IN THE CORONERS COURT
OF VICTORIA
AT MELBOURNE

Court Reference: **COR 2016 6193**

FINDING INTO DEATH WITHOUT INQUEST

Form 38 Rule 60(2)
Section 67 of the Coroners Act 2008

Findings of:	**MR JOHN OLLE, CORONER**
Deceased:	**KATHRYN MAREE JELBART**
Date of birth:	**6 OCTOBER 1956**
Date of death:	**25 MARCH 2016**
Cause of death:	**MULTIORGAN FAILURE AND POLYMICROBIAL SEPSIS SECONDARY TO SEVERE BONE MARROW FAILURE IMMUNOSUPPRESSION FOR PAST RENAL TRANSPLANT**
Place of death:	**AUSTIN HOSPITAL** **145 STUDLEY ROAD** **HEIDELBERG VICTORIA 3084**

HIS HONOUR:

BACKGROUND

1. Kathryn Maree Jelbart (Kathy) was born on 6 October 1956. She was 59 years old at the time of her death.

2. Kathy had an underlying diagnosis of spina bifida[1] at birth requiring an ileal conduit[2] at five years of age. In February 2015, Kathy underwent a renal transplant at the Austin hospital, the donor was her husband. Kathy had additional medical history of deep venous thrombosis, depression, hepatitis B, basal ganglia haemorrhage 2005 with residual left hemiparesis[3], supraventricular tachycardia[4] and a stable cerebral communicating artery aneuryism[5].

3. Kathy required immunosuppression[6] with mycophenolate[7], prednisolone[8] and tacrolimus[9] following her renal transplant. One of the side effects of mycophenolate chronic diarrhoea. Kathy was managed by the Renal Unit at the Austin Hospital and supported by her general practitioner in Bendigo.

THE PURPOSE OF A CORONIAL INVESTIGATION

4. On 30 December 2016, Dr Natasha Brown, Clinical Geneticist at the Austin Hospital, reported Kathy's death after meeting with her daughters regarding the possibility that they may be at risk of a genetic condition causing impaired thiopurine methyltransferase (TPMT). After review of the materials in relation to Kathy's death and a review of the medical literature around TPMT testing and azathioprine use, Dr Brown became concerned that Kathy's death may be classified as a reportable death and subsequently reported Kathy's death to the Coroner.

5. Kathy's death constituted a '*reportable death*' under the *Coroners Act 2008* (Vic), as her death occurred in Victoria includes deaths that occur during a medical procedure or

---

[1] A developmental congenital disorder caused by the incomplete closing of the embryonic neural tube. Some vertebrae overlying the spinal cord are not fully formed and remain unfused and open. If the opening is large enough, this allows a portion of the spinal cord to protrude through the opening in the bones. There may or may not be a fluid-filled sac surrounding the spinal cord.
[2] A surgical technique for the diversion of urine after a patient has had their bladder removed.
[3] Brain haemorrhage or 'stroke' leading to mild arm and leg weakness
[4] Occasional bursts of rapid heart rate.
[5] Swollen blood vessel within the brain under regular observation.
[6] Essential 'anti rejection' medications after a transplant in order to allow the body to tolerate a foreign transplanted kidney.
[7] A component of the anti-rejection medication regime.
[8] A component of the anti-rejection medication regime.
[9] A component of the anti-rejection medication regime.

following a medical procedure where the death is or may be causally related to the medical procedure and a registered medical practitioner would not, immediately before the procedure was undertaken, have reasonably expected the death..[10]

6. The jurisdiction of the Coroners Court of Victoria is inquisitorial[11]. The purpose of a coronial investigation is independently to investigate a reportable death to ascertain, if possible, the identity of the deceased person, the cause of death and the circumstances in which death occurred.

7. It is not the role of the coroner to lay or apportion blame, but to establish the facts.[12] It is not the coroner's role to determine criminal or civil liability arising from the death under investigation, or to determine disciplinary matters.

8. The "cause of death" refers to the medical cause of death, incorporating where possible, the mode or mechanism of death.

9. For coronial purposes, the circumstances in which death occurred refers to the context or background and surrounding circumstances of the death. Rather than being a consideration of all circumstances which might form part of a narrative culminating in the death, it is confined to those circumstances which are sufficiently proximate and causally relevant to the death.

10. The broader purpose of coronial investigations is to contribute to a reduction in the number of preventable deaths, both through the observations made in the investigation findings and by the making of recommendations by coroners. This is generally referred to as the 'prevention' role.

