



Critique of the Vaccination Alternatives Society flyer "Important Meningococcal Update" December 2004.

SUMMARY

The questions repeatedly raised by this group have been considered and researched in depth. The unfounded claims are addressed once more below from the body of research that is publicly available.

1. Will this vaccine protect my child?

Yes the vaccine is expected to protect your child. Based on international experience with very similar vaccines we know that a correlate of protection is a 4-fold rise in Serum Bactericidal Assay (SBA) antibody following immunisation. The MeNZB vaccine studies show that 75% of toddlers and children and 91% adults developed a four-fold rise from pre-vaccination levels six weeks following the 3rd dose.

2. Is this vaccine safe?

Yes, ongoing safety monitoring on over 200,000 children shows there has been no life threatening, unexpected or concerning events related to MeNZB™ vaccination.

There are several methods employed to monitor safety beyond the 7-day diary used. This includes reviewing, each day, emergency department consultations and admissions at Middlemore Hospital and admissions at Auckland City Hospital for everyone aged from four weeks to 20 years. Also actively reviewing all children's records from selected general practices. CARM (Centre for Adverse Reactions Monitoring) received only 88 spontaneous reports of adverse events following MeNZB™ vaccination during the first two months, which suggests the rate of concerning vaccine events is low.

3. Adverse reactions caused by the Norwegian vaccine

In the Norwegian vaccine trials a few serious events were observed following the immunisation. However these were also observed at the same level in those who did not receive the vaccine indicating that these events were not caused by the vaccine.

4. Secret ingredients

There are no secret ingredients. All the ingredients are public knowledge. These are listed on the data sheet, websites and other printed resources. The process used to manufacture the vaccine is also discussed. The use of aluminium hydroxide in vaccines has a very longstanding safety profile (more than 70 years).

5. The Norwegian vaccine was never released, as it was not effective enough.

The Norwegian epidemic had waned by the time the clinical trials were completed. The vaccine came too late for the Norwegians.

6. There is not really an meningococcal B epidemic in New Zealand

The peak of the epidemic appears to be waning. However it does continue at very high rates in New Zealand leaving more people dead or with life-long disability with each year that passes. New Zealand has the highest rate of the disease in the developed world. Our epidemic is expected to take many years still to abate.

7. The cause of meningococcal disease

Meningococcal B bacterium is the cause of our epidemic disease. There is no doubt. Although not every one who carries the organism becomes sick, the carriage of our epidemic strain is around 5% or less suggesting it is very virulent.

8. Will there be unforeseen future adverse effects?

This is extremely unlikely according to the body of vaccine research to date. Long term safety monitoring is in place.

9. Scientists disagree about vaccines

Scientific evidence is unanimous about the benefits of well-researched vaccines such as those used in NZ.

For more information Ask your doctor, nurse or midwife. Contact the dedicated information lines:

0800 20 30 90 or visit www.immunise.moh.govt.nz
www.immune.org.nz

0800IMMUNE (466863)

Critique of the flyer by the Vaccination Alternatives Society “Important Meningococcal update” December 2004

This is a rapid response to a flyer that has been distributed by an anti immunisation organisation. Responses are in the order they appear in the flyers. Claims made are in italics, the response follows. This information has been prepared to help health care professionals respond when people ask them about this flyer that has been distributed by mail drop in some Auckland suburbs. The flyer contains a large number of potentially dangerous inaccuracies. The claims are not new and have been made continually since the licensure of the MeNZB™ vaccine.

The Vaccine Alternatives flyer does not reflect the body of scientific information on the MeNZB™ vaccine and a refusal to vaccinate based on this flyer would be based on personal opinion, and not constitute informed refusal.

1. “Will this vaccine protect my child...there is no proof that the vaccine will in fact prevent meningococcal B disease”

Yes there is evidence that the vaccine will work. **The true test of the vaccine is in the field, in the population in whom it has been designed to protect.** It requires many people to be vaccinated and then exposed to the disease to determine the true effectiveness of a vaccine, simply by observing the difference in vaccination status in cases of disease.

In the NZ trials, blood is taken from vaccinees and the ability of the antibodies made in response to the vaccine to kill the meningococcal bacteria is assessed. Data from other similar vaccines, which have been used extensively internationally, is relevant and applicable to understanding MeNZB™. The data indicates that if the majority of those vaccinated mount an immune response to the vaccine, measured in this way, then a high proportion of vaccine recipients are likely to be protected. The measure of protection is a 4-fold increase in Serum Bactericidal Assay antibodies. Vaccines using the same or similar technology to the NZ vaccine have been used effectively and safely to control epidemics of meningococcal B disease in South America.

