CORONERS ACT, 2003

SOUTH *AUSTRALIA*

FINDING OF INQUEST

An Inquest taken on behalf of our Sovereign Lady the Queen at Adelaide in the State of South Australia, on the 12th day of November 2013 and the 31st day of January 2014, by the Coroner's Court of the said State, constituted of Mark Frederick Johns, State Coroner, into the death of Marjorie June Rowan.

The said Court finds that Marjorie June Rowan aged 52 years, late of 16 Montacute Street, Elizabeth Downs, South Australia died at Elizabeth Downs, South Australia on the 3rd day of May 2009 as a result of ischaemic and hypertensive heart disease. The said Court finds that the circumstances of her death were as follows:

1. Introduction

1.1. Marjorie June Rowan died on 3 May 2009 at her home in Elizabeth Downs. She was 52 years of age.

1.2. An autopsy was performed by Dr John Gilbert, forensic pathologist, who provided a report dated 14 January 2010[1], in which he gave as the cause of death 'dothiepin toxicity'.

2. Background

2.1. Ms Rowan had a history of diabetes, hypertension and major depression which required admission to the Adelaide Clinic in 1995 and 2001. She was on a number of medications for her depression, dothiepin being one of them. She had undergone electroconvulsive therapy in the past. She was also taking benzodiazepines to control her anxiety and anti-hypertensive medication for her high blood pressure.

[1] Exhibit C11

2.2. Ms Rowan had been a patient of psychiatrist Professor Robert Goldney between 2000 and 2005 after the death of her long-term psychiatrist, Dr Lloyd, in 2000. Professor Goldney was able to stabilise Ms Rowan's depression with a combination of dothiepin (225mg) and solian 400mg nocte. Ms Rowan had been trialled on a higher dose of dothiepin (up to 350mg) to achieve stability of mood however this had caused side effects such as a dry mouth and lack of co-ordination. Ms Rowan had also been trialled on lower doses of dothiepin (lower than 225mg) however this had brought about a rapid recurrence of severe depressive symptoms. With the combination of dothiepin at 225mg and Solian at 400mg, Professor Goldney achieved stability in Ms Rowan's mood and, after 2001, she was not hospitalised again for psychiatric issues. When Professor Goldney retired from private practice Ms Rowan's psychiatric management was handed to Dr Renata Maruszczyk.

2.3. Early in 2009 Ms Rowan was referred to a surgeon, Mr David Scott Watkin, by her general practitioner, Dr William Lees, for ongoing pain caused by her gallbladder. Ms Rowan was seen by Dr Watkin on 30 March 2009 and her liver function was analysed. She was found to have raised GGT[2] and ALP[3]. She was scheduled for laparoscopic cholecystectomy[4] due to the suspected presence of gallstones in the gallbladder. It was also expected that there were stones in the bile duct.

2.4. The surgery took place on 21 April 2009 and, as well as the scheduled procedure, a choliangiogram[5] was undertaken which indicated that there may be stones in the bile duct. The gallbladder was removed and further surgery was booked to remove the gallstones from the bile duct in three weeks.

2.5. On 28 April 2009 Ms Rowan saw her general practitioner, Dr Lees, complaining of persistent pain due to her gallbladder disease. Dr Lees was aware that there was a stone or stones remaining in her common bile duct which were due to be removed on 12 May 2009. On this day Ms Rowan complained of nausea and a sensation of heat. She had a slight fever and Dr Lees prescribed her antibiotics, endone analgesia and took her blood pressure, which was raised at $^{160}/_{90}$. She was referred for a 24 hour blood pressure monitor to assess the efficacy of her hypertensive medication and an

[2] Gamma-glutamyltransferase
[3] Alkaline Phosphatase
[4] Removal of the Gallbladder
[5] Imaging of the bile duct by X-ray

echocardiogram. Dr Lees did not inform Ms Rowan's treating psychiatrist (Dr Maruszczyk) of her liver dysfunction, although Ms Rowan informed Dr Maruszczyk that she was to have gallbladder surgery. Dr Maruszczyk made a statement[6] in which she said she would like to be informed of any and all test results relating to her patients, but acknowledged that this does not always happen.

