CORONERS ACT, 1975 AS AMENDED

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 13th and 14th days of August and the 8th day of November 2001, before Wayne Cromwell Chivell, a Coroner for the said State, concerning the death of Margaret May Stewart.

I, the said Coroner, find that, Margaret May Stewart aged 77 years, late of 7 Persic Street, Largs North, South Australia, died at the Repatriation General Hospital, Daw Park, South Australia on the 27th day of April, 1998 as a result of multi-organ failure due to massive transfusion-induced coagulopathy following retroperitoneal haemorrhage of unknown source. I find that the circumstances of the death were as follows:

1. Introduction

1.1. Mrs Stewart was admitted to the Repatriation General Hospital on 23 April 1998 for elective knee replacement surgery. The surgery was uneventful, and no excessive bleeding was noted at the time (see the statement of the surgeon, Mr Darby, exhibit C3a, p3).

1.2. At about 10am on 24 April 1998, Mrs Stewart collapsed and a massive intra-abdominal haemorrhage was diagnosed. Mrs Stewart was taken to theatre, and a laparotomy was performed. The source of the bleeding could not be found. Mrs Stewart received massive transfusions, but the bleeding could not be controlled. A total of four operations were performed over a two day period, but the bleeding continued.

1.3. The final operation on 26 April 1998 was discontinued as Mrs Stewart had developed an ischaemic bowel which was inconsistent with her survival. Her condition

continued to deteriorate, and her life was pronounced extinct at 3:40am on 27 April 1998.

2. Treatment administered to Mrs Stewart

2.1. As I have indicated, Mr Darby indicated that Mrs Stewart's knee surgery was uneventful, and she appeared to be making an appropriate post-operative recovery until her collapse on 24 April 1998.

2.2. At 12:30pm on 23 April 1998 Mrs Stewart was given 5000 units of Fragmin, an anti-coagulant, in order to guard against the development of deep-vein thrombosis, which is a recognised complication of knee surgery.

2.3. Mrs Stewart received another 5000 units of Fragmin at 10pm on 23 April 1998. Questions arise as to whether this would have played a part in the development of Mrs Stewart's intra-abdominal haemorrhage, and I will examine that issue in more detail later.

2.4. After Mrs Stewart's collapse on 24 April 1998, Mr Peter Dupont, vascular surgeon, was asked to examine her. He did so and decided that an urgent laparotomy was necessary. This was performed, and Dr Michael Jones was the anaesthetist. Mr Dupont found free blood in the peritoneal cavity and bleeding from the retro-peritoneal space. He could not pinpoint the precise bleeding point, so the area was oversewn. Following the operation Mrs Stewart was retuned to the Intensive Care Unit (ICU).

2.5. Prior to the first laparotomy, Mrs Stewart had received 5 units of blood, and 2 units of fresh frozen plasma. During the operation, she was given 18 units of blood, 5 of platelets and 1 unit of fresh frozen plasma.

2.6. Mrs Stewart's bleeding continued after the first laparotomy, so a second operation was performed at about 6pm on 24 April 1998. Again, Mr Dupont found a large amount of bleeding in the peritoneal cavity without obvious cause. Again, the area was oversewn, and this time packs were left in the cavity in an attempt to control the bleeding.

2.7. By the end of 24 April 1998, Mrs Stewart had received a total of 44 units of blood, 14 units of fresh frozen plasma, and 10 units of platelets.

2.8. The second laparotomy was also unsuccessful, and so a third operation was performed, on 25 April 1998, commencing at 11:10am. This time the spleen was removed and Mr Dupont explored the area further to locate the source of the bleeding, but again to no avail. The area was oversewn again, repacked and closed.

2.9. Mrs Stewart's condition continued to deteriorate, and on the morning of 26 April a further operation was performed by Mr Dupont, commencing at 8:55am. By this time the bowel had become necrotic due to poor blood supply, and her generally moribund condition prevented further treatment, so the operation was discontinued and Mrs Stewart was returned to the ward for comfort care. As I have said, her condition deteriorated further, and Mrs Stewart died early the next morning.

