella syndrome. Reactivation of latent varicella infection in the elderly and immunocompromised causes considerable morbidity due to shingles(76). In the US, routine varicella immunisation has reduced varicella-related hospital and ambulatory care admission rates(77). There is some evidence for the cost-effectiveness of selectively vaccinating adults susceptible to varicella, especially healthcare workers and some immunocompromised patients(78).

Varicella – Anna and Lily’s story: <http://www.immune.org.nz/?t=708>

Oral Polio Vaccine

In her chapter “informed choice- the key concept”, Hilary Butler cites a Ugandan radio broadcaster to supposedly demonstrate that oral polio vaccine (OPV) causes children to “die in droves”. Evidence from West Africa actually indicates mortality reductions from the use of OPV(79)

OPV is used in some countries overseas where wild-type poliovirus still remains endemic.. The OPV vaccine virus tends to circulate in the community, and very rarely can cause vaccine-associated paralytic polio (VAPP). There is little doubt that OPV has been largely responsible for the huge reduction in polio cases world wide. Once wild-type virus transmission is eliminated or sufficiently contained within a region, inactivated polio vaccine (IPV) may be used as the vaccine virus does not circulate in the community or carry the risk of VAPP. The WHO continues to closely monitor the circulation of vaccine-derived polioviruses in countries that use OPV(80).

OPV is no longer used in New Zealand, as the Western Pacific is free of endemic polio. The inactivated polio vaccine used in New Zealand (to protect individuals in the event of a case of imported wild-type polio) carries no risk of VAPP(81).

Polio: Sheryl’s Story: <http://www.immune.org.nz/?t=705>

Diphtheria Vaccination

Hilary Butler believes diphtheria immunisation to be an ineffective strategy for the prevention of diphtheria. In regards to the diphtheria epidemic, she states that “contrary to publicity, the highest rates of deaths occurred in predominantly well-vaccinated people who became

susceptible, not through lack of vaccines, but because of war, social dislocation, food shortages.” While socioeconomic factors appeared to contribute to the spread of diphtheria in the former Soviet Union (81), it can be demonstrated that a large proportion of the adult population was susceptible to diphtheria through waning immunity(82). The effectiveness of diphtheria vaccination in controlling this epidemic was demonstrated in a Ukrainian case-control study(84). In developed countries, mass diphtheria immunisation has conferred herd immunity and reduced transmission of diphtheria. The decline in diphtheria cases was accelerated by mass immunisation(85). A good case can therefore be made for vaccination against diphtheria.

Diphtheria – Joy’s Story: <http://www.immune.org.nz/?t=707>

Aluminium, thiomersal, and viral contamination of vaccines

Hilary Butler states that vaccine manufacturers and the medical profession “haven’t tested the toxicity of adjuvants and other compounds in vaccines, because they assumed there was none.” In the book concerns about the safety of aluminium and thiomersal are raised. The safety of both compounds has been examined and established:

- Aluminium levels in vaccination do not exceed currently accepted safe levels in humans. Humans absorb more aluminium from the food chain than vaccination. The aluminium from vaccines is excreted soon after vaccination(86). Aluminium use has a 70 year safety record.
- Thiomersal - a previous IMAC publication thoroughly addresses the safety of thiomersal (no longer used in childhood vaccinations in New Zealand). This document can be downloaded at <http://www.immune.org.nz/?t=721> .

The author also suggests that vaccines are contaminated with harmful viruses, including SV40 virus and the so-called “stealth virus”. Some polio vaccine batches in the 1950’s and 1960’s were contaminated by SV40 virus. Since 1963, manufacturing processes have eliminated this virus as a contaminant(3). Long-term follow-up of a vaccinated cohort exposed to SV40 virus has not demonstrated an increased rate of cancer(87). The FDA also considers there to be an absence of evidence for contamination of any vaccine with the so-called stealth virus, a cytopathic variant of Cytomegalovirus (CMV) that has been found in patients with chronic fatigue syndrome, neuropsychiatric and autoimmune diseases, as well as in apparently healthy individuals(88). Notably, vaccination has not been linked to Chronic Fatigue Syndrome(43).

