Personal Statement – Dibigatran Etexilate – Mrs. S J Rawden

My Story

In June 2005, my Husband and I flew back from Kuala Lumpur to London, after a two-week holiday. The flight lasted twelve hours and fifty-five minutes, not that I saw much of it; I fell asleep over the Malaysian-Thai boarder and woke up as the plane started its descent into Heathrow. On awaking I felt, what can only be described as a cramp like feeling in my left leg, so I walked around for a while which seemed to ease it slightly. On landing, the pain was still there, but more of a niggling pain, than what can be the first severe pain of cramp. At home, three hours later the pain had still not eased and I remember the thought crossing my mind, "Could I have DVT?" quickly followed by " Don't be silly, you've just pulled a muscle or got cramp."

The following morning was a Monday, and due to the pain in my left leg, when I tried to get out of bed the pain was agonising, standing made it worse and walking was almost impossibility. I was still sure I'd just pulled a muscle as there were no external signs that I had done anything more. It was not until the Tuesday morning, when the pain still persisted that I tried to book an appointment with my GP. They were fully booked and it was not until the Wednesday morning that I was seen.

I was lucky enough, that when I did get to see a G.P, it was a young locum doctor who had just spent six months working on the medical emergencies ward with DVT cases. When I told her I had been on a long flight, and the pain had started during the flight, she immediately suggested DVT and booked me in for an ultrasound scan at the local hospital.

At the Medical Emergencies ward at the local hospital I saw another doctor, who after looking at and measuring both my legs and feeling for any increased warmth, told me that in his opinion there was no way I could have DVT, as I didn't have any of the classic symptoms, but he would send me for the Ultrasound as it had been booked. I must admit he made me feel like I was wasting his time as well as that of the hospitals.

My ultrasound was positive; I had a blood clot in the lower part of my left calf. On returning to the ward, I saw the same doctor, who said, "I told you they wouldn't find a clot" to which I informed him that he was wrong. I have never seen anyone move so fast to get my notes.

I was 31, an ideal weight, no previous history of DVT, no family history (that I was aware of, at the time), hadn't had any recent surgery, not what you would call in a high-risk category. I had fallen asleep for twelve hours on a plane, whilst being on the combined contraceptive pill. At the time we thought this combination was the possible cause.

It wasn't till I got home that my mother mentioned that my uncle had died of a blood clot, aged 41, 2 years before I was born, after being in hospital for an operation on his varicous veins. I've since discovered, that his daughter, my cousin has had three episodes of DVT in 18 years, one caused by immobility after an operation, one by pregnancy, and one six months after mine with no known cause, but the one which underlines both hers and mine, Family History.

Anyway, back to the hospital, a blood test was taken, and my INR came back as 0.9, not overly low. The doctor decided on duration of treatment of 3 months and a desired therapeutic INR range of 2 to 3. I was injected with Clexane, a low molecular weight heparin, in the stomach wall lining, and given a Warfarin dose of 10mg for the first two days, and told to self inject with Clexane, the following day and go back to the hospital the day after. The hospital also prescribed tablets for pain and said there was no way I was flying on the Sunday to the U.S for a meeting.

It took eight blood tests in the next nine days for the hospital to be happy enough with my INR levels to reduce the testing to once a week; by this time my arms were black and blue with the needle marks from the injection to draw blood. I was still in pain and couldn't walk. Every time I put my legs below my waist, the pain increased. I was on painkillers every six hours.

A few weeks later I saw a consultant who was a heart specialist who was surprised that I was still in pain, but looking at my notes decided that the cause of the clot had been not moving on a plane for twelve hours and being on the pill. They decided to keep my on the Warfarin till the end of the three months.

I was still going to the hospital on a weekly basis for blood tests when on a visit to my GP's they said they could do the testing there. Which made thing so much easier, as they use a portable machine

when all they need is a drop of blood, which can be got from a finger prick. I heard nothing further from the hospital.