2.10. Dr Michael Jones, the anaesthetist in the first, third and fourth laparotomies, pointed out that the coagulation studies taken at 10:50am before the first operation on 24 April 1998 were normal, although the haemoglobin levels were low, indicating that Mrs Stewart had been bleeding for some time (T50).

2.11. Similar studies taken at 1:40pm (ten minutes after the operation had started) show that the haemoglobin had improved and was within normal limits, but the coagulation factors had deteriorated. Platelets had dropped from 149 to 50, and the clotting factors INR (international normalised ratio) had jumped from 1.1 to 2.5, and the APTT (activated partial thromboplastin time) from 26.2 to 83.1 (see exhibit C6a).

2.12. Dr Jones said that he knew at that point that he needed more plasma, which was still being thawed out (T52). He discontinued using Haemacel, which might have been diluted what clotting factors Mrs Stewart still had. He said that Mrs Stewart had received a total of 23 units of blood, 5 units of platelets and 6 units of fresh frozen plasma - 5 were given before the operation started, and the sixth in theatre at 1:20pm, just before administration of anaesthesia (T54).

2.13. Following the second coagulation study, Dr Jones ordered more plasma from the laboratory. This did not become available until the operation was over, at about 2:30pm. He decided to wait until Mrs Stewart was fully set up in the ICU before giving these 2 further units of plasma.

2.14. A further coagulation study taken at 3:15pm showed improvement in all respects. The haemoglobin was in the high range of normal, and platelets, INR and APTT had all improved (T60).

2.15. Two more units of fresh frozen plasma were given to Mrs Stewart at 3:30pm, and the coagulation studies at 5:25pm showed that the haemoglobin had dropped again, but the INR and APTT were close to normal (T61).

2.16. Dr Jones did not anaesthetise for the second laparotomy on 24 April, commencing at about 7:10pm. However, he noted that further coagulation studies taken at 9pm were 'very worrying'. Mrs Stewart's haemoglobin was down to 56, platelets were also low, and the INR and APTT had increased considerably, suggesting that she had developed coagulopathy by then. Dr Jones attributed this deterioration to a susceptibility to coagulation problems, an insufficiency of fresh frozen plasma, the fact that Mrs Stewart's coagulation ability was already 'on the brink' before the second laparotomy, and the fact that Mrs Stewart received 4 more units of Haemacel during the second laparotomy, thereby diluting the clotting factors again (T65-66).

2.17. A further coagulation study taken at 11:45pm showed some improvement. The haemoglobin had recovered to 79, platelets had deteriorated to 64, and INR and APTT had both improved somewhat.

2.18. By the time of the third laparotomy on 25 April, Mrs Stewart's condition was worse. She had progressed to renal failure. However, the coagulation studies taken at 4am and 7:30am had improved back to within normal limits (T69). These readings remained at those acceptable levels until Mrs Stewart died.

3. Issues arising at inquest

3.1. Dr John Lloyd, a consultant haematologist at the Royal Adelaide Hospital provided me with an expert evaluation of the treatment administered to Mrs Stewart. He commented at the outset that he encountered a good deal of difficulty in establishing precisely how much of each type of blood product was transfused to Mrs Stewart (T100).

3.2. Dr Lloyd commented that the dose of Fragmin administered to Mrs Stewart was higher than appears on standard protocols, although the risk of that producing bleeding from a site remote from the operation site was quite small (0.4%) (T103).

3.3. Dr Lloyd was not critical of the use of Fragmin in Mrs Stewart's case. He said the choice of anticoagulant was appropriate, and there was no need to administer another

drug, Protamine, when the haemorrhage became apparent. He said:

> 'So I would give Protamine if someone was bleeding after an injection of Fragmin, within say 4-6 hours or 3-6 hours when the peak blood levels occur. It would not have occurred to me to use Protamine in this situation where the Fragmin was given over 12 hours previously.' (T104)

3.4. Dr Lloyd said that when Mrs Stewart collapsed on the morning of 24 April 1998, prompt and appropriate action was taken to investigate the problem (T103).