Vaccination and *E. coli* endotoxaemia

Hilary Butler suggests a link between infant immunisation (particularly pertussis vaccination) and *E. coli* endotoxaemia that she believes is more common in formula-fed infants due to overgrowth of *E. coli* in the gut. The study which she uses to draw this conclusion does not actually prove a link between the DPT vaccination and endotoxaemia(89). NB the P component of DPt is the whole cell component which is no longer used in NZ. Acellular pertussis vaccines used in NZ since 2000 do not contain endotoxins. It simply indicates that E-coli lipopolysaccharide and the pertussis component of DTP cause similar alterations in liver metabolism in mice. Whether this occurs in humans is not clear.

Nutritional therapy, including high-dose vitamin therapy, prevents infection

As discussed above, poor nutrition does increase morbidity and mortality from infectious disease. Hilary Butler is a strong advocate for high dose vitamin C therapy. A meta-analysis has failed to demonstrate a protective effect against the common cold from high dose vitamin C therapy(90). Vitamin C has been shown to alter immune response to respiratory infection, but this does not imply prevention of infection in the first place(91). Contrary to Hilary Butler’s claims, there is little support for the use of vitamin C to treat pertussis infection.

IMAC funding

In her chapter “In front of the scenes, facing the media,” Hilary Butler alleges that IMAC cannot provide impartial advice because of funding from vaccine manufacturers, which she inferred from a letterhead “which had at the bottom the names of the vaccine companies that funded IMAC and the Goodfellow Unit”.

IMAC wishes to clarify the role of funding from the pharmaceutical industry. No funding from vaccine manufacturers is used in the provision of any services for the public including the operation of the 0800 IMMUNE hotline, website or other communications. Advice provided from IMAC in publications such as this one is a summary of the current orthodox medical literature and is not submitted to any vaccine manufacturer before its release. IMAC have used industry funding to conduct surveys of health professionals and run conferences.

Conclusion

IMAC finds this work by Hilary and Peter Butler to raise some valid points about the importance of nutrition, hygiene, sanitation and breast-feeding as important strategies in relieving the burden of infectious disease in our society. They also raise some valid points with regard to BCG vaccination.

While IMAC commends the authors’ efforts to examine the orthodox medical literature concerning vaccination, and would encourage others to do so, many of their conclusions are not consistent with the overall tenor of the current state of evidence from orthodox medical literature. IMAC is therefore concerned about the generally misleading nature of this work and its potential to unfairly undermine public confidence in vaccination.

References

1. Vitral, L., Gaspar, A., Souto, F., Epidemiological pattern and mortality rates for hepatitis A in Brazil, 1980-2002 – A review. *Mem Inst Oswaldo Cruz, Rio De Janeiro*. 2006;101(2): 119-127.
2. Mortimer, E., Jones, P., An evaluation of pertussis vaccine. *Rev Infect Dis*. 1979; 1(6):927-934 cited in *NZ Immunisation Handbook, 2006; Ministry of Health, Wellington, NZ p163*.
3. Ministry of Health, 2006. *NZ Immunisation handbook 2006. Ministry of Health, Wellington, New Zealand*.
4. Australian College of Paediatrics. Policy statement: vitamin A supplementation in measles. *Journal of Paediatrics and Child Health*. 1996; 32:209-210. cited in *NZ Immunisation Handbook, 2006; Ministry of Health, Wellington, NZ p221*.
5. Bhaskaram, P., Micronutrient malnutrition, infection and immunity: an overview. *Nutrition Reviews*. 2002; 60(5):S40-S45.
6. Cunningham-Rundles, S., McNeely, D., Moon, A., Mechanisms of nutrient modulation of the immune response. *J Allergy Clin Immunol*. 2005; 115:1119-1128.
7. Parvez, S., Malik, K., Kang, S., Kim, H.-Y., Probiotics and their fermented food products are beneficial for health. *Journal of applied microbiology*. 2006; 100:1176-1185.
8. Schwartz, J., Air pollution and children’s health. *Pediatrics*. 2004; 113:1037-1043.
9. Bernier, J., Brousseau, P., Kryzstyniak, K., Tryphonas, H., Fournier, M., Immunotoxicity of heavy metals in relation to great lakes. *Environ Health Perspect*. 1995; 103(Suppl9):23-34.
10. Blakly, B., Brousseau, P., Fournier, M., Voccia, I., Immunotoxicity of pesticides : a review. *Toxicology and Industrial Health*. 1999; 15:119-132.
11. Ban, M., Hettich, D., Bonnet, P., Effect of inhaled industrial chemicals on systemic and local immune response. *Toxicology*. 2003; 184:41-50.
12. Ahmed., S., The immune system as a potential target for environmental estrogens (endocrine disrupters): a new and emerging field. *Toxicology*. 2000; 150:191-206.