11. Coroners are also empowered:

    (a) to report to the Attorney-General on a death;

    (b) to comment on any matter connected with the death they have investigated, including matters of public health or safety and the administration of justice; and

    (c) to make recommendations to any Minister or public statutory authority on any matter connected with the death, including public health or safety or the administration of

[10] Section 4, definition of 'Reportable death', *Coroners Act 2008.*
[11] Section 89(4) *Coroners Act 2008.*
[12] *Keown v Khan* (1999) 1 VR 69.

justice. These powers are the vehicles by which the prevention role may be advanced.

12. All coronial findings must be made based on proof of relevant facts on the balance of probabilities. In determining these matters, I am guided by the principles enunciated in *Briginshaw* v *Briginshaw*.[13] The effect of this and similar authorities is that coroners should not make adverse findings against, or comments about individuals, unless the evidence provides a comfortable level of satisfaction that they caused or contributed to the death.

MATTERS IN WHICH THE CORONER MUST, IF POSSIBLE, MAKE A FINDING

Identity of the Deceased pursuant to section 67(1)(a) of the *Coroners Act 2008*

13. The Deceased was Kathryn Maree Jelbart. Identity was not in issue and required no further investigation.

Medical cause of death pursuant to section 67(1)(b) of the *Coroners Act 2008*

14. A Forensic Pathologist has not been involved as the reporting of Kathy's death. The death was reported on 30 December 2016, which was several months after her death and was initiated by the Clinical Geneticist Dr Natasha Brown in response to her concerns that Kathy's death was reportable to the Coroner.

Circumstances in which the death occurred pursuant to section 67(1)(c) of the *Coroners Act 2008*

15. In January 2016, Kathy travelled overseas and developed progressively worsening diarrhoea, which had been a fluctuating problem since the kidney transplant. Kathy was admitted to Noumea Hospital with severe diarrhoea, dehydration and acute kidney injury[14]. A renal specialist at Noumea Hospital substituted the mycophenolate with azathioprine 50mg twice per day, which had not been previously prescribed. Initially Kathy's condition improved and she was discharged from Noumea hospital and returned to Australia, where she was reviewed by the renal clinic at the Austin Hospital.

---

[13] (1938) 60 CLR 336.

[14] Deterioration in her transplanted kidney function as measured by blood test.

16. Professor David Power, Director of Nephrology at the Austin Hospital stated that Kathy was seen at the Austin Health outpatient clinic on the 19 February 2016 by Dr Peter Mount (consultant nephrologist) and that Dr Mount's notes indicated that a discussion of the advantages and disadvantages of the continuation of azathioprine were discussed with Kathy who elected to continue with azathioprine.

17. Professor Power writes:

> "Pathology taken on that day showed that the number of white cells in the blood was 4.2 and within normal limits (normal 4-11), while the haemoglobin (which is a measure of the number and quality of red cells in the blood) was low at 91 (normal 115-165) compared with a previous value of 104 about 6 weeks earlier. The platelet count (platelets are one of the formed element of the blood and responsible for clotting) was 354, which is normal (normal 150-400)."

18. Further blood tests were ordered and these were done on 27 February 2016 showed a dramatic change with a marked reduction in all the blood components. These results were conveyed to the general practitioner who arranged urgent admission to the Bendigo Hospital Emergency Department and Kathy was then transferred to the Austin Hospital.

19. On 1 March 2016, Kathy was admitted to the Austin Hospital with a diagnosis of sepsis in the setting of pancytopenia[15] ascribed to azathioprine toxicity. Despite family concerns that azathioprine was not immediately ceased, Professor Power and a review of the medical records was able to confirm that azathioprine was not administered to Kathy on any occasion during this admission to the Austin Hospital.

20. Kathy's bone marrow suppression[16] continued to deteriorate despite the cessation of azathioprine and the use of filgrastim[17] and other measures to support her blood count and treat infection and she was transferred into the Intensive Care Unit. Kathy's condition continued to deteriorate. On 22 March 2016, a family meeting was convened to discuss the palliative care service and to withdraw active treatments.

21. On 25 March 2016, Kathy died from multiorgan failure in the setting of polymicrobial[18] sepsis secondary to bone marrow failure.

---

[15] Abnormally low counts of all the blood components made by the bone marrow including red cells, white cells and platelets.
[16] Bone marrow inactivity leading to the pancytopenia (above).
[17] Medication used post chemotherapy to boost bone marrow to produce white cells.
[18] Multiple infections.

22. Genetic and enzymatic testing of thiopurine methyltransferase (TPMT) was performed and Kathy was homozygous[19] for a low functioning allele[20] within the TPMT gene (designated *3A/*3A) which is associated with extreme sensitivity to the bone marrow suppressive effects of azathioprine. With the permission of the family and the Coroner, the Austin Health team published a 'case review of fatal azathioprine toxicity'.

