

Penrose Inquiry: Questions for Dr. Willoughby

Question number:

- 1.1 Firstly, I must say that I was appointed to Yorkhill in late 1963 to establish a diagnostic haematology department. Having been taught haematology in Dr. Bigg's and Professor Macfarlane's department at the Radcliffe Infirmary, Oxford, as in their department, we used capillary blood samples from finger-prick samples for most tests, sparing the children's veins. This was valuable in the management of many blood disorders including haemophilia, as well as leukaemia.

There was no question of me establishing a Haemophilia Centre. Children from the West of Scotland with all types of blood disorders attended or were referred to Yorkhill, including those with known Haemophilia (congenital Factor VIII deficiency) or Xmas Disease (congenital Factor IX deficiency). My first duty was to establish those laboratory coagulation tests to confirm such diagnoses, and then Factor VIII and Factor IX assays on their peripheral blood to determine the level of severity of their coagulation disorder. If the level was 1% to 2% or so it meant that the disease was a severe form and was likely to be accompanied by frequent, and often severe, haemorrhagic manifestations. Milder forms of the disease had levels consistently below 50% of normal, but more usually around 5 to 25%.

As the years passed I became increasingly involved with the clinical management of blood disorders, particularly with the different types of leukaemia at the Children's hospital, But I also came involved with some of the problems at the adjacent Queen Mother's Maternity teaching hospital such as maternal anaemias, acute obstetric haemorrhagic states and infantile haemolytic anaemias, usually due to Rhesus or similar immunisation.

Of course the treatment of many of these haematology disorders was continuously evolving over the 19 years I was at Yorkhill, and has continued to do so since.

Regarding the treatment regime which operated at Yorkhill for children with haemophilia from 1 January 1974 onwards, I do not recall that specific date but have looked up what I was writing in my textbook "Paediatric Haematology" around that time (published in 1977 and referred to by Dr. Brian McClelland on 6th May 2011, pages 121-124). I describe in Chapter 18, 'Hereditary Coagulation Disorders' on page 320 the use of fresh-frozen plasma, by then largely superseded by cryoprecipitate, and also concentrates. Their preparation and average activity in units/ml is given. Cryoprecipitate, introduced after around 1965, is stated as having, on average, around 75 units in UK. But it could vary from bag to bag, and it was not practical to measure the level in each bag administered. So in 1968 Dallman and Pool, (Judith Pool had originally developed Cryoprecipitate for haemophilia treatment) recommended that it was a good practice to double the calculated dose to ensure adequate dosage (my page 321). I stated that 1 bag of cryo per 10 kg body wt raises the factor VIII by 15%.

On this basis I think we used to recommend 1 to 2 bags of Cryo per 10 kg for superficial cuts or lacerations, but higher doses of 6 or so bags per kg for treatment of more severe bleeding such as haemarthrosis (my page 322). In the early days these infusions would probably have been set up by the general Yorkhill medical staff, usually after consultation with myself or other haematology medical staff. But as time progressed, and particularly after being joined by Dr. Anna Pettigrew, I think we were more often involved with treating these patients ourselves. This would have been particularly so after we had started setting up the home-therapy program, in 1979 I believe.

I must also state that, although not apparently referred to by Professor Hann, my successor, or by Dr. Pettigrew, my colleague, the Yorkhill haemophilia patients received regular dental follow-up by our Dental colleague, a Mrs. Dunn (as I remember), largely for dental procedure prophylaxis.

Also patients were monitored, primarily for hepatitis C, previously termed non-A non-B hepatitis, by serum samples sent to the Virology department at Ruchill. I understand that these were retrospectively tested for HIV when that virus was subsequently discovered.

