Witness Name: Dr Elizabeth Mayne
Statement No.: WITN0736008
Exhibits: NONE
Dated:

INFECTED BLOOD INQUIRY

SECOND WRITTEN STATEMENT OF DR ELIZABETH MAYNE

I provide this statement in response to a request under Rule 9 of the Inquiry Rules 2006 dated 20 May 2019.

I, Dr Elizabeth Mayne, will say as follows: -

Section 1: Introduction

1. I would refer to paragraphs 1.1 to 1.3 of my written statement dated 20th May 2019.

Section 2: Response to criticism raised by Maria Conway

2.1 I have not had sight of Ms. Conway's medical notes and records. This statement is therefore based on my recollection of events to the best of my octogenarian memory.

2.2 The statement of the witness is seemingly straight-forward, however, it conceals a lengthy period of scientific investigation and analysis which took place in 1992. In order to ensure understanding of the Conway family results, it is pertinent to trace briefly the chronology of change which occurred both globally and locally in Haemophilia care over nearly three decades.

2.2 During 1968, after completion of my doctorate, Professor M.G. Nelson (the Head of Department), suggested that I took over as a special interest in the care of the Haemophilia patients. At that time the "Haemophilia Centre" had no physical location, dedicated staff or in-patient facility. Forty-Four families were listed in "the Register" of Haemophilia patients.

2.3 Although I had represented Professor Nelson at several Haemophilia Centre Directors meetings in Oxford at that time, it would be true to say that my knowledge

of Haemophilia and its problems were scanty. I did, however, realise that the numbers of families registered was a significant underestimate. The world-wide incidence of Haemophilia is 1:5000 of male births. The population of Northern Ireland was approximately 1.5 million at that time. The Registered families, GP's and the local hospitals were contacted. Domiciliary visits were made to those who lived a distance from Belfast. I first met the Conway family in this way. The person I met would have been the maternal grandmother of the witness. From her and others I learned of the graphic problems of dealing with severe crippling joint bleeds without active available treatment. She said something I have heard repeatedly since that time, that members of Haemophilia families do not mind the "general public" not knowing about their bleeding disorder but they are frustrated that many doctors have little knowledge about their problems. It would be true to say that this period of peripatetic visiting inspired me to improve the lot of Haemophilia patients.

2.4 As time progressed, through obtaining various grants and financial support the Haemophilia centre changed. The number of patients increased. The staff grew to include a part-time physiotherapist, a full-time nurse, a secretary and a part time social worker. During the mid-eighties there was a full time Medical Registrar, a second nurse, a part time aromatherapist and reflexologist, another secretary, receptionist and finally a full time scientist was appointed to establish new techniques for carrier detection.

2.5 With respect to carrier detection, the change wrought by the availability of active treatment completely altered the social lifestyle of patients with Haemophilia. Individuals went to school regularly, attended Colleges of Further Education, and went to University. Locally there was an increased incidence of weddings! Perhaps it was the latter which triggered the increased interest in the genetics of the condition and the queries for the advice about carrier detection, and how females were affected.

2.6 Family history is of vital importance. Often haemophilic fathers do not realise that all sons born to a haemophilic father and a "normal" mother are "normal" because their sex chromosomes are XY. The father's Y chromosome determines maleness and the son's X chromosome is derived from a "normal" mother.

2.7 Likewise it is of importance to know that certain female members within a family can be designated as obligate carriers.

i. All daughters born to a haemophilic father are obligate carriers. They will have his haemophilic-affected X chromosome in addition to the "normal" X contributed by the unaffected mother = XX.

ii. All mothers with more than one haemophilic son are obligate carriers (Thus the mother of the Conway family is an obligate on two counts in that her father had Haemophilia and she has two sons that are haemophiliacs).

iii. All mothers with one haemophilic son and a family history of Haemophilia in another generation.

There will be doubt in the case of:

a) Daughters of an obligate carrier, as they will have a 50:50 chance of being a carrier. The daughters of the Conway family fall into this category.

b) Families with no previous haemophilia history and one haemophilic son.

2.8 With respect to methods of detecting carrier status; up until the late 1960's obligate carriers for Haemophilia were regarded as asymptomatic. However, at a meeting of all doctors in the UK who cared for patients with Haemophilia, I presented a case history of an obligate carrier who had severe haemorrhage requiring hospitalisation and blood transfusion. At the time 1968/9 (I am unsure of the exact year), I was a junior doctor, and was most apprehensive of presenting data to experienced Doctors, and in some cases, of international repute. However, it transpired that many present had had similar experience! Thereafter carriers of severe haemophilia were regarded as potentially symptomatic.

