STATE CORONER'S COURT

OF NEW SOUTH WALES

Inquest:	**Inquest into the death of Josephine Lambert**
Hearing dates:	**24 and 25 June 2014**
Date of findings:	**8 August 2014**
Place of findings:	**State Coroner's Court, Glebe**
Findings of:	**Deputy State Coroner HCB Dillon**
Catchwords:	**CORONERS** – Cause and manner of death – Death of psychiatric patient – Whether death due to clozapine toxicity – Whether treating clinicians observed protocols for administering clozapine – Recommendation concerning communication between treating clinicians and forensic pathologists conducting post mortem investigations

File number:	2011/390164
Representation:	Sgt S Korneluk (Advocate Assisting) Mr R Sergi instructed by Avant (Western Sydney Local Health District & Drs Popova and Sampson) Ms Robertson, Nurses Association (RNs Fanuc and Maples)
Findings:	I find that Josephine Lambert died at the Cumberland Hospital, Parramatta, New South Wales on 28 July 2011 due to natural causes, possibly a cardiac arrhythmia, while an inpatient at the hospital.
Recommendations:	***To the Minister for Health:*** I recommend that, in relation to hospital deaths reported to coroners, the NSW Forensic and Analytical Health Service consider methods of improving routine communication between forensic pathologists conducting post mortem investigations and the patient's treating clinicians. This would be with a view to forensic pathologists being given as complete a relevant history as is practicable in a timely fashion so as to enable as accurate a post mortem diagnosis as is reasonably possible to be given.

IN THE STATE CORONER'S COURT
GLEBE
SECTION 81 CORONERS ACT 2009

REASONS FOR DECISION

Introduction

This is an inquest into the death of Josephine Lambert who died at the Cumberland Hospital on 28 July 2011. Josephine was a long-term patient and was in her 8th admission at the hospital when she died. She had suffered treatment-resistant schizophrenia for most of her life and had a number of other physical conditions that were problems for her, including diabetes, asthma, hypertension and morbid obesity. Because her schizophrenia was treatment-resistant, she was prescribed clozapine, a last-line medication that it is required to be carefully administered and monitored.

Despite her illnesses, Josephine was able to enjoy her life when she was stable on her medications. She was much-loved by her family because she was affectionate, warm-hearted and had a sense of fun. Her sister Kim and her daughter Louise, both warm and kind-hearted people themselves, were present throughout the inquest and spoke movingly about how much she was missed by her family

Role of the coroner

The coroner's role is to investigate sudden and unexpected deaths. The coroner must seek to identify a deceased person, when and where that person died, the physical cause of death and how that death came about.

In NSW, coroners also have special jurisdiction to investigate the deaths of patients of a psychiatric hospital. All such deaths must be reported. Preliminary investigations are carried out by police officers and, if the coroner believes that there are further issues to be examined, an inquest may be ordered.

Mentally-ill involuntary patients are by definition vulnerable and in need of protection. Coronial investigations of the death of such patients are one way that our society seeks to ensure that hospitals remain accountable and that patients are properly cared for. If fault is found in that care and treatment, systems can be improved to reduce the risk of further similar deaths.

The issues

In any inquest the coroner seeks to identify the person who has died, the date and place of the death and the cause and manner or circumstances of the death. The principal issue in this case is whether Josephine died as a result of 'acute clozapine toxicity 'as was reported in the autopsy report of Dr Istvan Szentmariay, the forensic pathologist who conducted the post mortem examination of Josephine's body.

The background

Josephine was 44 years old when she died. She had first been diagnosed with schizophreniform psychosis in 1988. In 1989, this diagnosis was changed to bipolar disorder. In 1991, however, a firm diagnosis of schizophrenia was made. Over the next 20 years or so, until her death, she had multiple presentations and admissions to psychiatric hospitals, including eight at Cumberland Hospital.

A number of anti-psychotic medications and treatments, including ECT, were trialled with Josephine but without significant success. In 1995 and 1996, she was trialled on clozapine. The second trial, from 1996 to 2000, proved highly successful until she became non-compliant with her medication regime.

In January 2009, Josephine was readmitted to Cumberland Hospital under the care of Dr Anna Popova. Dr Popova commenced Josephine on clozapine after consulting a cardiologist to ensure that it was safe to do so.