13. Bryant, P., Trinder, J., Curtis, N., Sick and tired: does sleep have a vital role in the immune system? *Nature Reviews. Immunology*. 2004; 457-467.
14. Majde, J., Krueger, J., Links between the innate immune system and sleep. *J Allergy Clin Immunol*. 2005; 116:1188-1198.
15. Vitetta, L., Anton, B., Cortizo, F., Sali, A., Mind-body medicine. Stress and its overall impact on health and longevity. *Ann. N.Y. Acad. Sci.* 2005; 1057:492-505.
16. Pressman, S., Cohen, S., Miller, G., Barkin, A., Rabin, B., Treanor, J., Loneliness, social network size and immune response to influenza vaccination in college freshmen. *Health Psychology*. 2005; 24(3):297-306.
17. Phillips, A., Burns, B., Carroll, D., Ring, C., Drayson, M., The association between life events, and antibody status following thymus-dependent and thymus-independent vaccinations in healthy young adults. *Brain, Behavior and Immunity*. 2005; 19:325-333.
18. Hanson, L., Breastfeeding provides passive and likely long-lasting active immunity. *Ann Allergy Asthma Immunol*. 1998; 81:523-537.
19. Silfverdal, S., Bodin, L, Ulanova, M., Hahn-Zoric, M., Hanson, L., Olcen, P., Expression of idiotypic antibodies -1 and -2 and breastfeeding in relation to antibodies against *Haemophilus influenzae* type b in children. *Scandinavian Journal of Immunology*. 2006; 63:371-375.
20. Oyedele, O., Odemuyiwa, S., Ammerlaan., W, Muller, C., Adu., F., Passive immunity to measles in the breastmilk and cord blood of some Nigerian subjects. *Journal of Tropical Pediatrics*. 2005; 51(1): 45-48.
21. Coe, C., Lubach, G., Schneider, M., Dierschke, D., Ershler, W., Early rearing conditions alter immune response in the developing infant primate. *Pediatrics*. 1992; 90(3):505-509.
22. Colditz, G., Berkey, C., Mosteller, F., Brewer, T., Wilson, M., Burdick, E., Fineberg, H., The efficacy of Bacillus Calmette-Guerin vaccination of newborns and infants in the prevention of tuberculosis: a meta-analysis of the published literature. *Pediatrics*. 1995; 96(1):29-35.
23. Fine, P., Primary prevention of leprosy. *International Journal of Leprosy and Other Mycobacterial Illnesses*. 1996; 64(4):S44-S49.
24. Cherry, J., Epidemiology of pertussis. *Pediatr Infect Dis J*. 2006; 25:361-362.
25. Salmaso, S., Mastrantonio, P., Tozzi, A., Stefanelli, P., Anemona, A., degli Atti, M., Giammanco, A., Sustained efficacy during the first 6 years of life of 3-component acellular pertussis vaccines administered in infancy: the Italian experience. *Pediatrics*. 108(5):e81.
26. Mitchell, E., Stewart, A., Clements, M., Ford, R., Immunisation and the sudden infant death syndrome. *Archives of Disease in Childhood*. 1995;73(6):498-501.
27. Stratton, K., Howe, C., Johnson, R., DPT and chronic nervous system dysfunction: a new analysis. Washington, DC, Institute of Medicine, National Academy Press *quoted in NZ Immunisation Handbook, 2006; Ministry of Health, Wellington, NZ p378*.
28. Greenberg, D., von Konig, C.-H., Heininger, U., Health burden of pertussis in infants and children. *Pediatr Infect Dis J*. 2005; 24:539-543.
29. Baker, M., Martin, D., Kieft, C., Lennon, D., A 10-year serogroup B meningococcal disease in New Zealand: descriptive epidemiology, 1991-2000. *J. Pediatr Child Health*. 2001; 37:S13-S19.
30. Trotter, C., Gay, N., Edmunds, W., The natural history of meningococcal carriage and disease. *Epidemiol infect*. 2006; 134:556-566.
31. Stephens, D., Uncloaking the meningococcus: dynamics of carriage and disease. *Lancet*. 1999; 353:941-942.
32. Health Research Council, 2004. Safety following MeNZB™ immunisation. Health Research Council Report., Wellington, NZ, 20 Dec 2004.
33. O'Hallahan, J., 2006. Letter to health professionals. Ministry of Health, Wellington, NZ, 18 October 2006.
34. Ministry of Health, 2001. An integrated approach to infectious disease: priorities for action 2002-2006. Ministry of Health, Wellington, NZ.
35. Gust, I., Epidemiology of hepatitis B infection in the Western Pacific and South East Asia. *Gut*. 1996; 38(Suppl2):S18-S23.

