Patient Name: Eileen O'Hara.

Date of Birth: 9th October 1930.

Date of Death: 7th May 2003.

This lady had a very complex medical history. Her problems began with rheumatic fever as a child. Subsequently, she developed significant mitral valve stenosis and required cardiac surgery on three occasions. In 1963, at the age of 33, she underwent closed mitral valvotomy. That appears to be an uncomplicated procedure. It is possible that blood transfusion was required at that time. However, one of my learned colleagues informs me that this was a procedure which could frequently be performed without the need for blood transfusion. That provided excellent palliation. As a consequence, she was able to achieve a number of pregnancies during the 1960s and early 70s. In 1985, she developed symptoms of cardiac failure. Therefore, she was referred for mitral valve replacement. This was performed in June of 1985 and apparently was an uncomplicated procedure. She received a porcine prosthesis. This would have been performed with cardiac bypass surgery and blood transfusion would be routine. There was good palliation of symptoms but further problems developed during 1990 and 1991. It was decided that she needed further mitral valve surgery. A prosthetic valve was inserted in October 1991. Once again, that would have required cardiac bypass and blood transfusion. It appears this was an uncomplicated procedure. The fact that the procedure was uncomplicated implies that liver disease if present was not severe and cirrhosis was unlikely. There was no subsequent cardiac surgery. Therefore, she underwent three major operations. All three may have required transfusion and certainly transfusion is routine for cardiac bypass. Two of those procedures were performed before the introduction of screening for hepatitis C of blood products.

There was a complex obstetric and gynaecological history. The patient had a couple of miscarriages. Subsequently, there were four successful deliveries. In 1965, 1967 and 1968, she successfully delivered three babies vaginally. In 1972, she required Caesarean section to deliver her baby. According to the anaesthetic record, she required transfusion with a single unit of blood at that time. In December of 1979, she underwent vaginal hysterectomy. The medical records indicated she was transfused with two units of blood at that time. Surgery in 1972 and 1979 required blood transfusion and the blood would not have been screened for hepatitis C virus. Therefore, she may have acquired hepatitis C at that time.

In the available files, the first reference to abnormal biochemical liver function tests is in February of 1984. At that time, she was being reviewed for her cardiac problems. Her AST was 51 and her ALT was 67. The cause of the abnormal liver function tests was not clear. It was suggested that this mild abnormality might have represented some hepatic congestion secondary to the cardiac disease. That seems a reasonable suggestion. It appears that the General Practitioner may have pursued this problem in 1990. There was a letter from the Cardiologist to the General Practitioner which thanks the GP for bringing the mildly abnormal liver function tests to his attention. It was the view of the Cardiologist, at that time, that cardiac failure did not explain the abnormal liver function tests. In September of 1990, the patient was reviewed by a Gastroenterologist at Glasgow Royal Infirmary. Apparently, the patient suffered with abnormal bowel habit at that time. Abnormal liver function tests (AST 108, ALT 160) were again noted. According to the Gastroenterologist, the liver function tests were abnormal despite abstinence from alcohol (though it sounds as if alcohol intake was never significant). The patient was subsequently reviewed in the Gastroenterology Clinic in November of 1990 and a screen for causes of abnormal liver function tests was performed. The blood was tested for hepatitis B, hepatitis A and hepatitis C. The tests used to screen for each of those viruses was negative. The negative hepatitis C antibody test is a surprising result. This would have been one of the first available hepatitis C screening tests. It may represent a false negative reaction. However, these early tests were quite sensitive. Therefore, it is possible that hepatitis C infection was not present in November of 1990. The possible liver problems were not pursued at that time. Possibly, the focus switched to the cardiological problems since mitral valve replacement was required the following year.

In 1994, the patient was noted to have hepatosplenomegaly. According to correspondence, an ultrasound examination suggested hepatic cirrhosis and portal hypertension with quite significant splenomegaly. Further investigations were performed. In March of 1995, the clinic letter from Cardiology to the General Practitioner confirms that the hepatitis C antibody test was positive. Indeed, the files contain the results of the blood test performed in the regional virus laboratories in February of 1995. The hepatitis C antibody result is positive with screening and confirmatory assays. However, a PCR test to confirm the presence of the virus may not have been performed. I cannot find a PCR result in any of the patient's medical records. It will be important that this is checked. I would suggest that the records at the regional virus laboratory and the Glasgow Royal Infirmary are checked to see if a PCR test was ever performed.

Liver biopsy and bone marrow examination were performed in June of 1995. The liver biopsy report shows cirrhosis with lymphocytic infiltrate consistent with hepatitis C infection.