Clozapine is a very effective drug but has serious potential side-effects. They include possible cardiomyopathy or myocarditis. Cardiomyopathy is a condition in which the heart muscle becomes inflamed and enlarged. This means that it is stretched and weakened and does not pump blood efficiently. Myocarditis is an infection of the heart muscle. It also weakens the muscle and may interfere with the electrical conduction system of the heart that maintains a healthy heartbeat.

For these reasons, clozapine is prescribed cautiously and is administered only under strictly monitored conditions.

In January 2010, Josephine went absent without leave from the hospital. About a week later, she was brought back to the hospital by police in a poor mental and physical state and was re-admitted. She was restarted on clozapine. Once back on clozapine, she began to recover steadily.

Over the next year and a half, she attended the Mental Health Review Tribunal on a number of occasions and each time was required to remain in hospital for treatment of her mental illness. During this time, her dosage of clozapine was varied. At one point, it became necessary to increase the dose to the maximum

recommended (900mg per day) to manage her symptoms adequately. By July 2011, however, her daily doses were 150mg in the morning and 500mg at night.

The events of 28 July 2011

In July 2011, Josephine was residing in Jarrah House, part of the rehabilitation section of the hospital. This section caters for long-term, chronically ill patients.

At about 11pm, a nurse did a bed check of the patients in Jarrah House. Josephine was in bed asleep at that time. After the checks, the nurse returned to the staff cottage nearby. At about 11.35pm, another patient came to the staff cottage to say that Josephine was lying unconscious in the hallway of Jarrah House. Her fall had not been witnessed by anyone.

Nurses immediately rushed to Jarrah House and simultaneously called a 'Code Blue' alert – a medical emergency requiring the 'crash team' to rush to the scene to provide life support and resuscitation. During this process, an ambulance was also called. The Medical Emergency Team arrived to find nurses conducting CPR on Josephine. CPR and other first aid measures continued for some time but the MET team and Ambulance Service paramedics were unable to resuscitate Josephine.

Police investigators were called and her death was notified to the Coroners Court.

The post mortem examination report

When a person dies suddenly and the cause of that death is not known or cannot easily be diagnosed, an autopsy is usually conducted by a forensic pathologist and a report is prepared for the coroner. Quite commonly the diagnosis of the cause of death is a diagnosis of exclusion. This means that the pathologist considers the person's medical history and patient records, looks at the person's body and does tests and, by doing this, is able to exclude various conditions as the likely cause of death. For example, there may be no history of cancer, no visible signs of cancer and no evidence in the blood tests of cancer.

Sometimes a person dies suddenly without there being any physical damage that is left behind as evidence of what happened. Cardiac arrhythmia is probably the most common of these types of deaths. This means that the person's heartbeat runs out of control and the blood stops circulating. The heartbeat is kept in proper rhythm by the body producing electrical current. If a fault develops in that electrical conduction system, the heart's timing can be thrown out rhythm.

While Josephine had a number of co-morbidities, the forensic pathologist found nothing that stood out as the anatomical cause of death. Blood tests revealed that, at the time the samples were taken, Josephine had relatively high levels of clozapine. Because there was no other obvious cause of death, and the blood test

levels of clozapine (2.6 mg/L) fell within the 'toxic' range specified in toxicology reference tables used by the pathologists, Dr Szentmariay concluded that the most likely cause of Josephine's death was clozapine toxicity.

The challenge to the toxicology findings

Because this opinion suggested that something had gone wrong at the Cumberland Hospital and that Josephine may have been overdosed on clozapine, or may have overdosed herself, further inquiries were made.

Dr Popova, Josephine's treating psychiatrist, gave evidence that she had been prescribed clozapine within the recommended range. She also gave evidence that the protocol for administering clozapine had been strictly followed. This protocol requires that patients receive regular blood tests while on clozapine. Unless the blood tests are done, and are properly documented, the hospital pharmacy will not dispense the drug. This evidence was supported by evidence from the hospital pharmacist Ms Nancy Zaki and by Dr Peter Cohen, the Medical Director of Mental Health Services, Western Sydney Local Health District. And, of course, patients are closely monitored by nursing and medical staff for signs and symptoms of their mental illnesses but also for their response to medications. If Josephine had been developing increasing blood concentrations levels of clozapine that were too high, she would have been observed to become excessively drowsy, there may have been blood pressure irregularities and possibly increased temperatures. There is no evidence of any of these signs manifesting themselves in the period shortly before her death.