Medical Investigation

23. There is broad agreement that Kathy died as a result of severe azathioprine toxicity related to a genetic susceptibility which caused fatal bone marrow suppression and fulminating sepsis.

24. The following extract is from the published case report in relation to Kathy's death:

> "Azathioprine, a prodrug of mercaptopurine, is a purine antimetabolite which suppresses the immune system. In addition to preventing the rejection of organ transplants it can be used to manage a range of autoimmune and inflammatory conditions such as inflammatory bowel disease and system lupus erythematosus.
>
> The enzyme thiopurine methytransferase (TPMT) is important for converting azathioprine and mercaptopurine into inactive metabolites. This reduces the consequent risk of myelosuppression[21]. In 0.3-0.6% of Caucasians there are genetic polymorphism[22] which leads to markedly reduced TPMT activity. During her final admission, our patient was found to have a genetic polymorphism, which resulted in low TPMT activity. This made her extremely sensitive to the myelosupressive effects of azathioprine."

25. Kathy's case was discussed extensively within the Austin Hospital and Professor Power states that the severity of Kathy's reaction to azathioprine was unprecedented in the experience of the renal unit at the Austin Hospital. Professor Power states that the Austin Hospital renal unit policy was subsequently amended to mandate TPMT testing prior to the prescription of azathioprine in all renal patients.

---

[19] Two identical genes.
[20] Genetic sequence within the chromosome.
[21] Refers to bone marrow suppression, but particularly the white cell component.
[22] The simultaneous occurrence in the same locality of two or more discontinuous forms of a gene.

26. Dr Natasha Brown described the benefits of genetic testing prior to starting treatment with thiopurine containing medications including azathioprine:

> "Dose optimization can occur for all patients, and the likelihood of a catastrophic outcome can be reduced in a small number. This means that the 0.3% at extremely high risk (low/absent TPMT activity and homozygous or compound heterozygous[23]) can consider therapeutic alternatives or drastic dose reduction, the 11% who are intermediate metabolisers or are heterozygous can be offered dose reduction, while those with normal genotype can commence the usual full dose to maximize therapeutic response."

27. Prior to Kathy's death, the Austin renal unit did not have a policy to perform TMPT testing when prescribing azathioprine.

FINDINGS

28. Having investigated the death of Kathryn Maree Jelbart and having considered all of the available evidence, I am satisfied that no further investigation is required.

29. I make the following findings, pursuant to section 67(1) of the *Coroners Act 2008*:

(a) that the identity of the deceased was Kathryn Maree Jelbart, born 6 October 1956;

(b) that Kathryn Maree Jelbart died on 25 March 2016, at the Austin Hospital, 145 Studley Road, Heidelberg, Victoria from multi organ failure and polymicrobial sepsis secondary to severe bone marrow failure immunosuppression for past renal transplant; and

(a) that the death occurred in the circumstances described in the paragraphs above.

[23] Two abnormal genes of different types.

COMMENTS

30. Pursuant to section 67(3) of the *Coroners Act 2008*, I make the following comments connected with the death:

    1. At present, there is no Australian guideline regarding TPMT testing, and the decision to perform routine genotyping or enzymatic analysis prior to prescription of thiopurine[24] medication is determined by individual clinician or health care service.

    2. Access to testing should not be considered a significant barrier since genotyping and TPMT functional assays are now readily available, and the cost of such testing is not high.

    3. A significant barrier that may remain is the lack of knowledge amongst prescribers regarding access to testing and the implementation of specific recommendations at a clinical level, across the different subspecialty groups that are largely responsible for prescribing these medications

RECOMMENDATION

31. Pursuant to section 72(2) of the *Coroners Act 2008* (Vic), I make the following recommendation connected with this death:

    1. that TPMT genotyping for the common alleles should be mandatory for patients prior to the commencement of thiopurine containing medications.

32. I convey my sincerest sympathy to Kathy's family and friends.

33. Pursuant to section 73(1) of the *Coroners Act 2008,* I order that this Finding be published on the internet.

---

[24] A broader group of compounds which azathioprine belongs.

34. I direct that a copy of this finding be provided to the following:

(a) Kathy's family, senior next of kin;

(b) Prof. David Power;

(c) Dr Natasha Brown;

(d) Therapeutic Goods Association;

(e) Safer Care Victorian Department of Justice;

(f) Royal Australasian College of Physicians;

(g) Interested Parties.

Signature:

MR JOHN OLLE

CORONER

Date: 8 January 2018