Also I regularly joined my Orthopaedic surgeon colleague Mr Ian McPherson (decd.) in the general outpatient department where he had his other clinics. I think these were held monthly on Friday afternoons for our mutual convenience. Also attending was the haematology home-visiting nurse but not, I believe Dr Pettigrew because, being 6 sessions part-time, she would not have usually been available at that time; which is probably why she did not refer it. We did not regard these dental or orthopaedic joint follow-up meetings as "Haematology Department" meetings but felt they were valuable for collaborating with our professional colleagues in their own departments for the patients' clinical benefit. (We had never regarded our haematology department at Yorkhill as being a 'Haemophilia Centre'. I had never been asked to institute that.)

I remember the orthopaedic follow-up well because one of the first things I did on setting up my new unit at Princess Margaret's Children's Hospital (PMH) in Perth, Western Australia, was to initiate a combined joint orthopaedic/haematology follow-up clinic primarily for haemophilia patients. Initially this was with the Professor of Orthopaedics attending from Sir Charles Gairdner Hospital, a major Perth teaching hospital. Subsequently this has continued with a PMH consultant paediatric Rheumatologist attending.

- 1.2 As I explained in the 6th paragraph of my earlier statement the reason we chose the 'Hemofil' commercial Factor VIII concentrate for use in the home-therapy program was in order to make things as simple as possible for the parents being initiated into the challenge of them preparing the product and giving their young children an intravenous injection in the own home. It was easier to reconstitute in a few minutes in a volume small enough to be given via a 10-20ml syringe, could be stored at home in a regular refrigerator, and stated the number of Factor VIII units per vial. This compared with Cryoprecipitate which had to be stored deep-frozen, thawed out in a 37 degree water-bath over around 30 minutes or so, required an intravenous drip with

drip-stand etc, and contained a variable Factor VIII dose per bag. All these points were made in both Dr. Pettigrew's evidence (Page 17, 1, 14, 17 and page 21, 15 and Professor Hann's evidence (Page 28, 19, 22, 23, 24). Professor Hann stated that the Scottish product was more likely to produce transfusion reactions (page 28, /24, page 31, 13). We warned the parents regarding possible reactions from the Hemofil, and gave them chlorphenamine for treatment of such, with instructions to call us. But I do not remember this really being a problem with Hemofil.

- 2.1 I do not recall the name of the drug company making Hemofil. In my book (page 321) I refer to it as being Hyland Laboratories. (perhaps naming the drug firm in case readers wanted to know where to obtain it. I had no other motive.) It was a product designed for intravenous therapy of haemophilia patients, which was what we were planning, and I naively believed it was satisfactory for this purpose. It certainly proved efficacious in controlling and preventing bleeding in these patients (Dr. Pettigrew, page 20, 2/3), Professor Hann, page 28, 6/7).
- 3.1 Those patients with the severe form of haemophilia and with frequent bleeding problems. The rationale for intermittent prophylactic replacement therapy is that spontaneous haemorrhage is only seen in patients with Factor VIII levels below 1-2 per cent, and infusions of concentrates at 36 to 48-hour intervals can keep the concentration above this level for most of the time (see page 325 in my book).
- 3.2 Our prime concern at that time was to treat the haemorrhagic events as expeditiously as possible, such as instituting therapy at home rather than having to travel, often some distance, to hospital. And in the prophylactic home program the aim was to prevent serious joint and muscle pathology, and to transform these children's quality of life, and that of the family.

Professor Hann expressed these views well when stating (Page 21, /17) "Our energies were first and foremost to prevent serious bleeding, --."

In this context he went on to say (Page 21,/22) "Non-A non-B hepatitis virus risk was not seen as something which dwarfed the risk of serious bleeding." And then: (Page 22,/1) "It didn't dwarf it for the simple reason that all blood products, and certainly all concentrates, both commercial and NHS, were known to carry a very high, or virtually total, risk of transmitting hepatitis, non-A non-B, as it was then called ----." Then (Page 22/15) re pooled plasma "sadly that was a problem that came to light later". And (Page 22 7/9) re Did hepatitis risk ever justify giving up u the use of concentrates? To which he replied "No."

As far as I can remember back then these were also my thoughts regarding the risks. This risk assessment was made before we knew either directly or indirectly of the existence of the HIV virus.