Evidence was also given that clozapine and other S4D drugs are kept in a locked cupboard in a treatment room that is also locked when not in use. Whenever S4D drugs are administered a check is done by two nurses. Records of drugs in and out and administered are kept. There was no evidence of any irregularity in the quantities of clozapine used or supplied during the period leading up to Josephine's death.

According to the nurses who managed the administration of prescribed drugs, patients are given their medications in the treatment room and must take the drugs at the time they are administered in the presence of the nurses. This is checked by the nurses. No hoarding is permitted. Patients are not allowed to take drugs away with them. No drugs are left in patient's rooms. During the police investigation, Josephine's room was searched and no drugs, or medication bottles or packets or empty containers were located. This evidence demonstrates that it is highly unlikely that Josephine had a secret 'stash' of clozapine and had overdosed herself.

Professor Olaf Drummer, the head of the Department of Forensic Medicine at Monash University and Head of Forensic Scientific Services at the Victorian Institute

of Forensic Medicine, provided an independent expert report and oral evidence at the inquest.

In his report dated 3 October 2013, Prof Drummer stated (at [17]):

> *Deaths following the misuse of clozapine have occurred at post mortem concentrations ranging from 1.2mg/L, however most cases have exceeded 3 mg/L… This has also been observed at the Victorian Institute of Forensic Medicine in that clear deaths from overdose to clozapine usually have quite high blood concentrations, often much higher than 5mg/L in the leg blood (range 8-100mg/L). Moreover, deaths have usually occurred following an overdose to the drug, i.e., ingestion of a single large amount leading to death, rather than as a consequence of long-term therapy. Deaths occurring from misadventure or suicide but unrelated to clozapine administration have ranged up to about 4.8mg/L.*

He also commented:

> *It is not possible simply to assume that because clozapine concentrations are seemingly high they have necessarily caused a death, primarily due to significant changes in blood concentration that occur after death. If [Josephine] was on a stable dose and she had not shown signs of toxicity then death caused by this drug is much less likely, particularly in that there was no evidence of myocarditis, a rare disease sometimes associated with users of clozapine.*

Prof Drummer also gave important evidence concerning the redistribution of drugs following death. At the inquest, he explained that following death, levels of drugs found in blood samples are often artificially elevated above the levels ordinarily found in living people.

This is because quantities of the drug(s) that have been absorbed into body tissue (muscle and fat) leach out of the tissue cells into large blood vessels where they increase the concentrations found in the circulating bloodstream. He stated in his report that blood concentrations can be artificially elevated by two or three times above the actual concentrations found in living people when tested.

Prof Drummer also observed that individual people respond differently to drugs. Some respond to lower doses than others. In some people, like Josephine, need relatively high doses to obtain a therapeutic effect. Individual people are different in size, Body Mass Index, metabolic rates and other things. Some may suffer from kidney, heart or lung disorders that reduces the rate at which drugs are cleared from the body. These factors all affect the dosages that will be prescribed and therefore the concentration levels that will be found in patients while they are alive and after death.

In Prof Drummer's opinion, there are three hypotheses that could explain the high concentration levels found in Josephine's blood samples following her death:

- That she ingested an excessive quantity of clozapine in the day or two before her death;
- That, due to a heart, liver or kidney disorder she developed an inability to clear the drug from her system; or
- That the blood concentrations found post mortem were elevated due to changes that occurred after her death.

There is no evidence of over-dosage and no evidence of kidney, liver or heart disorders that would cause a drug to accumulate in her body. It follows that the elevation of concentration levels was most likely due to changes that occurred after her death.

Finally, Prof Drummer commented in his report that:

> *It is known that person with mental illness including schizophrenia can die suddenly, presumed to be related to an irregular heart rhythm (arrhythmias). While this association has been reported for clozapine, it is not clear to what extent the disease itself contributes to this process.*

Dr Szentmariay provided a letter supplementing his autopsy report after he had seen Prof Drummer's report.

