

Virus in the system

KIRSTEN and Mick Button were looking forward to a family holiday in Bali when the letter landed in their mailbox.

<http://www.theaustralian.com.au/news/features/virus-in-the-system/story-e6frg8h6-1226063484330>

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Saba Button when she was a "perfectly happy and healthy baby". *Source:* The Australian



Kirsten Button with baby Saba, 2, who has brain damage. Picture: Frances Andrijich *Source: The Australian*

From the West Australian Health Department, it urged them to vaccinate their children against the flu. A killer new strain of influenza, a mutant mix of human, avian and swine influenza viruses, had swept the country the previous winter, and WA was taking no chances. It offered the flu vaccine free to all children, the only state or territory to do so. “It encouraged us to protect our children,” Kirsten says of the letter. “Our four-year-old, Cooper, has asthma so we thought it was the best thing to do. When you get that letter, you are in a situation where if you don’t vaccinate, you feel like you’re not doing the right thing.”

Kirsten took Cooper and his 11-month-old sister, Saba, to their local GP for the flu shot at lunchtime on April 19 last year. On the way home in the car, Saba would not stop screaming. Back in their beachside home in the Perth suburb of Watermans Bay, Kirsten gave her little girl some Panadol to soothe her, and “she was fine all afternoon”.

After dinner, Kirsten went out for a pilates class, leaving Mick to give Saba a bottle and put her to bed at 7pm. An hour later, he heard moaning over the baby monitor. When he checked on Saba in her upstairs cot she was, Kirsten relates, “burning hot,

limp like a rag doll”. Mick called his wife to let her hear their daughter’s whimpers over the phone. “I’d never heard anything like it,” Kirsten says. “I was hysterical. I couldn’t drive; my dad had to drive me back home.” While her fretful parents waited for an ambulance, Saba’s temperature was 40.2 degrees, a high fever.

“She was lying very still and groaning and moaning,” Kirsten says. “She was so white.” In the wailing ambulance, as diarrhoea seeped from Saba’s nappy, her parents panicked as they listened to the machine monitoring their baby’s heart, racing at 238 beats per minute – double the usual rate. When the ambulance arrived at Perth’s Princess Margaret Hospital, doctors and nurses were waiting out the front. Kirsten remembers hearing one of them remark, “It’s another Fluvax baby.”

Flu pandemic

When swine flu emerged from Mexico in April 2009, initial reports were that it was killing one in every 20 people infected. Within eight weeks the virus had swept across four continents, Australia included, prompting the World Health Organisation to declare the first global flu pandemic of the century. In July 2009, federal health minister Nicola Roxon warned that in a “worst-case scenario” 6000 Australians could die from the new flu that had already infected 10,000 people, killed 22 and landed 60 others in intensive care. It was highly contagious and it was striking in unpredictable ways: fit, healthy young people normally strong enough to fight off the seasonal flu were being taken down. At its worst it was causing organ failure and brain damage and fears were held for pregnant women, the elderly and people with underlying medical conditions.

The race was on for a vaccine and CSL – the now-privatised Commonwealth Serum Laboratories, Australia’s biggest pharmaceutical manufacturer – was awarded a \$131 million government contract to supply the nation’s entire stockpile of swine flu vaccine. CSL began clinical trials of Panvax, which protected against swine flu but not the typical strains of seasonal flu, in 470 children in August 2009. It was approved for children in December by the Therapeutic Goods Administration – the Health Department agency that approves and monitors pharmaceutical products – and administered without any unforeseen side-effects.

Three months later, CSL rolled out a new vaccine, Fluvax, which many GPs promoted to parents as being superior to Panvax because it would protect against seasonal flu as well as swine flu. As the only Australian-made flu vaccine, Fluvax had been on the market for 42 years covering three strains of the most common flu viruses circulating each winter. But something about the 2010 “recipe” was different. In a world-first, CSL’s Fluvax mixed H1N1 swine flu with two strains of seasonal flu. Unlike Panvax, this new trivalent version of Fluvax had not been clinically tested in children before

the TGA gave doctors the green light for mass vaccinations of healthy babies, toddlers and pre-schoolers.

What followed has shaken public confidence in one of the world's most popular immunisation programs. In April last year, four days after baby Saba had her flu shot, Australia's Chief Medical Officer, Professor Jim Bishop, made the unprecedented decision to ban nationally all the seasonal flu vaccines for the under-5s. Fluvax, the predominant vaccine, was triggering febrile fits in one in every 100 children – 10 times the expected rate. The side-effects, in some cases, were severe, and no-one could explain what had caused them. As the mystery continues, even eminent scientists and medical specialists are now quibbling over the efficacy of flu vaccines, how they are tested and how well they are monitored. With another flu season upon us and the medical community divided, what are we, the public, to make of it all?