“...efficacy studies normally compare unvaccinated groups who receive a placebo, with vaccinated groups. However in New Zealand there was no real placebo given in the trial. Instead the Norwegian vaccine was given in place of a real placebo”

Efficacy studies **do not** usually use a placebo, they use a control, and usually it is another vaccine. As it happens however, the Norwegian trial did in fact use a placebo and these trials included over 360,000 doses, so we know the safety profile of the Norwegian vaccine.

2. “Is the MeNZB™ vaccine safe?...The follow up time to monitor “adverse events” was for only “up to seven days...”

This claim is repeatedly put forward by the anti immunisation lobby. It is completely untrue. The Independent Safety Monitoring Board (ISMB) established by the Health Research Council has reviewed safety data for the first 2 months of the MeNZB™

programme and states that it has no particular issues for concern in relation to the safety of MeNZB™. The safety monitoring includes reviewing, each day, emergency department consultations and admissions at Middlemore Hospital and admissions at Auckland City Hospital for everyone aged from four weeks to 20 years.

CARM (Centre for Adverse Reactions Monitoring) received only 88 spontaneous reports of adverse events following MeNZB™ vaccination during the same period, which suggests the rate of concerning vaccine events is low. There were no life threatening or unexpected events related to MeNZB™ vaccination.

For further details view the ISBM briefing on www.immunise.moh.govt.nz

To reiterate the safety monitoring being undertaken for MeNZB™:

The initial MeNZB™ NZ rollout process is being very closely monitored in the following ways for safety.

- Voluntary reporting of adverse events following immunisation by health care professionals and parents. Reports go to the Centre for Adverse Reaction Monitoring (University of Otago) as for other vaccines. Health professionals are actively encouraged to look out for and report any possible safety concerns.
- A range of general practices around NZ are being used to compare all their clinical notes on children and to compare any possible visits to the general practice with immunisation events, to see if there are any relationships with any conditions and immunisation.
- Any admissions to hospital and emergency department consultations in approximately 100,000 vaccinees under 5 years of age and 100,000 vaccinees over 5 years of age are being monitored. The National Immunisation Register will be matched against the hospital data to see if there has been a consultation within a certain period after vaccination.
- All hospital admissions and emergency department consultations in those aged under 20 years in Auckland and Northland are reviewed daily to identify pre selected rare conditions that may be potentially linked to immunisation. These are looking for any possible link between vaccination and these events. In depth investigations will occur for serious or unexpected cases.
- Ongoing data matching of hospital discharge data and immunisation data will occur so that any event or disease that may be of possible concern can be linked back to immunisation status. This gives the ability for follow up of any concerns that may arise in the longer term.

3. Adverse Reactions

See #2

“The Norwegian vaccine caused a number of serious side effects, including allergic shock, blood in urine, as well as some long term problems...”

What the anti immunisation lobby fails to mention is that these events also occurred in the placebo group, therefore there is no evidence to suggest that the Norwegian vaccine caused these effects.

4. Secret Ingredients. Many of the ingredients in the vaccine are considered to be “proprietary”. In other words, neither the Ministry of Health nor the manufacturer will disclose everything that’s in the vaccine...what agents were used to deactivate the bacteria, and what agents were used to purify the vaccine...”

The list of ingredients is published on websites and in other printed resources. The list of ingredients has been made widely available to the public and the media and has been sent to anyone who asks.

For the sake of clarity, each dose is 0.5 ml and contains **only** the following:

- 25 mcg of outer membrane vesicles from the Neisseria meningitidis group B strain NZ98/245
- 1.65 mg of aluminium hydroxide (an adjuvant)
- Histadine (to stabilise the pH)
- Normal saline

The vaccine does not contain any other ingredients. The vaccine does not contain any bacteria (alive or dead). The "outer membrane vesicles" it contains are a small part of the "skin" of the bacteria. MeNZB™ vaccine does not contain any human blood or bovine products, porcine products, egg products, neomycin or the preservative thiomersal.

The bacteria used to make the vaccine are grown in a nutrient rich synthetic broth that contains water, sugar, essential amino acids and essential elements such as iron and potassium. The bacteria and the nutrients are then placed in a big fermenter which is akin to a highly complex thermos that maintains optimal conditions for the bacteria to grow, including gas mixtures and temperature. The process is strictly controlled to ensure purity and safety.