36. Bond, W., Favero, M., Petersen, N., Gravelle., C., Ebert, J., Maynard, J., Survival of hepatitis B virus after drying and storage for one week. *Lancet*. 1981:550-551.
37. Tovo, P.-A., Lazier, L., Versace, A., Hepatitis B virus and hepatitis C virus infections in children. *Curr Opin Infect Dis*. 2005; 18:261-266.
38. Kremsdorf, D., Sussan, P., Patalini-Brechot, P., Brechot, C., Hepatitis B virus-related hepatocellular carcinoma: paradigms for viral-related human carcinogenesis. *Oncogene*. 2006; 25:3823-3833.
39. Ministry of Health, Report 5.4 The surveillance phase of the national hepatitis B carrier screening and surveillance programme. Ministerial Review of Targeted Policies and Programmes, 2005., Ministry of Health, Wellington, New Zealand.
40. Wong, V., Ip, H., Reesink, H., Lelie, P., Reerink-Brongers, E., Yeung, C., Ma, H., Prevention of the HBsAg carrier state in newborn infants of mothers who are carriers of HBsAg or HBeAg by administration of hepatitis-B vaccine and hepatitis-B immunoglobulin. *Lancet*. 1984; 8383:921-926.
41. European Consensus Group on Hepatitis B Immunity. Are booster immunizations needed for lifelong hepatitis B immunity? *Lancet*. 2000; 355:561-565.
42. Sadovnick, A., Schelfele, D., School-based hepatitis B vaccination programme and adolescent multiple sclerosis. *Lancet*. 2000; 355:549-550.
43. Zuckerman, J., Protective efficacy, immunotherapeutic potential and safety of hepatitis B vaccines. *Journal of Medical Virology*. 2006; 78:169-177.
44. DeStefano, F., Mullooly, J., Okoro, C., Chen, R., Marcy, S., Ward, J., Vadheim, C., Black, S., Shinefield, H., Davis, R., Bohlke, K., Childhood vaccinations, vaccination timing and risk of type 1 diabetes mellitus.
45. McMahon, B., Helminiak, C., Wainwright, R., Bulkow, L., Trimble, B., Wainwright, K., Frequency of adverse reactions to hepatitis B vaccine in 43,618 persons. *Am J Med*. 1992;92(3):254-6.
46. Ronchi, F., Cecchi, P., Falcioni, F., Marsciani, A., Minak, J., Muratori, G., Tazzari, P., Beverini, S., Thrombocypenic pupura as adverse reaction to recombinant hepatitis B vaccination. *Arch. Dis. Child*. 1998;78:273-274.