2.6. On Friday 1 May 2009 Ms Rowan's sister-in-law, Cheryle Rowan, attended at her home and found her to be in a depressed state. Ms Rowan was upset because she was about to become a grandmother for the first time and, due to her surgery, was unable to travel to Queensland to be with her daughter for the impending birth. Cheryle Rowan noticed on this occasion that her sister-in-law was dressed for the day and not in her pyjamas[7]. Ms Rowan told Cheryle on this day that she blacked out for a period of time on the Wednesday before.

2.7. The following day Cheryle Rowan spoke to her sister-in-law on the phone and she reported another black out. Cheryle offered to take her to the doctor and Ms Rowan said she would see if she could get an appointment. On the Sunday evening, 3 May 2009, relatives from Queensland attempted to contact Ms Rowan with no success. They tried again on the Monday morning, but when they could not raise her they contacted Cheryle Rowan. Cheryle was also unsuccessful in trying to contact Ms Rowan and so rang the doctors surgery, expecting that she had made an appointment for that day. No appointment had been made. At that point Cheryle Rowan rang the police and asked them to conduct a welfare check.

2.8. A welfare check was undertaken by Salisbury Patrols. They also asked for the SA Ambulance Service to attend. Cheryle Rowan met them at Ms Rowan's address. Ms Rowan was found deceased inside the premises. She was wearing pyjamas and socks. No suicide note was found and the medication that was located on the premises had all been prescribed to Ms Rowan. It was apparent from the prescribed doses, the date of the prescriptions and the quantities of medication that remained, that Ms Rowan had not taken more medication than she ought to.

[6] Exhibit C5a
[7] Exhibit C1d

2.9. It was the opinion of the investigating officer who attended the scene and located Ms Rowan that:

> 'There were no suspicious circumstances … It would appear that the deceased had got ready for bed and gone through to the living room to have a cigarette before going onto sleep. The fact that a cigarette, found in an ashtray, had been left to burn would indicate that the deceased collapsed to the floor from the 3 seat sofa and died on the floor.' [8]

3. Original opinion as to cause of death

3.1. Dr Gilbert's autopsy reported dated 14 January 2010[9] stated that at autopsy bloods were taken and there was a potentially lethal range of dothiepin in Ms Rowan's system (0.84mg/L). A sample of liver was also tested and returned a result of 32mg/kg which is was also considered to be potentially lethal. Dr Gilbert was aware that dothiepin is extensively metabolised in the liver and is contraindicated in hepatic failure. The prescribing information for dothiepin states that caution should be used in patients with impaired liver or renal function as toxic blood levels may develop. Additionally, a maximum daily dose of 200mg/day is listed. Ms Rowan was prescribed 225mg per day.

3.2. Dr Gilbert was aware from her medical records that Ms Rowan had deranged liver function before her gallbladder surgery. He therefore concluded that her impaired liver function predisposed Ms Rowan to developing dothiepin toxicity.

3.3. Another finding at autopsy was significant coronary artery disease. The right coronary artery and left diagonal branch artery were nearly completely occluded by atheromatous plaque (greater than 75% stenosis). Stenosis over 75% is recognised to predispose to lethal arrhythmias. It was noted by Dr Gilbert that Ms Rowan had a number of risk factors for ischaemic heart disease[10]. These markedly increased her risk of mortality from ischaemic heart disease.

3.4. Ultimately Dr Gilbert stated that:

> 'Death has been attributed to dothiepin toxicity … appearing likely that it resulted from mild liver impairment from common bile duct gallstones coupled with a relatively high dosage. Underlying ischaemic and hypertensive heart disease would therefore have

[8] Exhibits C3a and C3b
[9] Exhibit C11
[10] Diabetes, smoking and hypertension

> further predisposed to the development of cardiac arrhythmias and is therefore listed as a contributing factor in the death.' [11]

3.5. It will be recalled that Ms Rowan reported two blackouts to her sister-in-law before her death. These could have been explained by non-lethal arrhythmias.