Eleven days before Saba received her seasonal flu shot, across the continent in Brisbane, a family was in shock. David and Nicole Epapara had vaccinated their healthy twin toddlers, two-year-old sisters Ashley and Jaime, at 3pm on April 8. At midnight, Jaime vomited in her cot, while Ashley slept peacefully. When Jaime woke the next morning, her twin lay dead. "We don't know whether it was the vaccination or some other cause," David Epapara told *The Australian* a few weeks later. "It just seems too much of a coincidence, that's all, for a healthy girl to pass away like that. We're so shocked, we don't know what to think."

Nor does Brisbane Coroner John Lock, who was unable to determine a cause of death after a five-month investigation. "There was no finding to causally connect the young child's death with the flu vaccination," he said. "However, I have concluded that a link between the vaccination and the death cannot be absolutely excluded."

The child's death should have set off alarm bells, but Queensland Health had initially failed to investigate the case because Ashley did not die in a hospital, and the suburban GP who inoculated her had not notified authorities of any possible link with the flu shot.

Back in Perth, health workers were starting to notice an unusually high rate of fevers and febrile convulsions after children were vaccinated with Fluvax. The six-month-old son of Perth doctor Will Patterson was one of the first to be immunised at a government-run flu clinic in the city. Within hours, the baby was running such a high fever that Patterson feared he might have a fit. "I never thought of reporting it because I thought it was just an individual reaction," he says. But a couple of weeks later, receptionists at the Port Kennedy Medical Centre where he works began fielding calls from anxious parents. Dr Richard Choong alerted the health department after a child had to be sent to hospital.

As the vaccination program accelerated, so did the complaints. On March 31, 12 days after the program began in WA, the regional health service at Wickiepin, three hours' drive from Perth, alerted the public health nurse that six out of nine children vaccinated with Fluvax seemed feverish, with one sent to hospital. When the nurse notified WA Health the next day, she was reassured that "reactions are common", and was asked to report the matter to the TGA.

Perth mother Sharron Coppin was oblivious to the crescendo of complaints when she took her one-year-old twins Byron and Lateesha for a routine vaccination against measles, mumps and rubella in early April. Her three-year-old, Alivia, came along, and when the GP suggested she have all three children vaccinated against the flu – postponing the other shots for a few weeks – she took his advice. Soon after the family returned home, Alivia "just turned purple".

"Alivia went from being happy to suddenly very sick and shaking," Coppin recalls. "Then Teesha went into convulsions. Her eyes were fixated. It was like she was staring past you. It was really, really scary. I had the feeling I was losing her."

All three children had to be hospitalised for convulsions or vomiting. Coppin says her doctor called WA Health to report the side-effects, at least two weeks before Saba received her injection. "My kids had such a bad reaction and they kept on going, and now that little girl is severely damaged," she says. "It's sad that a child had to nearly die for them to take it off [the market]."

Sixteen hours after her flu shot, little Saba was in hospital on life support, breathing with the aid of a ventilator and drugged to stop the seizures. An MRI and a CAT scan revealed global brain injury and organ damage. Two doctors and two nurses took the frantic parents aside. "They said they didn't expect Saba to make it, and if she did she would have severe cerebral palsy and never walk or talk again," Kirsten says. "It was devastating. I remember I was on the floor, moaning." Saba spent 11 days in intensive care and eight weeks back in the children's ward before being sent home with brain damage.

Two days after Saba was admitted to intensive care, officials from WA Health, the hospital and the TGA held a teleconference to discuss the vaccine's side-effects. They talked about the "risk of damaging the program", according to the findings of an independent investigation ordered by WA Health Minister Kim Hames. Within two hours, Hames had suspended his state's free flu vaccination program; a day later, the federal Health Department announced a national ban on flu vaccines for the under-5s. By the time Fluvax was suspended, health departments across the country had notified the TGA of 410 adverse reactions among children younger than five, including 67 cases of febrile convulsions, as well as high fevers and vomiting. Most were in WA,

the only state with a free and recommended flu vaccine program. As well as Saba, another Perth child had been admitted to intensive care.