47. Maillfert, J., Sibilia, J., Toussiro, E., Vignon, E., Eschard, J., Lorcerie, B., Juvin, R., Parchin-Geneste, N., Piroth, C., Wendling, D., Kuntz, J., Tavernier, C., Gaudin, P., Rheumatic disorders developed after hepatitis B vaccination. *Rheumatology*. 1999; 38:978-983.
48. Langmuir, A., Bregman, D., Kurland, L., An epidemiological and clinical evaluation of Guillain-Barre syndrome and the 1992-1993 and 1993-1994 influenza vaccines. *J epidemiol*. 1984; 19:841-879. cited in *NZ Immunisation Handbook, 2006; Ministry of Health, Wellington, NZ p267*.
49. Lasky, T., Terracciano, D., Magder, L., Koski, C., Ballesteros, M., Nash, D., Clark, S., Haber, P., Stolley, P., Schonberger, L., Chen, R., The Guillain-Barre syndrome and the 1992-1993 and 1993-1994 influenza vaccines. *NEJM*. 1998; 339(25):1797-1802.
50. van der Wouden, J., Bueving, H., Poole, P., Preventing influenza: an overview of systematic reviews. *Respiratory Medicine*. 2005; 99:1341-1349.
51. Postma, M., Jansema, P., van Genugten, M., Heijnen, M.-L., Jager, J., de Jong-van den Berg, L., Pharmacoeconomics of influenza vaccine for healthy working adults. *Drugs*. 2002; 62(7): 1013-1024.
52. Burls, A., Jordan, R., Barton, P., Olowokure, B., Wake, B., Albon, E., Hawker, J., Vaccinating healthcare workers against influenza to protect the vulnerable – is it a good use of healthcare resources? A systematic review of the evidence and an economic evaluation. *Vaccine*. 2006; 24:4212-4221.
53. Nichol, K., Influenza vaccination in the elderly. Impact on hospitalization and mortality. *Drugs Aging*. 2005; 22(5):495-515.
54. Poole, P., Chaco, E., Wood-Baker, R., Cates, C., Influenza vaccine for patients with chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2006; 4.
55. American Heart Association, American College of Cardiology. Influenza vaccination as secondary prevention of cardiovascular disease. *J Am Coll Cardiol*. 2006; 48:1498-1502.