2.9 The explanation lay within what is termed lyonnisation. In a random manner, at any one time the "normal" or the "abnormal" X chromosome may be operative within the cells synthesising the Factor VIII clotting activity in females. If, at times, the abnormal gene is dominant, the Factor VIII clotting activity may be low enough to prolong or exacerbate physiological menstrual bleeding, or even cause post-surgical bleeding. Lyonnisation may lead to difficulties in trying to detect carriers but also within families it can lead to on and off bleeding problems related to menstruation. However despite lyonnisation female patients do not suffer from joint bleeding.

2.10 Analysis of Factor VIII clotting activity used to be the only test available to determine carrier status. It was fraught with problems as indicated, depending on lyonnisation. There can be extreme variation in the results of such studies ranging from 50% of normal up to 100% Factor VIII activity. When such tests were the only means of carrier detection it was agreed internationally that at least 3 measurements were necessary and they needed to be taken in the absence of extreme anxiety, infection or pregnancy as all conditions are associated with increased to high Factor VIII levels. As time progressed other more sophisticated clotting tests were introduced but it remained as uncertain methodology and no individual could be assured of non-carrier status.

2.11 With respect to DNA technology, the Factor VIII gene was cloned in 1984. Two years later, in 1986, whilst driving to a cabin in the woods of California, Kary B. Mullis had the flash of inspiration which led to the development of the Polymerase Chain Reaction (PCR) and a Nobel Prize. Simplistically this stroke of genius revolutionised molecular biology and enabled the rapid determination of mutation detection. It is said that the invention of PCR was to molecular biology what the invention of the telescope was to astronomy. Thus, in the late 1980's and in the case of the Northern Ireland Haemophilia Centre, the early 1990's, carrier detection proceeded via the Restriction Fragment Length Polymorphism (RFLP) technology utilising PCR methodology.

2.12 The procedure of this test is that venous blood samples are obtained from family members. Ultimately, via various procedures, DNA is obtained from the white blood cells within the samples. To enable successful gene tracking to be carried out by this technology it is necessary to obtain samples from the affected family member(s). There were two affected haemophiliacs in the Conway family, an obligate carrier i.e. the mother, and all the unaffected family members, which included the father and in this case an unaffected son and daughters. All the samples were labelled by a code at the bedside at the time of testing. There was no pre-labelling of sample tubes to avoid mistakes.

2.13 The Conway family travelled to Belfast for testing. As was customary we, myself, Sister Farrell, Nurse McAfee and Dr Winter, Haemophilia Centre Scientist, met in Ward 37. A lively discussion took place with Dr Winter especially making the science, at best understandable. The blood samples were taken and coded. No other blood tests were carried out. The samples were used solely to prepare DNA from each person.

2.14 The family realised that the process was time consuming and complex. Therefore the results would take some weeks before they became available. It was also explained that sometimes gene tracking by this method was unsuccessful. However, if it was possible then the results would be of the order of 99% accurate.

2.15 I remember analysing the results with Dr Winter but somewhat oddly I do not have any recollection of the family's return visit. The results were as follows:
A) The test detected two male members with Haemophilia. When the samples were decoded they were identified as the two haemophilic sons, Edward and Seamus.
B) Two males were identified as normal and not having Haemophilia. Mr Conway Senior and his unaffected son were identified.
C) The test identified three female carriers. The first was Mrs Conway Senior who was known to be an obligate carrier. Two of her remaining daughters also tested positive as carriers of the disorder.
D) The remaining daughters proved to be identified as normal and unaffected.

2.16 In view of the investigation showing that both Haemophiliacs and non-Haemophiliacs were clearly identified and furthermore that the obligate carrier had been accurately revealed it therefore seemed logical to believe that the results for all the daughters, i.e that two were designated carriers and two were non-carriers, were correct.

2.17 Subsequently two events happened; firstly one of the diagnosed potential carriers indicated, indeed, had a haemophilic son, giving an expected result considering the test. However, later a familial and scientific "bombshell" unexpectedly occurred. One of the daughters who tested as a non-carrier unexpectedly gave birth to a haemophilic son. Thereafter, although I had retired, I understand multiple investigations were undertaken to understand the occurrence of this totally unexpected phenomenon. A medico-legal case then ensued.

2.18 Ms. Conway states that she was erroneously told that she was not a carrier. As I have set out above, Ms. Conway was provided with test results based on knowledge

and information available at the time. During the 21st Century the necessity to carry out laborious RFLP testing was discontinued because advanced technology enabled the detection of specific family mutation causing the Haemophilia.

Section 3: Other Issues

3.1 I would refer to section 3 of my statement of 20th May 2019.

Statement of Truth

I believe that the facts stated in this witness statement are true.

Signed GRO-C

Dated 20th September 2019