4. Issues considered at Inquest

4.1. When this matter was first listed for Inquest the main focus was the communication between Dr Maruszczyk and Dr Lees and the prescription of the dothiepin medication. The issue to be ventilated was whether, given Ms Rowan's deranged liver function, the dothiepin should have been reduced or ceased in the lead up to and following her gallbladder operation. Prior to the matter being heard statements were produced from Dr Watkins, the general surgeon, Associate Professor Hugh Harley, Head of Clinical Hepatology at the Royal Adelaide Hospital, in the capacity as an expert, and Professor Robert Goldney.

4.2. It was the view of Professor Harley[12] that although there were elevations to the AST[13] and the ALT, this picture seldom reflects damage to the liver cells or inflammation of the bile duct and is consistent, in Ms Rowan's situation, with gallstones in the bile duct. If Ms Rowan had severely impaired hepatic function, a reduced albumin and an increased bilirubin would be present. These were consistently normal in the liver function tests undertaken. This supported the proposition that there was no severe liver injury in Ms Rowan.

4.3. Professor Harley commented on the macroscopic appearance of the liver at autopsy which was normal with a smooth capsular surface. The weight of the liver was also within normal range. He noted that upon microscopic examination there was no scar tissue of the liver and no evidence of cirrhosis. This suggested that there was no significant injury to the liver cells and therefore no significant impairment of liver function.

4.4. The statement from Professor Robert Goldney[14] noted that the dose of dothiepin prescribed to Ms Rowan at the time of her death was relatively standard and that

[11] Exhibit C11
[12] Exhibit C10a
[13] Aspartate amino transferase
[14] Exhibit C7a

much higher doses have been used therapeutically for depression. In some instances up to 600 mg per day.

4.5. Dr Watkins confirmed that he was aware of the medications that Ms Rowan was prescribed in the lead up to the surgery as it was his invariable practice to enquire. He was informed by Dr Lees. Dr Watkins stated:

> 'There was no clinical indication to reduce or stop the dothiepin and the concern is always that to reduce/cease medication which is clinically indicated may lead to an increase in the symptoms of depression which the medication itself is treating.' [15]

4.6. On receiving these additional statements, counsel assisting obtained an expert overview from Emeritus Professor Lindon Wing, Consultant Physician and Clinical Pharmacologist, who was furnished with all statements and casenotes. Professor Wing was asked whether the liver derangement that was present in March 2009 was such that it could adversely affect Ms Rowan's ability to metabolise the dothiepin leading to toxic levels in her liver and blood. Professor Wing's response was as follows:

> 'Although the test results in Ms Rowan during the period of interest indicated that her liver cells were under stress from a cholestatic process, the overall processing capacity of the liver was such that it could still break down bilirubin or synthesise albumin in a normal manner. Likewise the capacity for a drug such as dothiepin would be overall no different from that for bilirubin and thus on the basis of Ms Rowan's liver function test, results would be expected to be essentially normal.' [16]

5. Further consideration as to cause of death

5.1. These new reports and statements were referred by counsel assisting to Dr John Gilbert who revised his cause of death to 'ischaemic and hypertensive heart disease complicated by dothiepin toxicity'[17]. He acknowledged the opinions of both Professor Hugh Harley and Emeritus Professor Lindon Wing in doing so. He did note:

> 'The reason for the abnormally high post-mortem blood and liver levels of dothiepin is uncertain. Emeritus Professor Wing's suggestion that this may have arisen because Ms Rowan began taking a larger daily dose or took a single larger dose is a plausible hypothesis.' [18]

[15] Exhibit C8a, page 3
[16] Exhibit C9a, pages 2-3
[17] Exhibit C11a
[18] Exhibit C11a, page 1

5.2. Dr Gilbert apparently remained concerned that there was no discernible reason for Ms Rowan having such high levels of dothiepin in her liver and blood. He submitted a third supplementary report[19] detailing a new analytical method to measure the levels of the dothiepin metabolite nordothiepin in the blood and liver tissue. The purpose of this exercise was to establish whether Ms Rowan may have taken a deliberate overdose or whether the drug had somehow built up in her system to dangerous levels over time.