56. Smith, S., Poland, G., Use of influenza and pneumococcal vaccines in people with diabetes. *Diabetes Care*. 2000; 23(1): 95-108.
57. Melcher, L., Recommendations for influenza and pneumococcal vaccinations in people receiving chemotherapy. *Clinical Oncology*. 2005; 17:12-15.
58. Antonen, J., Pyhala, R., Hannula, P., Ala-Houhala, I., Santanen, R., Ikonen, N., Saha, H., Influenza vaccination of dialysis patients: cross-reactivity of induced haemagglutination-inhibiting antibodies to H3N2 subtype antigenic variants is comparable with the response of naturally infected young healthy adults. *Nephrol Dial Transplant*. 2003; 18:777-781.
59. Principi, N., Esposito, S., Pediatric influenza prevention and control. *Emerging Infectious Diseases*. 2004; 10(4):574-580.
60. Block, S., Role of influenza vaccination for healthy children in the US. *Pediatr Drugs*. 2004; 6(4):199-209.
61. Roberts, S., Hollier, L., Sheffield, J., Laibl, V., Wendel, G., Cost-effectiveness of universal influenza vaccination in a pregnant population. *Obstet Gynecol*. 2006; 107:1323-1329.
62. Bueving H., Thomas, S., van der Wouden, J., Is influenza vaccination in asthma helpful? *Curr Opin Allergy Clin Immunol*. 2005; 5:65-70.
63. Grau, A., Fischer, B., Barth, C., Ling, P., Lichy, S., Buggle, F., Influenza vaccination is associated with a reduced risk of stroke. *Stroke*. 2005; 36:1501-1506.
64. Wood, J., Developing vaccines against pandemic influenza. *Philosophical Transactions of the Royal Society. Biological Sciences*. 2001; 356(1416):1953-1960.
65. Mansoor, O., Blakely, T., Baker, M., Tobias, M., Bloomfield A., A measles epidemic controlled by immunisation. *NZ Public Health Report*. 1997. Ministry of Health, Wellington, New Zealand.
66. Tobias, M., Christie, S., Mansoor, O., Predicting the next measles epidemic. *NZ Public Health Report*. 1997; 4(1):1-3.
67. Roberts, M., 2004. A mathematical model for measles vaccination. Internal report to the Ministry of Health. cited in *NZ Immunisation Handbook, 2006; Ministry of Health, Wellington, NZ p210*.
68. Peltola, H., Heinonen, L., Frequency of true adverse reactions to mumps-measles-rubella vaccine. *Lancet*. 1986. Apr:939-940.
69. Miller, C., Deaths from measles in England and Wales, 1970-1983. *BMJ*. 290:443-444. cited in *NZ Immunisation Handbook, 2006; Ministry of Health, Wellington, NZ p207*.
70. Asaria, P., MacMahon, E., Measles in the United Kingdom: can we eradicate it by 2010? *BMJ*. 2006; 333(7574):890-895.
71. Weibel, R., Caserta, V., Benor, D., Evans, G., Acute encephalopathy followed by permanent brain injury or death associated with further attenuated measles vaccines: a review of claims submitted to the National Vaccine Injury Compensation Program. *Pediatrics*. 1998; 101(3):383-387.
72. Ray, P., Hayward, J., Michelson, D., Lewis, E., Schwalbe, J., Balck, S., Shinefield, H., Marcy, M., Huff, K., Ward, J., Mullooly, J., Chen, R., Davis, R., Encephalopathy after whole-cell pertussis or measles vaccination. Lack of evidence for a causal association in a retrospective case-control study. *Pediatr Infect Dis J*. 2006; 25:768-773.
73. Horwitz, O., Grunfeld, K., Lysgaard-Hansen, B., Kjeldsen, K., Epidemiology and natural history of measles in Denmark. *American Journal of Epidemiology*. 1974; 100(2):136-149.
74. Madsen, K., Vestergaard, M., MMR vaccination and autism. What is the evidence for a causal association? *Drug Safety*. 2004; 27(12):831-840.
75. Immunisation Advisory Centre, <http://www.immune.org.nz/?t=719>
76. Straus, S., Ostrove, J., Inchauspe, G., Felsler, J., Freifeld, A., Kroen, K., Sawyer, M., Varicella-Zoster virus infections. Biology, natural history, treatment, and prevention. *Annals of Internal Medicine*. 1988; 108:221-237.
77. Zhou, F., Harpez, R., Jumaan, A., Winston, C., Shefer, A., Impact of varicella vaccination on healthcare utilization. *JAMA*. 2005; 294:797-802.
78. Thery, N., Beutels, P., van Damme, P., van Doorslaer, M., Economic evaluations of varicella vaccination programmes. A review of the literature. *Pharmacoeconomics*. 2003; 23(1):13-38.