3.5. Dr Lloyd did acknowledge, however, that Fragmin may have been responsible for Mrs Stewart's original haemorrhage, even though it would no longer have been playing a part by the time of her collapse (T105).

3.6. In relation to the transfusion, however, Dr Lloyd said that Mrs Stewart should have received more than 6 units of fresh frozen plasma by the time the first laparotomy was completed. She had received 23 units of red cells by then, and the doctors should have been giving plasma at a rate of at least 1:2 of red cells (T107).

3.7. Dr Lloyd explained that a 'massive transfusion' is described as the replacement of total blood volume (5 litres or 10 units) within 24 hours. He said that once Mrs Stewart had lost 10 units of volume in about 6 hours, a massive transfusion was happening and the plasma needed to be given at 1:2 of red cells. He said that a protocol had been developed at the Royal Adelaide Hospital, a major trauma hospital, since this incident, which applies this principle (T108). He pointed out that if the anaesthetist gets too far behind, the haemorrhage increases as the concentration of clotting factors decreases, so the problem worsens (T109).

3.8. Dr Lloyd accepted that by the time of the second laparotomy in the evening of 24 April 1998, Mrs Stewart had received another 6 units of fresh frozen plasma, making a total of 12, and a total of 30 units of red cells. A ration of 12:30 was 'not bad' (T110). This is reflected in the acceptable coagulation study figures taken at 5:25pm that I have already described (T110, 138).

3.9. Dr Lloyd was unable to explain why Mrs Stewart continued to bleed at that point. He said that his approach would have been to try and improve the coagulation times even further by an even more aggressive program of fresh frozen plasma replacement (T113).

3.10. Following the second laparotomy on 24 April 1998, Mrs Stewart's cumulative totals were 12 units of fresh frozen plasma to 37 units of red cells, which is slipping back away from 1:2. This was reflected in the deterioration in the coagulation studies at 9pm that I have already described, although this may also have been the result of haemodilution because 2 litres of Haemacel was given during the second laparotomy (T139). Dr Lloyd said that she had a 'very very severe coagulation disturbance' at that point (T116). This was dealt with appropriately by giving more fresh frozen plasma (at midnight the ratio was 18:44), and cryoprecipitate early the next morning when fibrinogen levels were seen to be low (0.7 – normal range 1.5 to 3.8) (T113). As a result, the coagulation study taken at 11:45pm reflected improvements in clotting times again.

3.11. Although it would have been better had these levels not fallen back and caught up several times, Dr Lloyd said that it is very difficult to keep appropriate levels in these situations, because the testing and ordering and thawing processes take time, and the doctors are always trying to catch up. For this reason, the 1:2 rule of thumb is worth applying to try and 'keep ahead of the game' (T118, 135).

3.12. In my opinion, this answers Mr Homburg's submission that paying attention to the INR and APTT readings is more sophisticated than the 1:2 test (see Dr Jones' evidence at T72). Of course, Dr Lloyd was not advocating that the results of such tests should be ignored. Instead, he argued that because of the lag time between sample taking and test results becoming known, if you do not operate on the 1:2 basis, you run a substantial risk of getting behind, as Dr Jones did here.

3.13. From that point on, the ratio of plasma to red cells was appropriate, and Mrs Stewart's coagulation studies remained normal, despite the fact that she continued to haemorrhage uncontrollably. Dr Lloyd said:

> 'I probably said it before, I'll just say it again, this is a problem that we sometimes get into, that in these massive transfusion situations a patient continues to bleed, we don't know why. What usually happens is we support them with red cells and fresh frozen and platelets, heavily, as was done here, and I think more often that not we gradually win and the bleeding gradually slows and the situation resolves. Unfortunately this is a case where that didn't happen, and the reasons for that are totally unclear, basically.' (T122)

He added that if the ratios had been kept at satisfactory levels on 24 April 1998, Mrs Stewart would have had a 'reasonable chance' of survival (T124, 141).