5.3. The finding was of a high parent to metabolite ratio. This supported an acute overdosage as opposed to gradual accumulation of toxic levels due to chronic overdosage or impaired metabolism. However, Dr Gilbert noted that this finding had to be balanced against the lack of scene evidence of excessive tablet consumption and the fact that there were possible post-mortem causes for the results.

5.4. Dr Gilbert noted that Ms Rowan was prescribed dothiepin to be taken at night. She appeared most likely to have died overnight because she was found in her pyjamas. It is therefore possible that she died while there was a high concentration of dothiepin in her stomach. While she was not decomposed, the interval between her death and her autopsy was approximately three days. During this time it would have been possible that the post-mortem liver level of dothiepin became significantly higher than that present in life due to post-mortem diffusion from the stomach. The liver level of nordothiepin would not be expected to change significantly after death. Based on a study of a similar drug (distributed in the same way), the parent to metabolite ratio in the liver could rise substantially after death and give a misleading indication of acute overdose.

5.5. Based on this hypothesis Dr Gilbert requested a dothiepin level on Ms Rowan's gastric contents to determine whether or not dothiepin toxicity was a contributing factor to death. On 13 May 2013 Dr Gilbert issued his final supplementary report[20] stating that the analysis of the gastric contents showed a relatively high dothiepin concentration (34mg/L). This would be in keeping with dothiepin medication still being present in the stomach at the time of death. This would also predict the presence of significant concentrations of dothiepin in the duodenum and small intestine.

[19] Exhibit C11b
[20] Exhibit C11c

5.6. Dr Gilbert reasoned that, as dothiepin has a high volume of distribution and is structurally similar to amitriptyline, and as amitriptyline is known to be highly redistributed after death, the high concentration of dothiepin noted in the liver, while suggestive of overdosage, could also be explained by post-mortem diffusion of the drug from the stomach, duodenum and small intestine into the liver.

5.7. It was Dr Gilbert's opinion that there was now significant doubt that death arose primarily from dothiepin toxicity, particularly given that there had been no evidence of excessive consumption of dothiepin tablets at the scene.

5.8. He revised his opinion as to cause of death to 'ischaemic and hypertensive heart disease', although noting that dothiepin toxicity, due to the vagaries of the toxicological findings, could not be completely excluded as the cause of death or as a possible contributing factor. There was a possibility that the death was caused by, or contributed to, by QT prolongation[21] resulting from dothiepin at greater than therapeutic levels.

6. Conclusion

6.1. In my opinion there was no issue with respect to any of the treating doctors of Ms Rowan for not reducing or ceasing the dothiepin medication in light of the derangement of some aspects of her liver function. This has been expertly explained by Professors Harley and Wing. Ms Rowan's psychiatric illness was managed thoroughly by Professor Goldney and Dr Maruszczyk who gave careful consideration to the amount of dothiepin that she was prescribed over a number of years. Drs Lees and Watkins worked together to manage Ms Rowan's gallbladder difficulties in an attempt to rectify her pain. The perceived lack of communication between Dr Lees and Dr Maruszczyk in respect of the abnormal liver function tests had no bearing whatsoever on Ms Rowan's death.

6.2. There is no evidence to suggest that Ms Rowan took her own life and I reject that notion. The post-mortem distribution hypothesis is the most plausible and I find the cause of death was ischaemic and hypertensive heart disease.

[21] The QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle

7. Recommendations

7.1. I have no recommendations to make in this matter

Key Words: Dothiepin

In witness whereof the said Coroner has hereunto set and subscribed his hand and Seal the 31st day of January, 2014.

State Coroner