Professor Bryant Stokes, the eminent neurosurgeon and former head of WA Health who reviewed the events for the state's health minister, concluded in a report tabled in the WA Parliament last August that the "slow response" by federal and state authorities had "not served the public well". It was "disturbing", he noted, that Australia had not put in place the surveillance and reporting systems recommended by the World Health Organisation, which had advised all countries in August 2009 to "conduct intensive monitoring for safety and efficacy" of the pandemic vaccine, Panvax.

"It really was a shambles," Stokes recalls of the reporting chain. "Reports were coming in by phone and by paperwork. It was like a whisper going about, and no one was actually recording numbers. Information was received in dribs and drabs." Health workers could report on three different systems – by sending a fax to WA Health's Communicable Disease Control Directorate, by phoning a national hotline at the Mater Hospital in Brisbane, or by faxing or emailing the TGA. "Doctors just didn't know what to do," said Stokes.

More harm than good?

First do no harm. It's the medico's mantra, inspired by the Hippocratic Oath sworn by generations of doctors. Peter Collignon, professor of microbiology at the Australian National University and director of infectious diseases at Canberra Hospital, believes last year's flu vaccine might have caused more harm than good in otherwise healthy children. Awarded a Member of the Order of Australia last year for his work in clinical microbiology, infectious diseases and infection control, he has been taken aback by the controversy his comments created within the medical community. Citing data from NSW Health, he has found that the risk of a healthy child or teenager dying from swine flu in 2009, before a vaccine was available, was less than one in two million for those without underlying health problems such as asthma or heart disease.

"To stop two or three children going to intensive care we had to immunise 600,000 people," he says. "We need to be very careful before we recommend universal vaccination against influenza every year until we have better data. Otherwise we're talking about faith-based medicine, instead of evidence-based medicine."

The health official ultimately responsible for Australia's flu vaccination scheme was the Commonwealth Chief Medical Officer, Professor Jim Bishop, who strongly defended the program to *The Weekend Australian Magazine* in his final interview before retiring this month. He argues that the flu vaccination program "changed dramatically the flu outlook for this country", with admissions to intensive care from

swine flu falling from 681 in 2009 to just 60 last year, and hospitalisations dropping from nearly 5000 to 600. Swine flu killed 191 Australians in 2009 and 36 last year. In contrast, seasonal flu killed 1796 Australians that year – but, unlike swine flu, the victims were mainly the frail and elderly. Bishop cautions that one in every three hospital patients were “perfectly fit and well” before they caught swine flu, which was severe in pregnant women, teenagers who had lost their innate childhood immunity and indigenous people who tend to suffer underlying health problems. Three pregnant women died of swine flu, and 280 ended up in intensive care.

Worst-case scenario

Others lost their babies. Townsville woman Alma Palmer, 19, knows first-hand the terrible impact the flu can have on pregnant women. In April 2009, four weeks before the happily anticipated arrival of her third child, she came down with swine flu, which was raging around her then home on Palm Island in North Queensland. With blinding headaches and nausea she went to see her doctor, who sent her home with some Panadol. A day after the doctor’s visit, she started coughing up blood and collapsed. Airlifted to Townville, she blacked out on the tarmac and lapsed into a coma. As she fought for her life in the intensive care ward with acute pneumonia, her unborn baby was being starved of oxygen. Lorna Joyce died in utero while her mother was still in a coma. “I woke up a week later, and found out my daughter was dead,” Palmer recalls. “I just cried and cried. I couldn’t believe she was dead.”

Paediatric specialist and epidemiologist Professor Robert Booy also sees first-hand the misery caused by flu, which he says kills three to nine children in Australia each year. Booy heads the clinical research team at the National Centre for Immunisation Research and Surveillance based at the Westmead Children’s Hospital in Sydney. He says swine flu is the worst he has seen, three times more likely than seasonal flu to kill kids. “They come in looking like they’re dying of blood poisoning,” he says. “We had children with inflammation of the brain, with paralysis, children with severe pneumonia required to go onto machines to take over the work of their heart and lungs.” Fifteen children under the age of 15 died of swine flu in 2009.

Booy has attacked Collignon over his comments, declaring that “if parents are told by a reputable, responsible professor not to immunise, they might be very disappointed to find their children very ill, in intensive care or dying”.

Booy supervised CSL’s clinical trials of Panvax in 2009. He says the other flu vaccines on the market this winter are safe. “We’re not going to promote anything that will harm children,” he says. “That [Fluvax] vaccine was a bad vaccine. They still don’t know why, and it’s not to be used. [The TGA says Fluvax cannot be given to under-5s, and says it is to be used on children aged 5-10 only when there is no alternative vaccine]. We shouldn’t rake over old coals.”