Among other things he commented:

> *This case… illustrates the difficulties of formulating a cause of death not necessarily based on macroscopic or microscopic post mortem findings. The macroscopic findings were sparse…*
>
> *Post mortem identification of unwitnessed terminal seizures is a real challenge. Based on the history provided in this case, the patient was sleeping normally in her bed during the late evening hours (23.00), however, she was found lifeless shortly after in the hallway/lounge-room area. These events may indicate some substantial symptomatology which had prompted [Josephine] to wake up, leave her bed and subsequently collapse. The symptoms are not specific and they may represent a relatively sudden seizure or perhaps a cardiac event (arrhythmia? QT abnormality [an abnormality of the heart rhythm]? Can be caused by clozapine overdose).*

Dr Szentmariay also commented that, when formulating the cause of death for the autopsy report, he and his registrar had carefully used the words 'on the balance of

probabilities'. He said that he believed that clozapine 'played a role' in Josephine's death but agreed that this was not certain.

He also noted, like Prof Drummer, that schizophrenic patients are at higher risk of sudden death than the general population.

In the light of all this evidence, I have concluded that it is unlikely that Josephine died as a result of 'acute clozapine toxicity' and that it is much more likely that she died of natural causes. As her diabetes was being managed and she had no history of epilepsy, the most probable cause of her death appears to be a cardiac arrhythmia.

Communication between treating clinicians and forensic pathologists

Dr Szentmariay did not have the advantage I have had of receiving a full brief of evidence, particularly the statements of Dr Popova and others from Cumberland Hospital. Nor did he have Prof Drummer's report at the time of the autopsy.

In his supplementary letter, he showed intellectual integrity in admitting to the difficulties of diagnosis in a case like Josephine's and a willingness to revise his views in the light of fresh evidence.

This inquest illustrates not only the difficulties of diagnosis in some cases but also the possibility that a tentative diagnosis may imply a criticism of treating clinicians that cannot be corrected without an inquest drawing together fresh evidence.

In my view, it will ordinarily be helpful if, in cases such as this in which there is no clear or obvious cause of death, the forensic pathologists undertaking the post mortem examinations and the treating clinicians discuss the case before a final autopsy report is issued to the coroner. How that can best be done is not for me to determine.

Conclusion

The deaths of vulnerable people, especially those to whom the State owes a duty of care, are of special concern for coroners. Those who suffer psychiatric illness are often tormented by their illnesses, deprived of many of the satisfactions that normally flow from work and family and frequently live in poverty and die prematurely. Through no fault of their own, they are accorded a low social status. This makes them particularly vulnerable to neglect or abuse.

Yet they are equal in legal status with the rest of us as citizens and as our fellow human beings. The coronial system, including the forensic medicine system, is emblematic of our society's principled commitment to respect for human life and human dignity for all who live in this community.

So, too, is the public health system and, in particular, that part of the system dedicated to the care and treatment of the mentally ill. As all human systems are inherently imperfect, however, it is of great importance that the psychiatric health system is reviewed from time to time and those who manage it understand that they will be held to account for the care and treatment of their patients.

I hope that Josephine's family will find reassurance in the fact that their concerns have been listened to and addressed and that this inquest has reached a conclusion that she was not overdosed with clozapine. Rather, it is my impression that Josephine was well-cared for and treated appropriately and reasonably.

I also hope that they will accept my sincere and respectful condolences on the loss of a woman who, despite her illness, was much loved and respected by those closest to her.

Findings s 81 Coroners Act 2009

I find that Josephine Lambert died at the Cumberland Hospital, Parramatta, New South Wales on 28 July 2011 due to natural causes, possibly a cardiac arrhythmia, while an inpatient at the hospital.

Recommendation s 82 Coroners Act 2009

To the Minister for Health:

I recommend that, in relation to hospital deaths reported to coroners, the NSW Forensic and Analytical Health Service consider methods of improving routine communication between forensic pathologists conducting post mortem investigations and the patient's treating clinicians. This would be with a view to forensic pathologists being given as complete a relevant history as is practicable in a timely fashion so as to enable as accurate a post mortem diagnosis as is reasonably possible to be given.

Magistrate Hugh Dillon
Deputy State Coroner for NSW