MEDICAL REPORT ON

ALEXANDER BLACK LAING

DATE OF BIRTH 07.12.1923

DATE OF DEATH 04.09.2003

PREPARED BY

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I, Graeme Alexander, have been a Consultant Hepatologist at Addenbrooke's Hospital since 1991 and have a particular interest in the clinical and laboratory aspects of viral hepatitis including hepatitis C virus infection. I am a Fellow of the Royal College of Physicians, a member of the British, European and American Societies for the Study of Liver Disease and Chair the National Hepatitis C Virus Steering Group which has been following the natural history of patients who acquired hepatitis C virus infection at a single point largely through transfusion for close to two decades.

I have prepared my report with the advantage of the notes from the Aberdeen Royal Infirmary, the general practice notes, as well as a number of miscellaneous statements from those involved in his care.

In June 1990 Mr Laing was referred to Mr Keenan, a surgeon, with a long history suggestive of carcinoma of the bowel and after appropriate investigations he underwent an anterior resection in August of 1990. The histology later showed that he had a Duke's C carcinoma and that one of a number of nodes removed was positive for tumour. In April 1995 he was identified through the 'National Look Back' to have received blood that was positive for hepatitis C virus at the time of his operation. He was offered testing for hepatitis C virus subsequently and in June 1995 he was found to be hepatitis C antibody positive and subsequently hepatitis C virus PCR positive. At the time that he was advised that he might have hepatitis C virus infection there was nothing to suggest that he might have liver disease nor was he symptomatic. There is no recorded note (that I can find) to indicate that he had any other of the recognised risk factors for acquisition of hepatitis C virus infection.

In 1996 he was admitted for a liver biopsy under the care of the gastroenterologists. The clinical notes indicate that obtaining tissue at that biopsy was difficult and that two passes were required. The histologist commented specifically in the report that three samples of tissue measuring 0.2 cm in length, one piece measuring 0.3 cm in length and two further small strands of tissue were obtained. The report states that the findings were suspicious for cirrhosis. The report is dated January 1996. There are comments in the clinical notes subsequently in 1996 from Dr A S Bhutta, Dr Dominic Cox and subsequently Dr T S Sinclair in September 1996 that the biopsy changes showed mild fibrosis - but that is not what was commented upon in the final histology report.

I could find three instances subsequently in 1996 at which the possibility of treating his hepatitis C virus infection with Interferon-α had been discussed with the patient. In all three cases the letters indicated that the histological changes were mild and there was a relative likelihood that Interferon-α treatment would not be successful and that the long-term outlook, although uncertain, was probably benign in someone of his age. Each of those letters relating to clinic appointments documents further that he would prefer, under those circumstances, not to be treated.

There is not much further of note until December 2001 when he was admitted with a transient episode of what was labelled cholestatic jaundice. Very little helpful information is available from that admission except to note that he had mild jaundice with a bilirubin of 32 and an alkaline phosphatase that was just outside the normal range and at which time an ultrasound showed no evidence of intra- or extrahepatic duct dilatation, nor was there evidence that gall stones had been seen. A conclusion was made that this illness probably represented an episode of biliary obstruction due to gall stones which 'had passed away' (sic) and that he should be referred later to the surgeons.

In 2003 the liver function tests began to show deterioration and he presented in the summer of 2003 with very advanced liver disease manifest as ascites, peripheral oedema, jaundice and cachexia. The ultrasound features were compatible with cirrhosis and he was found to have portal hypertensive gastropathy with oesophageal varices at endoscopy. His condition deteriorated and he died finally in September 2003 as a consequence of end stage liver failure due to hepatitis C virus related infection.

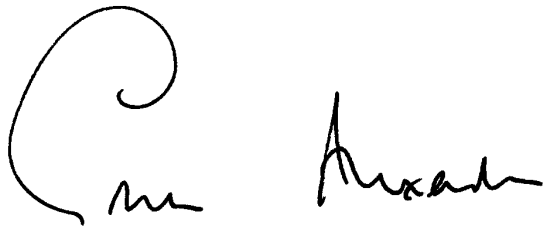
There is very little that is contentious in the history. He had an operation during which he was transfused. The anaesthetic records document that he received a transfusion. The blood transfusion service found subsequently that blood that Mr Laing had received in August 1990 had come from a donor who had been shown at a later date to be hepatitis C virus positive. Mr Laing was called back in 1995 when he was found to be hepatitis C positive. There were no other risk factors in his history that would account for hepatitis C virus infection. A liver biopsy in 1996 (which I have not seen) almost certainly shows cirrhosis and seven years later he died as a consequence of advanced liver disease due to hepatitis C virus infection.

The short interval of just six years between acquisition of hepatitis C virus infection and documentation of cirrhosis at liver biopsy and the seven years that followed thereafter to his death, are consistent with what we now know about the natural history of hepatitis C virus infection. The proportion of patients that go on to develop cirrhosis and the rate at which cirrhosis develops subsequently are greatly accelerated in the elderly and in particular in men over 60. The fact that he had been overweight earlier in life may have been an additional confounding factor increasing his chance of becoming cirrhotic and increasing the rate at which the disease would progress. The first large publications drawing attention to the importance of age on the progression of liver fibrosis were published around 1997 and would have been discussed in abstract form, probably in the preceding few months. Thus the information that was provided to Mr Laing at the time of his biopsy in 1996 was probably 'best known practice'.

The fact that he was told that his disease was benign and was likely to remain so may well have influenced his decision not to accept the offer of anti viral therapy and it seems clear to me from the letters around that time that he was likely to have been told that the Interferon-α treatment was not likely to offer him a cure. I agree that was certainly true at the time and the response rate to treatment with Interferon-α in our centre was just 9% of cases at that time and with an even lower rate in the elderly and those with cirrhosis.

I do think, however, that the biopsy (which I have not seen) is likely to have been under reported in terms of the stage of fibrosis and that the possibility that the biopsy might have represented a higher stage of fibrosis was not appreciated by the clinicians. A fragmented biopsy, such as that in this case, is not one on which to base a prognosis with confidence.

It must be noted that Mr Laing survived 13 years after his diagnosis of carcinoma of the rectum with Duke's C histology, which is an astonishing outcome. I do not feel that even if there had been a better indication of his fibrosis stage in 1996 that it would have been possible to modify the natural history of his hepatitis C virus infection as the treatment available at that time was relatively ineffective and more so in elderly males with cirrhosis. If he had presented now with Pegylated Interferon and Ribavirin available the chances are that he would not responded to treatment and if I was asked now to consider treatment I would very likely not offer him treatment with Pegylated Interferon and Ribavirin, the best available current therapy, because of his age and cirrhosis and the low probability of a response.



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18th August 2010