Commentary on coronial inquiry expert witness testimony

Background

Jasmine Renata died in her sleep in September 2009, aged 18 years. Her family believe her death was caused by the three doses of quadrivalent human papillomavirus vaccine (Gardasil®); she received between one year and six months earlier, as part of the National Immunisation Programme. Autopsy was unable to determine a cause of death and her case was referred to the Coroner.

Jasmine's family requested that evidence be given by two international professionals. Dr Christopher Shaw, a neuroscientist from Canada and Dr Sin Hang Lee, a pathologist from Connecticut, USA. Scientists at the Immunisation Advisory Centre at The University of Auckland have serious concerns about the scientific validity of information provided by Drs Shaw and Lee at the coronial hearing into the death of Jasmine Renata.

The Immunisation Advisory Centre has prepared this commentary, addressing the claims presented by Drs Chris Shaw and Sin Hang Lee. Most of the claims are centred on the purported role of aluminium in the vaccine at being able to cause brain disease. There is also the claim that the vaccine was contaminated and that this also played a role in Jasmine's death. The claims and assumptions are listed below followed by the facts and a brief précis of the scientific validity of the claim.

1. The role of aluminium

Claim: In a review of the literature on the safety of aluminium adjuvants in vaccines (1) the authors Lucija Tomljenovic and Christopher Shaw conclude that vaccine benefits may have been overrated and risk for adverse effects underestimated and that this matter has not been rigorously evaluated in the medical and scientific community.

Fact: Other reviews on the safety of aluminium adjuvants and vaccines in general (of which there are many) consistently support the safety of aluminium adjuvanted vaccines (2, 3). Tomljenovic and Shaw appear to have cherry picked the research to fit with their theory and omitted work by prominent experts in the field of aluminium adjuvants, most notably Professor Stanley Hem. There is no description of how the papers were selected for review or criteria for inclusion or exclusion. This is a serious flaw in any literature review and an unscientific approach to testing a theory. The paper also includes a range of erroneous assumptions. The World Health Organization considers the paper seriously flawed (http://www.who.int/vaccine_safety/reports/Jun_2012/en/index.html).

A few errors of fact and logic are listed on the following pages.

Claim: Aluminium is a neurotoxin

Fact: Aluminium is everywhere in the environment and the most abundant metal on the planet. Aluminium can be found in most body tissues from birth and exposure occurs throughout life without causing any health problems. Most aluminium (>95%) in the blood is cleared via the kidneys, following injection of aluminium directly into the blood around 0.001 – 0.01% finds its way to the brain via receptor mediated transport (vaccines are not injected into the blood). As with anything large amounts can be dangerous. People at particular risk of accumulating toxic levels of this metal are patients with renal problems receiving long term nutritional supplements directly into their blood (parenteral nutrition) (4).

Assumption: Vaccines contain large amounts of aluminium.

Fact: Vaccines do not contain large amounts of aluminium. Relative to daily intakes, vaccines contribute very little, even in babies who receive aluminium from both breast milk and formula. The amount of elemental aluminium in a dose of Gardasil vaccine is around 225 micrograms. We consume around 7,000-9,000 micrograms per day and around 0.1% is absorbed into the blood (or around 7-9 micrograms) (2, 4).

Assumption: Vaccines given to infants exceed FDA recommendations for maximum daily intakes.

Fact: The FDA guidelines pertain to parenteral nutrition given to premature infants and children with impaired renal function every day (hence the 'daily' limits). Vaccines are given as one offs, not every day (5).

Assumption: Aluminium accumulates in the body and reaches toxic levels.

Fact: Aluminium is excreted via the kidneys and urine; there is little build-up over a lifetime of exposure. Problems generally only arise in cases of regular high daily intakes coupled with renal failure (2, 4).

Assumption: Vaccine derived aluminium has a greater potential to induce neurological damage than that in diet because it is adsorbed to vaccine antigen and too large to be excreted via the kidneys.

Fact: The fate of most adsorbed aluminium in vaccines is 1) rapid disassociation following injection; 2) excreted via kidneys. Remaining aluminium is involved in the immune response and endures for longer. Aluminium adjuvants have been used in vaccines for over 80 years and there is a significant body of literature on their use. There are many studies now available that compare outcomes in people exposed and unexposed to aluminium adjuvants. They consistently support the safety profile of these adjuvants (3).