79. Aabya, P., Hedegaarda, K., Sodemanna, M., Nhantea, E., Veiruma, J., Jakobsena, M., Lissea, I., Jensena, H., Sandstroma, B., Childhood mortality after polio immunisation campaign in Guinea-Bissau. *Vaccine*. 2005; 23(14):1746-1751.
80. World Health Organisation. Inactivated poliovirus vaccine following oral poliovirus vaccine cessation. *Weekly epidemiology record*. 2006; 81(15):137-144.
81. Turner, N., Vaccinators booklet – some changes are being made. 2002. Immunisation Advisory Centre, Auckland, New Zealand.
82. Golaz, A., Hardy, I., Strebel, P., Bisgard, A., Vitek, C., Popovic, T., Wharton, M., Epidemic diphtheria in the Newly Independent States of the former Soviet Union: implications for diphtheria control in the United States. *Journal of Infectious Diseases*. 2000; 181(Suppl1):S237-S243.
83. Chen, R., Hardy, I., Rhodes, P., Tyshchenko, D., Moiseeva, A., Marievsky, V., Ukraine, 1992: first assessment of diphtheria vaccine effectiveness during the recent resurgence of diphtheria in the former soviet union. *Journal of Infectious Diseases*. 2000; 181(Suppl1):S178-S183.
84. Chen, R., Hardy, I., Rhodes, P., Tyshchenko, D., Moiseeva, A., Marievsky, V., Ukraine, 1992: first assessment of diphtheria vaccine effectiveness during the recent resurgence of diphtheria in the former soviet union. *Journal of Infectious Diseases*. 2000; 181(Suppl1):S178-S183.
85. Fine, P., Herd immunity: history, theory, practice. *Epidemiologic Reviews*. 1993; 15(2): 265-302.
86. Lindblad, E., Aluminium adjuvants – in retrospect and prospect. *Vaccine*. 2004; 22:3658-3668.
87. Strickler, H., Rosenberg, P., Devesa, S., Hertel, J., Fraumeni, J., Goedert, J., Contamination of poliovirus vaccines with simian virus 40 (1955-1963) and subsequent cancer rates. *JAMA*. 1998; 297(4):292-295.
88. CDC, 2006., <http://www.cdc.gov/nip/vacsafe/concerns/gen/contamination.htm#Stealth>
89. Ansher, S., Thomson, W., Snoy, P., Habig, W., Role of endotoxin in alterations of hepatic drug metabolism by diphtheria and tetanus toxoids and pertussis vaccine adsorbed. *Infection and Immunity*. 1992; 60(9): 3790-3798.
90. Douglas, R., Hemila, H., Chalker, E., D'Souza, R., Treacy, B., Vitamin C for preventing and treating the common cold. *Cochrane Database of Systematic Reviews*. 2006; 4.
91. Khaw, K.-T., Woodhouse, P., Interrelation of vitamin C, infection, hemostatic factors and cardiovascular disease. *BMJ*. 1995; 310(6994):1559-1563.
92. Grant CC, Roberts M, Scragg R, Stewart J, Lennon D, Kivell D, et al. Delayed immunisation and risk of pertussis in infants: unmatched case-control study. *BMJ*. 2003;326(7394):852-3.
93. Essery SD, Raza MW, Zorgani A, MacKenzie DA, James VS, Weir DM, et al. The Protective Effect of Immunisation against Diphtheria, Pertussis and Tetanus (DPT) in Relation to Sudden Infant Death Syndrome. *FEMS Immunology & Medical Microbiology* 1999;Vol. 25(1-2):183-192.
94. Fleming PJ. The UK Accelerated Immunisation Programme and Sudden Unexpected death in Infancy: Case-Control Study. *British Medical Journal*. *BMJ* 2001;322(7290):1 - 5.
95. Henderson-Smart DJ, Ponsonby AL, Murphy E. Reducing the risk of sudden infant death syndrome: a review of the scientific literature. *Journal of Paediatrics & Child Health* 1998;34(3):213-9.
96. Institute of Medicine. Immunisation Safety Review - Vaccinations and Sudden Infant Death in Infancy. *National Academy of Sciences* 2003.
97. Ministry of Health. 2003. NZ Food NZ Children: Key results of the 2002 National Children's Nutrition Survey. Wellington: Ministry of Health. <http://www.moh.govt.nz>