4. Cause of death

4.1. A post-mortem examination of the body of the deceased was performed by Drs Somers and Vaska at Repatriation General Hospital on 28 April 1998. Their diagnosis of the cause of death was 'disseminated intravascular coagulopathy' (exhibit C2a).

4.2. The pathologists' clinicopathological correlation was as follows:

> 'Margaret Stewart was a 77 year old woman admitted for an elective knee replacement. Post operatively she developed an intra-abdominal haemorrhage requiring surgical intervention, blood transfusions and clotting factor transfusions. Treatment was withdrawn following the development of an ischaemic bowel. Autopsy finding showed an extensive retroperitoneal and intra-abdominal hematoma, making assessment of the intra-abdominal blood vessels impossible. There was extensive necrosis of the bowel. Death was a result of disseminated intravascular coagulopathy causing haemorrhage and complicated by bowel ischaemia and pulmonary oedema.' (Exhibit C2a, p4)

4.3. Like Dr Jones (T77), Dr Lloyd did not consider that disseminated intravascular coagulopathy (DIC), was the cause of Mrs Stewart's death, as suggested by the pathologists. He said that the deficit in supply of fresh frozen plasma was sufficient to explain her coagulopathy without resort to that diagnosis (T125).

4.4. DIC is defined as a condition which results from the uncontrolled activation of clotting factors and fibrinolytic enzymes throughout small blood vessels; fibrin (which should polymerise to form a clot) is deposited, platelets and clotting factors are consumed and fibrin degradation products inhibit fibrin polymerisation resulting in tissue necrosis and bleeding (Stedman's Medical Dictionary).

4.5. Dr Lloyd said that there may have been signs of DIC at post-mortem, but these would have been associated with the multi-organ failure Mrs Stewart suffered at the end-stages of her illness (T126).

4.6. Dr Lloyd suggested that the appropriate cause of death was multi-organ failure due to massive transfusion-induced coagulopathy following retroperitoneal haemorrhage of unknown source (T127). I accept Dr Lloyd's evidence on this topic and find that the cause of Mrs Stewart's death was as he described.

5. Record keeping

5.1. I have already mentioned that Dr Lloyd had great difficulty tracing the amounts of blood and other fluids transfused into Mrs Stewart during this crisis.

5.2. Dr Lloyd suggested that when transfusions are given in the ward, in ICU, in theatre and in recovery, they can all be recorded differently. One suggestion to overcome these difficulties was the establishment of a transfusion record, either written or computerised, which stays with the patient. He referred to the National Blood Review which came out with recommendations that there needs to be better regulation and auditing of transfusions, not only for these purposes, but also in case viruses are transmitted (T128).

5.3. Dr Jones acknowledged that he found himself in difficulty during the first laparotomy on 24 April 1998, because he had been told that 2 units of fresh frozen plasma were available, but once the operation started, he found that this had already been given to Mrs Stewart in ICU. This was emergency surgery and so delaying surgery was not an option. Dr Jones said that if he had known that the 2 units had already been given, he would immediately have ordered more. He emphasised that he was not criticising the nurses, who no doubt recorded the transfusion on the fluid balance sheet. His problem was that he did not know that they were the last 2 units they had available (T74).

5.4. Dr Jones said that the way he keeps track in theatre was to place all the empty bags on a towel on the floor and physically count them (T90).

5.5. Dr Lloyd acknowledged the practical difficulties of such recording (T130-132). He said that the best way to develop a better system would be to establish a consultative process involving anaesthetists, intensivists, ward clinicians, haematologists and the transfusion services. He said that 'Transfusions Committees' had been established in some hospitals following the National Blood Review, and that these committees might be the appropriate vehicle for such consultation (T133).