The possibility of antiviral therapy was considered. The opinion of Dr John Forrest (local consultant Gastroenterologist) was sought. It was his advice that the patient was not a good candidate for antiviral therapy. At that time, the only available treatment was Interferon. He suggests that the chance of successful treatment was of the order of 20%. I think that his assessment is correct. Indeed, the chance of successful treatment may have been significantly less. In July of 1997, she underwent upper gastrointestinal endoscopy. This showed that she had small oesophageal varices consistent with portal hypertension. Specific complications of cirrhosis were not experienced by the patient from the time of diagnosis until the time of her admission to hospital with her final fatal illness in 2003. Specifically, she did not bleed from varices, she did not develop significant ascites and there was no encephalopathy. Between 1997 and 2003, she continued to attend medical clinics for management of her diabetes and cardiac disease. It is my impression that her health deteriorated slowly during that period. In December of 1999, she was described by the Cardiology SHO as "a rather frail lady". She developed some chest pains which may have been angina. Her medication was changed accordingly. In December of 2002, the GP requested a wheelchair for the patient. In January of 2003 (after the death of her husband), application was made for sheltered housing on medical grounds.

Mrs O'Hara was admitted to Stobhill Hospital on 26th March 2003 and died on 7th May. Diagnosis at admission was pancreatitis. It was thought that the pancreatitis was due to choledocholithiasis. Therefore, endoscopic clearance of the bile duct was attempted on three occasions. Eventually, that was successful. There was intermittent sepsis including significant cellulitis of the lower limbs. There were positive blood cultures and the tip of her central venous line was also infected. Severe sepsis required aggressive resuscitation including the use of adrenaline. Under these circumstances, it is not surprising that there were great difficulties in fluid management. The patient developed significant fluid retention with lower limb oedema and ascites. This would be predictable in a patient with significant cardiac disease and with cirrhosis. Despite all of that, her biochemical liver function tests remained remarkably good. There was little jaundice until the last days of her life. With cessation of Warfarin, her prothrombin time returned to almost normal values. These observations suggest that the liver coped reasonably well during the stresses of this illness. It seems likely that the final event was profound sepsis. The blood tests on 7th May showed that her white cell count rose rapidly to a value of 40.

The cause of death is complex and multifactorial. She has significant cardiac disease and liver cirrhosis. There was longstanding diabetes. There was severe pancreatitis and choledocholithiasis. Fluid management was very difficult and the patient was extremely susceptible to infection for many reasons. Cirrhosis may have contributed to her eventual demise. However, it

is quite possible that death would have been the outcome even in the absence of cirrhosis.

It is likely that she had hepatitis C infection. The conflicting hepatitis C antibody tests are difficult to reconcile. It seems most likely that the test performed in 1990 was a false negative result. Certainly, there was a history of blood transfusion and repeated and complex admissions to hospital for management of obstetric and cardiac conditions. Blood transfusion prior to the availability of screening for hepatitis C was required. That blood may have been a source of hepatitis C. It is also possible that the infection, though nosocomial, was not a direct result of transfusion. I cannot see that the patient was quizzed concerning other possible routes of infection. The most common source of infection is intravenous drug use. It seems extremely unlikely that this lady would have been exposed in that way.

In summary, I believe this lady was exposed to hepatitis C at some stage in her life and probably during one of her hospital admissions. Infection may have been acquired from blood transfusion. The discrepant hepatitis C antibody tests are hard to explain. The earlier test may have been inaccurate. It seems likely that hepatitis C did contribute to the development of cirrhosis. Once diagnosed, the management of her hepatitis C infection seems quite appropriate. The cardiac condition and her diabetes may have predisposed her to the development of cirrhosis. At the age of 72 and with significant cardiac disease, she suffered a bout of pancreatitis. Cardiac disease, diabetes and cirrhosis were significant co-morbidities. Under that circumstance, death with multiple organ failure is not surprising. It seems unlikely that hepatitis C infection made a major contribution to shortening this lady's life.

In preparation of this report I have referred to the following documents.

1. Principal Stobhill Hospital Records (1971 – 2002)
2. Principal Stobhill Hospital Records (2003)
3. Copy Glasgow Royal infirmary records (1985 – 1999)
4. Principal GP records (1952 – 1997)
5. Principal GP records (1997 - 2004)
6. File of documents from the SNBTS (comprising correspondence in relation to the previous Crown Office investigation into this woman's death).
7. Folder of miscellaneous material:
   (a) Copy death certificate
   (b) Copy letter from Dr F G Dunn, Consultant Cardiologist, Stobhill Hospital to Leanne Cross, COPFS dated 19 September 2005
   (c) Copy letter from NHS Scotland, Central Legal Office to Leanne Cross, COPFS dated 13 September 2005

(d) Police sudden death report

Yours sincerely

Dr David Mutimer

Consultant Hepatologist