Claim: Dr Lee claims that more women suffer adverse events from the HPV vaccine than die from cervical cancer. He quotes incidence and mortality rates for cervical cancer per 100,000 women. He cites a paper by Tomljenovic and Shaw that uses raw data (total number of adverse event reports) from passive vaccine safety surveillance systems from several countries and compares it to mortality rates.

Fact: Passive safety surveillance systems receive reports of events that occur following a vaccine from a number of sources including health professionals and the public. These reports include any adverse event that occurs following receipt of a vaccine regardless of what caused the event. There is no denominator in these systems (how many people were vaccinated) and no causality (what caused the event). These events can range from minor injection site reactions to death. They serve as warning systems for unusual or

unexpected patterns. If a passive safety system raised a signal about a new, unexpected or more frequent event, then other methods are required to assess whether this is a real association or just a coincidence. Genuine vaccine-associated events are assessed using other methods that compare outcomes between vaccinated and unvaccinated people. Using only passive reporting data in the way that Tomljenovic, Shaw and Lee have done suggests they are either deliberately trying to mislead or have very limited understanding of basic epidemiology and vaccine safety surveillance. The World Health Organization (WHO) Global Advisory Committee on Vaccine Safety provides a scientific review of the same data on a regular basis and this is available on their website. (http://www.who.int/vaccine_safety/reports/Jun_2012/en/)

Claim: Dr Shaw claims that he tested post mortem samples of Jasmine Renata's tissues and found aluminium in all of them. He also claims he found human papillomavirus (HPV16) in her brain. Dr Lee, who was also sent samples, claims to have found "unnatural results".

Fact: As mentioned, aluminium is the most common metallic element and third most common element on earth. It is present in our food, water, breast milk and we are born with aluminium in our bodies. Aluminium in the brain would not be an unexpected find. There are reported values for the presence of aluminium in various human tissues including the brain.

2. The theories of linking vaccine to sudden death

The theories as to how the HPV vaccine could have caused Jasmine Renata's death are convoluted and contradictory. They are almost exclusively based on speculation and require that many unlikely biological events occur in order for harm to arise. Below we examine a few of them.

Claim: Dr Lee claims to have tested samples of Gardasil from nine countries each with a different lot number. He claims to have found HPV DNA in them using special techniques. http://sanevax.org/gardasil-vaccine-found-to-be-contaminated/

Fact: Fragments of vaccine virus DNA for the L1 gene are to be expected in the vaccine as this DNA is present during the manufacturing process, as with any vaccine. This genetic material is highly degraded and fragmented and would be expected to be present in miniscule amounts. These fragments are inactive, not contaminants and do not pose a risk to those vaccinated. Our bodies come into daily contact with DNA from external sources from both food and microbes. This is eaten, inhaled and, in the case of microbes, distributed throughout body.

Theory one – HPV DNA is joined to the aluminium adjuvant

Dr Lee theorises that these fragments of DNA are bound to the aluminium adjuvant present in the vaccine.

Fact: There is no evidence to prove or disprove this theory. How was this tested? Given that the DNA and the adjuvant have opposite charges it seems theoretically possible that they may bind together but this has not been demonstrated. Normally within the vaccine formulation a proportion of the vaccine antigen (in this case the HPV viral-like proteins) are adsorbed to the adjuvant via electrostatic interactions. Once the vaccine has been administered there is a rapid disassociation of antigen and adjuvant into the extra cellular fluid at the injection site (6).

Theory two – HPV DNA remains joined to the aluminium adjuvant

Dr Lee speculates that these hypothetically bound DNA fragments remain firmly adhered to the aluminium adjuvant.
Fact: There is no evidence to prove or disprove this theory. No one else has observed these complexes. There is no description of the methods used to arrive at these results.

Theory three – new complex with unknown effects

Dr Lee claims that this DNA and adjuvant complex may constitute a new chemical compound with unknown effects.
Fact: There is no evidence to suggest such a new chemical compound.

Theory four – phagoctytosis by macrophages and failure of intracellular degradation causing on going inflammatory response

Dr Lee claims that these adjuvant-DNA complexes would be phagocytised (taken up) by tissue macrophages after injection and that these DNA fragments, protected from degradation within the cell, may behave as long acting stimulators to activate the production of inflammatory products such as tumour necrosis factor (TNF). He then goes on to point out that TNF is a known myocardial depressant capable of causing hypotension and lethal shock in animals and humans as well as the symptoms reported by girls who received Gardasil.