Collignon realises he is “in the bad books” over his criticisms of flu vaccination. “I’ve had people ring me from various sources and various levels of government to make it very clear I would be responsible for the deaths of large numbers of people if I kept on talking to the media,” he says. “There’s been a lot of pressure on me. Like a lot of medical people, I believe vaccines are terrific – but it has come to the situation where it’s almost like motherhood, that you cannot question it, especially in the public arena, for fear you’ll undermine the vaccination program.”

Bishop admits he did phone Collignon to “discuss the fact it’s up to all of us to realise the huge gains that have occurred through vaccination”. “When I was a child,” Bishop says, “my classmates were dropping off with polio. Vaccination has made a huge impact on our ability to look after diseases. Things that damage people’s trust in vaccines are problematic.”

What is telling, however, is how lackadaisical health professionals – those in the front-line of any pandemic – have been about vaccinating themselves. The Australian Institute of Health and Welfare has discovered that barely one in four health and community workers bothered to get the free pandemic flu shot in 2009 – compared to 19 per cent of the adult population generally. Last year, just 6 per cent of children and 18 per cent of adults had been vaccinated against the flu. Asked why they shunned the flu shot, one in every six people cited “problems”, saying they thought the vaccine was “rushed and unsafe”.

While Collignon advocates the vaccination of at-risk children, he worries that healthy kids are still being immunised when so little is known about what went wrong with Fluvax. He is pushing for an independent surveillance system, funded through a levy on vaccines, to ensure last year’s debacle is never repeated. “We don’t know why it happened,” he says. “The mere fact we can’t explain it is, to me, of concern.”

A year after the Federal Government banned Fluvax for younger children, the company that manufactured it still does not know what caused the febrile convulsions. Nor does the TGA, which launched an international investigation that examined everything from the ingredients to the manufacturing process. Bishop says the evidence points to an excess of the enzyme neuraminidase within the H1N1 strain of flu used in the vaccine, which triggered an overreaction in children’s immune systems. The TGA is still trying to work out whether CSL’s manufacturing process gave Fluvax a higher concentration of the enzyme than other vaccines on the market. But CSL’s director of clinical development of vaccines, Dr Michael Greenberg, insists the investigations “do not point to a manufacturing issue... It seems to be something about what’s in the vaccine, the strains involved,” he says.

The 2009 version of Fluvax was not tested in children, Greenberg explains, because “it is not routine to do clinical trials in children, it’s not required”. (Australian health

authorities do not require clinical trials of the seasonal flu vaccine on the grounds that four decades of use have not revealed any safety issues, and it would slow down production. But clinical trials for children are required in Europe.) Yet a scientific paper published in October 2009 reveals that a previous version of the vaccine, which did not include the swine flu strain, had been linked to the hospitalisation of two of the 298 children tested in a clinical trial in Melbourne and Perth four years earlier. Its co-authors were Professor Terry Nolan – the Federal Government’s chief adviser on vaccines – and Dr Peter Richmond, a fellow adviser who headed vaccine trials at the hospital where Saba was treated. Neither would be interviewed, but CSL’s Greenberg insists the results were not a “red flag” for severe side-effects.

Since last year’s Fluvax suspension, which was also imposed in the US and Europe, CSL has not sought TGA approval to use Fluvax in the under-fives. (Greenberg says he has vaccinated his own three-year-old son with a rival company’s brand.) CSL does not intend to produce any more Panvax on the grounds that it was designed as a pandemic vaccine and has been superseded by Fluvax. Now the only option for parents who choose to vaccinate their children against swine flu this year is to use Abbott Products’ Influvac, made in The Netherlands, or Sanofi Pasteur’s French-made Vaxigrip, the only two brands recommended for use in children younger than 10. Both combine the same three flu strains used in Fluvax, but Bishop considers them safe on the grounds they have not produced the same high rate of side-effects during worldwide use over the past year. “I think it is safe,” he asserts. “Millions of people have now had the vaccine.”

Collignon has also upset the nation’s top medico by suggesting that regular flu shots for healthy people could weaken their natural immunity against any new wildfire influenza. Bishop scoffs at the theory – “that’s like saying you weaken people’s immunity against smallpox by immunising them” – but Collignon’s view has a foothold within the scientific community. Research from Canada and Hong Kong indicates that people who received a seasonal flu vaccine in 2008 had double the risk of contracting swine flu when the pandemic struck a year later.