5.6. Mr David Roxby, the Manager Medical Scientist at the Flinders Medical Centre Transfusion Service, prepared a very useful computerised chronology of Mrs Stewart's transfusions (exhibit C6a), working from computerised records and laboratory worksheets.

5.7. From his records, Mr Roxby was able to confirm that Mrs Stewart received the appropriate type of blood product at all stages of the process (T14), and that the product arrived undamaged at Repatriation General Hospital (T33).

6. Conclusions

6.1. From all the above information, I think that the following conclusions can be drawn:

1. The administration of Fragmin to Mrs Stewart on 23 April 1998 was appropriate, but carried with it a risk of haemorrhage remote from the operation site of about 0.4%. This may have precipitated Mrs Stewart's haemorrhage which led to her collapse.

2. By the time of Mrs Stewart's collapse at around 10am on 24 April 1998, the concentration of Fragmin would have been so low as to be discounted as a cause of continued haemorrhage.

3. During the first laparotomy on 24 April 1998, the bleeding site could not be found. Mr Jones, the anaesthetist, fell behind in the ratio of fresh frozen plasma to red blood cells because the 2 units he thought were available had already been given, and a delay until 3:30pm was experienced in obtaining more.

4. A further laparotomy in the evening of 24 April 1998 also failed to locate the bleeding site. The fact that 2 litres of Haemacel were administered during that operation may have resulted in haemodilution, further weakening Mrs Stewart's clotting ability. By that time Mrs Stewart had developed transfusion-induced coagulopathy.

5. A third laparotomy on 25 April 1998 was similarly unsuccessful. The bleeding could not be stemmed, even though Mrs Stewart's clotting factors had been brought back under control and remained appropriate until her death. The reason why Mrs Stewart continued to bleed in these circumstances cannot be ascertained.

6. By 26 April 1998, Mrs Stewart had developed multi-organ failure, as a result of the ongoing bleeding. The cause of her death was multi-organ failure due to massive transfusion-induced coagulopathy following retroperitoneal haemorrhage of unknown source.

7. Recommendations

7.1. Having regard to the evidence of Drs Lloyd and Jones, it is apparent that improvements should be made to the way transfusion data is stored and made available to doctors during a transfusion procedure, particularly, as here, where the transfusion is occurring in an emergency situation.

7.2. I note Dr Lloyd's comments that a recent inquiry had recommended the establishment of Transfusion Committees in hospitals to consider such issues.

7.3. Mr Homburg, counsel for Mr Roxby and Dr Jones, kindly undertook some further inquiries, and has advised me as follows:

'I have ascertained that Flinders Medical Centre has a Transfusion Committee with representation from South Path, the Departments of Haematology, Anaesthetics, Intensive Care, Emergency, Surgery, Medicine, Nursing and the Red Cross.

I am instructed that the Committee is the appropriate entity to entertain any recommendation the Coroner makes.

At present, the Committee does not have direct representation from the Repatriation General Hospital. I understand that since the Inquest, Mr Roxby has approached the Clinical Director of the Repatriation Hospital to explore the possibility of its representation.'

(Letter dated 21 August 2001)

7.4. I therefore recommend, pursuant to Section 25(2) of the Coroner's Act 1975, that:

1. The Repatriation General Hospital either gains representation on the Flinders Medical Centre Transfusion Committee, or establishes a Transfusion Committee of its own;

2. The Transfusion Committee consider ways in which transfusion data might be better recorded and made contemporaneously available to clinicians, particularly in cases of massive transfusion and emergency surgery.

Key Words: Hospital treatment; Blood transfusion; Coagulopathy

In witness whereof the said Coroner has hereunto set and subscribed his hand and

Seal the 8th day of November, 2001.

……..……
Coroner

Inq.No. 19/01 (0975/1998)