- 3.3 The children were brought up to the Accident and Emergency Department at Yorkhill where they were probably first seen by the general medical staff on duty and treated along the lines described in the 4th paragraph of my answer to

your question 1.1. Often we would be consulted. As our clinical involvement grew we may have been more directly responsible for their clinical management, particularly after Dr. Pettigrew joined the haematology department (see her statement Page 13,/18).

Additionally these children had dental follow-up by the hospital dentist (Mrs. Dunn I believe), and a joint follow up by an orthopaedic surgeon (Mr. Ian MacPhearson) and myself and the haematology home-visiting nurse.

- 3.4 As referred to in my answer to question 3.2 I think our concerns, and those of the parents, was how we might try to improve the treatment and quality of life for these unfortunate children. We warned them of the risk of infusion-related reactions, and what they should do, as mentioned in my answer 1.2.
- 4.1 I cannot recall any difficulties with either type of product, in particular none with hemofil. We held an adequate stock of this and many other drugs, such as anti-leukaemic ones, in our purpose-built haematology department 'Cold Room'. As these supplies were getting in need of replenishment our Technical Head of Haematology, Mr. Fred Jewell, would order some topping-up supplies from the hospital pharmacy, who supplied all our other drug requirements. Perhaps if we had not got our stock-up supply and a doctor had suddenly wanted to have a dose there and then for a particular patient who had just attended there might have been a problem. Namely, it might have taken a day or so ordering things like hemofil. But our system obviated that sort of problem. Mr. Jewell was very experienced, and had come to Yorkhill having worked with me for 3 years at my previous hospital (Glasgow Southern General) and knew well the sort of rate at which our growing department used a wide range of these drugs. There was never any problem.
- 4.2 I cannot recall if any commercial company provided guarantees in relation to supplies. And I cannot recall any supply problem.
- 4.3 The main problem with Cryoprecipitate was its storage deep-frozen, slow thawing out in a 37 degree water-bath, IV drip type infusion and somewhat uncertain dosage, all referred to above (see my 1.2 answer as well as Dr. Pettigrew's and Professor Hann's statements). I cannot remember if these problems also applied to other NHS blood products.
- 4.4 No, I cannot recall anything related to that.
- 5.1 I well recall Mr. Jewell's helpful assistance with these matters, as mentioned in 4.1 above. Thinking about the different drug firms that must have produced the wide range of drugs we used for these diseases, and leukaemia and other oncology disorders, there must have been dozens. I would only be thinking: we must make sure we have enough for the regular in-patient and out-patient therapy, as well as for possible planned Allogeneic Bone-Marrow transplants etc. There were many drugs: Vincristine, prednisolone, dexamethasone, L-Asparaginase, 6-mercatopurine, methotrexate, daunorubicin, adriamycin, cyclophosphamide, thiotepa, CCNU, BCNU. immunoglobulins etc.. I presume each had a drug firm's name on the product. But, although I suppose one could

read that off the label, I never really remember thinking about the drug firms involved. This must have been an issue for the Yorkhill pharmacy department. I presume that all these drugs must have been paid for by the hospital through the hospital pharmacy department.