Epidemiologist John Mathews, from the School of Population Health at the University of Melbourne and a former senior adviser to the federal Health Department, agrees that natural infection with the flu grants broader immunity than vaccination. “Seasonal vaccines do not boost the broadly reactive protection that can be induced by infection with live virus. We need more research to better understand the interactions between the immunity induced by natural infection with seasonal virus, and that induced by vaccination.”

Parents’ dilemma

As another winter descends, parents contemplating what is best for their children can

take little confidence from the controversy brewing in the scientific community. The Chief Medical Officer has tempered last year's advice to vaccinate everyone, although he is adamant that those most at risk – the elderly, the indigenous, pregnant women and anyone with an underlying medical problem – should get the flu shot. “We've put it back on the parents, to say ‘if you think flu is important to your child, have a chat to your doctor’,” Bishop says. “The government isn't the right person to give medical advice.”

Mathews thinks it is a cop-out for the government to leave the recommendation entirely to doctors. “How should a GP give you a better decision than the national [immunisation] committee?” he asks. Despite his expertise, even Mathews is unsure if his young grandchildren should have the flu jab this winter. “I am sitting on the fence,” he concedes. “If their mother asked me, I'd say I don't think it's essential they get vaccinated but I don't think it would be harmful.”

WA's Health Minister is continuing to recommend flu vaccination for all children this year on the grounds that “the disease itself can be severe, unpredictable and life-threatening”. The Australian Medical Association's official line is that children with underlying medical conditions should be vaccinated – a climb-down from the initial push to immunise everyone. “It's probably true that we're not as pushy, but we would not dissuade anyone from having the vaccine,” says AMA vice-president Steve Hambleton.

Booy is predicting a “moderate” flu season this year, as one in every three or four children will have gained natural immunity to swine flu, which has replaced the other flu types as the dominant strain of flu. “I'm not pushing parents to have the vaccination ... I just want them to feel they have a choice,” he says. “I don't see that they should be told not to because of safety concerns that are all about last year's vaccine, and not this year's.”

The World Health Organisation is keeping close watch on what went wrong in Australia. David Durrheim, professor of public health medicine at the University of Newcastle and a member of the WHO Strategic Advisory Group of Experts on Immunization, says Australia's “passive” system of reporting side-effects has been “effective” but could be improved. Rapid reporting of unusual or unexpected side-effects, prompt investigation and openness with the public are “essential to maintain public confidence in vaccine programs”.

In March, WA Health changed its fax-based reporting system to let patients, parents and medical staff report side-effects online. For the first time, CSL is being made to monitor the vaccination of 600 children and report any side-effects to the TGA.

Collignon concedes it would be impractical to run clinical trials of a flu vaccine that changes composition every year. “You’d never get the vaccine out in time,” he says. But he wants active surveillance of any complications. “Parents could fill out a diary for seven days, and the results could go into a database so the government can quickly see any side-effects. This is the sort of thing governments should do, with a levy on the vaccine to pay for the cost.”

Bishop defends the existing “passive surveillance” regime, which is being reassessed. “This was a new side-effect,” he says of the one-in-100 rate of febrile fits. “The world wasn’t aware of it. The current reporting system worked in the sense it was picked up and reported and was acted upon. The debate is whether it was fast enough. There are some things that probably could be improved upon.”

A year after the flu shot landed Sharron Coppin’s three children in an emergency ward, WA Health has invited her to try it again – this time with a different vaccine, and in a hospital. A big believer in the benefits of vaccination, she is understandably nervous. “They reckon it would be beneficial but I’m so scared it’s going to happen again,” she says of the side-effects. “I think the flu vaccine has got more of a risk than the risk of actually getting the flu.”

Saba Button recently turned two, but cannot hold up her head or crawl, let alone walk or talk. In the past year she has returned to hospital 11 times with respiratory problems. Kirsten, a primary school teacher, and Mick, an entrepreneur, dote on her constantly. “She can sneeze and fall down from her chair,” Kirsten says, swallowing her tears. “She was perfectly healthy and happy, the most beautiful baby. She slept like clockwork, ate well, she felt very secure and loved. We were blessed.”

The family has hired Perth malpractice lawyer Julian Johnson to sue the WA Government for compensation. WA Health would not discuss any specifics of the case. “We’re not going to just sit back and let this happen to other people,” Kirsten insists. “How could there be so many people presenting [with fits] and nobody said a word? I would never have risked my healthy baby’s life and future. How could they muck around with babies?”