Fact: This is all speculation as no evidence has been provided to support any of these contentions. However it seems highly unlikely that such a very small quantity of DNA hypothetically bound to aluminium adjuvant could remain highly bonded and then induce such a massive inflammatory response. Both foreign DNA and aluminium are ubiquitous in our environment and exposure to both occurs daily from many sources.

Summary Statements

What does the presence of aluminium in brain tissue mean?

- Any presence of aluminium in brain tissue samples simply tells us that like the rest of the population, there was aluminium in Jasmine's tissue.
- The presence of aluminium does not inform us about why Jasmine died.
- We do not know that the tests carried out by Lee and Shaw were appropriate or with proper controls, as they have not presented their methods for scrutiny and peer review.

What does the presence of HPV DNA in the brain mean?

- The claimed presence of human papillomavirus type 16 in the brain tissue is difficult to comment on. What methods were used to detect it? Is this the virus itself or do they mean fragmented DNA?
- The amount of residual fragmented DNA in the vaccine is miniscule. It is very hard to believe that such a tiny amount could find its way throughout the body and be present in a high enough quantity to be detected by even the most sensitive of methods.
- Another fundamental problem is that the theory about DNA binding to aluminium and the theory about this complex being found in the brain contradict each other. Dr Lee states that the proposed DNA-adjuvant complex is phagocytised by macrophage where it resides causing an inflammatory response. The blood-brain barrier restricts passage of blood-borne cells. It is debateable whether or

not peripheral macrophage can enter the brain in the first instance and if they do it is likely only to occur under diseases states and probably limited. So how can this hypothetical complex enter the brain? This is an error in logic based on several assumptions, none of which have been demonstrated.

Given the tiny amount of DNA present in the vaccine and the fact most aluminium is excreted and the fact that this hypothetical DNA-aluminium complex is apparently residing inside macrophage and that peripheral macrophage do not usually access the brain then detecting this complex in the brain tissue seems **extremely improbable**.

The 'Experts'

Scientific credibility of Drs Shaw and Lee

Dr Shaw has published two pieces of rodent research on the role of aluminium in neurological damage and several reviews (funded by anti-immunisation lobby groups) on the safety of aluminium adjuvants in vaccines (1, 7-9). These review articles are not original research and simply cite a range of material that appears to support a pre-established position. This is not scientific. There are many articles published that use a systematic approach to evaluating the safety of vaccines and review articles meeting a strict set of criteria for quality that address a particular research or clinical question. This repeated failure to use the scientific method to assess the safety of vaccines and aluminium draws the scientific credibility of Dr Chris Shaw into serious question.

Dr Lee appears not to have been employed by the Milford Hospital in Connecticut since 2010 and he has filed a lawsuit against the hospital claiming wrongful termination (http://sanevax.org/dr-sin-hang-lee-a-case-study-in-ethics-dont-pay/). Despite this, his name is still being used in association with Milford hospital (http://www.stuff.co.nz/dominion-post/news/7445193/Foreign-DNA-found-in-teenagers-blood). Dr Lee has made some erroneous statements about the Gardasil vaccine and also has a major conflict of interest.

- Dr Lee claims that the Gardasil vaccine trials demonstrated an increased risk of cervical disease if women were already infected with the virus.
- Dr Lee therefore recommends a test prior to women receiving HPV vaccine. He offers a service on line (for a USD$50 fee) to test them for evidence of existing HPV infection. http://sanevax.org/pre-vac-hpv-testing-2/
  http://www.weeklyblitz.net/949/dr-sin-hang-lee-joins-forces-with-sane-vax-inc-in

There are two serious issues here.

- Firstly, the trials did not demonstrate an increased risk of cervical disease in vaccinated women who had pre-existing infection. The fact is there was a cluster of women in a sub-study with pre-existing infection who appeared to have an increased risk after vaccination. However on careful examination of that small study and of all the other studies it was found that the vaccinated group had different baseline risk factors such as smoking which probably contributed to this anomaly. Apart from the small sub-group the rest of the trials did not find any increased risk.
- There is a conflict of interest when Dr Lee profits from the proceeds of the testing he recommends. He is the President and a shareholder in HiFi DNA Tech (http://www.hifidna.com) which provides the tests he recommends. Dr Lee's criteria for this HPV DNA testing and its use in clinical decision making have been highly criticised by other pathologists (10).

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