- 5.2 I am absolutely unaware of any discounting arrangement.
- 6.1 Totally unaware. None.
- 6.2 Totally unaware. None.
- 6.3 Totally unaware. None.
- 7.1 I feel I can add little to my answer to question 3.2 on this issue.
- 7.2 Believing that virtually all blood products carried some risk we were more concerned with using a product that would permit the establishment of a home therapy program, rather than with the ‘pool size’ etc. of commercial products which I do not recall being informed about then. Much more attention was paid to pool size following discovery of HIV.
- 7.3 No. I think I was unaware of this.
- 7.4 I cannot recall how much detail we went into in regard to viral risks. It might have been brought up more by some parents than by others. The risks from hepatitis B were, of course, well known. But we thought that was now behind us, and hepatitis non-A non B was generally thought to be less serious (again see answer 3.2). The patients on home therapy, at least, had regular viral screening tests. And because of the uncertain relation between these and liver function test (LFT) abnormalities Dr. Pettigrew took advantage of incidental venous blood samples to look at LFTs, as mentioned in her statement.
- 8.1 Because I thought that this was a relevant issue I specifically addressed it in the 2nd paragraph of my initial statement to Tracy Turnbull (attached). The treatment of childhood leukaemia progressively became my main interest from that time on, and well after leaving Glasgow. I cannot give an accurate ratio of my time as I simply responded to emerging issues related to all the patients as they arose throughout the day. There were two haematology out-patient (OPD) clinics per week, mostly for leukaemia follow-up and OPD treatment, and the monthly (I believe) joint orthopaedic clinic (see 1.1). A lot of time was of course spent in the wards with patients, including sometimes post-bone-marrow transplant patients being, nursed under sterile conditions etc. But, as I said in my initial statement, I also felt responsible for the haemophilia patients attending Yorkhill (even although not a ‘Haemophilia Centre’). With regard to the time I spent looking after haemophilia patients, this grew with the institution of the home therapy program. One had to spend a lot of time with the parent being trained to reconstitute and give an IV injection in their young child. Others helped me in this regard; Dr. Pettigrew in particular, but also the home-visiting haematology nurse. We all became enthusiastic about this when we saw the transformation of the these severe-haemophilia patient’s life style, like playing football for the first (legal) time in their lives, and not missing school like they used to. I believe that we managed patients with haemophilia and other bleeding disorders to the best of our ability

bearing in mind the on-going problem of medical understaffing in the haematology department referred to by Professor Hann below.

Towards the end of his evidence Professor Hann states that he thought Yorkhill haematology department was the most under-funded such unit in the UK. Although a number of excellent trainees circulated through my department over the years I felt there had been chronic under-staffing in all fields, but I had been unsuccessful in gaining the needed extra staff. But this was not the main reason I left.

- 8.2 I am rather sorry that you ask me why I left Yorkhill and Glasgow, because it echoes in the end of a most challenging and also rewarding part of my medical career. It was not primarily because of staff shortage, and not because of problems with haemophilia care.

I had built up my whole department over 19 years as a team approach between doctors, nurses and technical staff, with every member individually appointed by myself, and with subsequent on-going long-term commitment on their behalf. We came from not existing at all, to performing, together with my radiotherapy consultant wife, some of the first Allogeneic Bone Marrow transplants outside London hospitals. (Glasgow Royal Hospital staff used to attend our transplants to see how we did them! re Prof. Hann's questions about the relationship between the two departments!)

Professor Hann (Page 28./10) mentions 'industrial action issues' as one of the reasons I left. Well, he is correct:

On of the imperative reasons that our department had been originally established was to provide a twenty-four-hour emergency blood transfusion service for the adjacent Queen Mother's Maternity Hospital under Professor Ian Donald. We trained at least a dozen laboratory technical staff who were rostered and continuously undertook that responsibility that they recognised as important, including the head Mr. Jewell and other senior technical staff.

Industrial action in the Glasgow NHS was rife in June 1982.

This included one night when not a single one of the on-call haematology staff would come in to cross-match blood needed for a new-born infant requiring urgent neonatal surgery that night. This was in spite of me individually telephoning every one of those on the on-call transfusion roster. They all either refused or were said to be out.

Eventually a group of haematology doctors (myself included), probably not nearly as good at doing cross-matches compared to the staff doing it all the time, congregated in the haematology department at the nearby Western Infirmary, and managed to provide the blood.

The next morning I told the entire staff that I could no longer work with them professionally, and would be looking elsewhere.

After one phone call to PMH Perth, where I happened to know that they were looking for a new head of department (I was a referee for one such), and the

next day they called me to say that they wanted me to establish a 'state-of-the-art' paediatric haematology/oncology unit at their Children's University teaching hospital, and I think they were even more keen to employ my wife in the Sir Charles Gairdner teaching hospital radiotherapy department. They flew us out to Perth WA 10 days later.