Once the seed bacteria have multiplied many times they are killed with a detergent that acts by breaking the cell wall into many fragments, most of which then re-aggregate into vesicles (Outer Membrane Vesicles) – much like detergent breaks up grease and oil. This detergent is sodium deoxycholate; a compound made from carbon, oxygen, hydrogen and sodium (salt) and is a normal by-product of bile metabolism.

Those vesicles that are the best components for the vaccine are separated out by centrifugation (spun at a very high speed until all fragments are separated into layers according to weight). The characteristics of these fragments are known well as they have been intensively studied for their immune generating properties.

The selected fragments are purified by ultra filtration and then added to the other constituents that make up the vaccine. The other major component necessary is the adjuvant, which acts to boost the immune response to the fragments of bacteria. The adjuvant in this vaccine is aluminium hydroxide, which is used in many other vaccines and considered by the US Food and Drug Administration to be the safest possible adjuvant. The other ingredient is histadine, which is an essential amino acid used to buffer the vaccine so that its pH (acidity) is the same as the pH in human blood.

“The MoH admits that the vaccine contains aluminium hydroxide, a proven neurotoxin (nerve poison), and that there is no safety data on its use with other vaccines.”

This is scaremongering by anti-immunisation campaigners. All elements can be toxic at high levels but harmless in trace quantities. The issue is what levels are safe. Aluminium is most definitely not a proven neurotoxin at the levels used in vaccines. Aluminium is one of the most common elements on earth. It is part of human bodies, in water, in breast milk, in most things we ingest. Aluminium is a necessary ingredient

in many vaccines to elicit a strong immune response. It assists the immune system to respond to the active ingredient in the vaccine. Aluminium in vaccines has a long-standing safety record of over 70 years. There have been many studies supporting the safety of aluminium-based adjuvants in vaccines. As with almost anything, dose is a critical factor in toxicity. The amount of aluminium in vaccines is miniscule and shown to be safe.

5. *The Norwegian “Parent Vaccine”...was never released after researchers concluded from the clinical trials that it wasn’t effective enough to justify a national campaign.*

Whether or not the Norwegian parent vaccine was used in epidemic control is irrelevant to the data about its safety and efficacy. It was tested on more than 178,000 people with approximately 360,000 doses. The testing showed it was safe and that it helped make people immune to meningococcal disease. The Norwegian vaccine is called the parent vaccine to NZ’s because it provided much of the early research that made our vaccine possible. Norway was unlucky that the technology and research was not available in time to change the course of their epidemic, which lasted about 20 years. It takes years to build this scientific knowledge and their vaccine came too late for their epidemic. It is not too late for MeNZB™ vaccine to make a significant difference to the New Zealand epidemic, preventing suffering, saving potentially hundreds of lives and preventing potentially more than a thousand cases of permanent disability. The Norwegians undertook a large randomised controlled trial on Norwegian teenagers and showed the vaccine had a good safety profile and was effective. However by the time they had completed the trials they were into year 19 of their epidemic, which was waning by then. NZ has since profited from their work and our researchers have taken the Norwegian research work further (amongst other) to the current situation where we have a vaccine with a good safety and efficacy profile ready in time to make a difference in our epidemic.

6. *Is there really an ‘epidemic’ of the disease in New Zealand?’ ...in New Zealand, where both deaths and notifications from meningococcal disease have reduced by 75% and 50% respectively, in the last three years (with no vaccine).’*

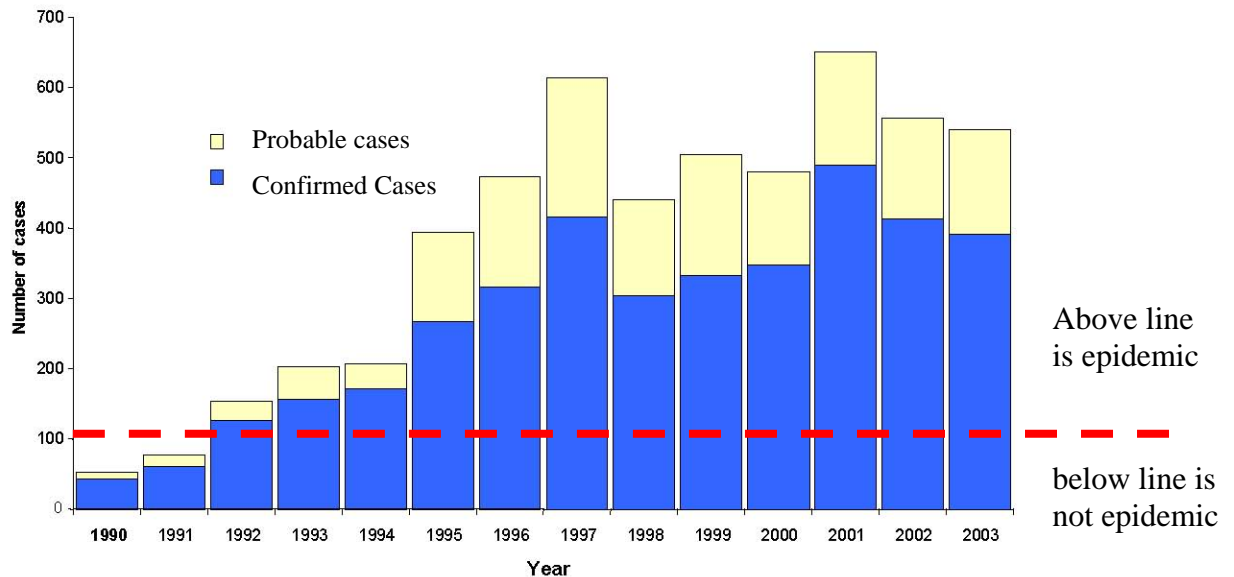
This is not correct.

The provable existence of the epidemic is inconvenient for anti-immunisation campaigners. All epidemics will subside eventually although they do not disappear overnight. The Norwegian Meningococcal epidemic took almost 20 years to go away. The question is at what point should we intervene with a vaccine, if we have one, to save both lives and lifetimes of disability.

Below is a graph illustrating confirmed and probable cases since 1990. As you can see there was a high rate of disease recorded in 1997, which then dropped only to appear at an even higher rate in 2001. There has been a drop since then, however it is far from being a 50% reduction. The epidemic is continuing to affect NZ children in high numbers. In 2004 to date 75.1% of confirmed cases were caused by the epidemic strain. It is reasonable to assume a similar ratio in the sero-unknown cases (see Table 1)

Full information about the ongoing epidemic is available from the report *The Epidemiology of Meningococcal Disease in New Zealand in 2003* available from the Ministry of Health website. www.moh.govt.nz. 300 cases of meningococcal disease have been notified from 1st January to 29th October 2004.

Meningococcal Disease Cases 1990-2003



There has certainly been a reduction in the rate of deaths. However deaths are the “tip of the iceberg” when compared with the severe disability incurred in 20% of cases and to a lesser extent in a further 25%.

Table 1. Deaths from Meningococcal disease: (Martin D, Mcdowell R. 2004)

YEAR	Group B.	Other (C,Y)	Serogroup Unknown	TOTAL
1999	11	2	10	23
2000	12	1	4	17
2001	18	4	4	26
2002	5	5	8	18
2003	7	5	1	13
2004				<i>To date 8</i>

Reduction in deaths is likely to be due to greater awareness among both the public and health professionals resulting in prompt treatment in more cases. NZ has very effective health services and one of the lowest rates of death in the world for this disease, and this is a credit to our health services, however death and disability continues despite the best medical treatment possible because it is such an aggressive, rapidly progressive disease.

7. The Cause of Meningococcal Disease

There is no doubt that Meningococcal B bacterium does cause this disease. Infection with Meningococcal B causes septicemia, and meningitis. Not everyone who carries the bacteria becomes infected, but many do. Studies currently being undertaken indicate that while NZ has a carriage rate of meningococci comparable to

other countries i.e. in the order of 20-30% carriage, the actual carriage of our epidemic strain is around 5% or less. This suggests that when the organism spreads to a vulnerable host that person may get the disease, as they are not immune to the organism. This is a disease with very high rates in children, the younger the child the higher the rate. NZ rates are five times higher than the level at which the World Health Organisation calls an epidemic – this is not a ‘tiny’ minority.

8. A disagreement among scientists...Science and medicine are by no means unanimous about vaccines...

An overwhelming majority of scientists and scientific evidence is completely unanimous about the benefits of well-researched vaccines such as those used in NZ, including MeNZB™. People may choose to claim otherwise for their own personal gain, self-promotion or because of fear driven by a poor understanding of the science, but science does not choose sides. The science on vaccines is abundant and comprehensive. There is no contention around the safety and effectiveness of the meningococcal B vaccine. The science to date shows it is safe. No one can credibly claim that the meningococcal B vaccine is not effective when the NZ research to date and the considerable international experience of the same kind of vaccines gives NZ confidence that the vaccine is safe and effective. The vaccine is being closely monitored both for safety and effectiveness. This is an established scientific process that is being used to develop, test and then deliver vaccines to control a disease. It is not a contentious process.

December 2004