By the September, I was still in pain, couldn't walk, couldn't drive and thus couldn't go to work. I was fed-up and decided to take matters into my own hands. I was lucky, I had private medical cover, and on phoning my medical insurer they booked an appointment for me to see the same consultant privately. I did ask why a heart specialist, but was told he covered DVT cases.

My consultant decided that the reason I was still in pain was due to muscle degeneration and damage to the calf caused by the increase blood flow to other vessels, while I had the clot, but ordered another ultra scan to be on the safe side. It came back negative, the clot had gone. He then booked a course of Physiotherapy for me which over 10 weeks, eased the pain and got me back walking again. I was back at work in the second week of November, it had been five months, and I was still on Warfarin.

I saw the consultant again in the beginning of January, who said it was time for me to come off the Warfarin, when I asked, "Why?" he explained, "The current policy is not to put people who have only had one clot on long term Warfarin". I asked what the policy was, and he replied "We wait and see if you get another clot" When I asked "What happens if the second clot results in me no longer breathing?" He didn't have an answer.

I've been looking into my Family Tree for twenty years, I know this sounds morbid, but I looked back through all the death certificates I had and discovered that my paternal Great Grandfather, Great Great Grandmother and Great Great Grandfather had died of different types of Thrombosis. The case for family history was very strong.

Due to this we agreed that it would be advisable that I have the genetic test done to see if I had a hereditary form of Thrombophilia. This involved coming off the Warfarin for four weeks, so my blood was not chemically altered. As soon as I had the test I could go back on the Warfarin and go back and see my consultant when the test results were through.

It took six weeks from the test being done. They were negative. My GP said I was clear; there was nothing I'd inherited. This was a case of lack of awareness. We are currently aware of five genetic mutations that cause hereditary Thrombophilia; there could be more gene mutations that we are not aware of. Molecular Biology to gene level is still in its infancy, there is still so much we do not know.

On visiting the consultant in the April, he decided that due to my incessant questioning, it would be a good idea if I saw a real specialist.

What had I been doing for 10 months?

So an appointment was booked for me to see a Haematologist. Why it had taken so long I don't know.

After 11 months I finally met with a consultant who not only understood what I had, but could advise me accordingly. He understood my situation and the fact that I had a knowledge of the science led to a very constructive discussion. We decided that although I have no identifiable Thrombophilia, my family history was too strong to ignore it. The plane flight and the pill contributed to me getting a clot, but it was the family history, which was probably the main reason. We came to the conclusion that for me, staying on Warfarin was the best thing to do.

It has now been 2 years since I was diagnosed with DVT; I'm still on Warfarin, I'm now self testing my INR. I still haven't flown for more that three hours, but this is predominantly a mental thing rather than there being any danger, but I feel DVT is now something I understand and, most importantly, can live with.

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The current of treatment for most patients who have had Knee or Hip surgery is mechanical prophylaxis. One option can be the use of graduated elastic compression stockings, which are uncomfortable for the patient especially after surgery. These are inexpensive, but not necessarily truly effective.

In certain cases intermittent pneumatic compression devices, which inflate and deflate, which again caused discomfort to the patient, especially at night. These pneumatic compression devices are expensive to run and are not readily available.

Mechanical foot pumps are also used, and although more cost effective than the pneumatic compression devices, can only be used on patients that have a degree of mobility.

The Final Scope for this Health Technology Appraisal states “Patients at increased risk of venous thromboembolism (VTE) should be offered low molecular weight heparin (LMWH)”.

Firstly, Low molecular weight heparin can only be given as a sub-cutaneous injection into the stomach wall lining. This is a very uncomfortable procedure, and from a patient’s point of view it is an evasive treatment. Heparin should be given for 10 days following major surgery. This is not always done, especially once the patient has been discharged from hospital and have to self inject. The FDA approved heparin in 1937 making it a drug, which is now 71 years old.

Fondaparinux (Arixtra®), like heparin is also given daily as a sub-cutaneous injection, the potential advantage of using Fondaparinux is the risk of heparin-induced thrombocytopenia being reduced. Approved in 2001, it does not give huge advantages over Heparin.

Secondly, how are patients measured to be at increased risk? Most patients that require these operations are over 40, which put them in a higher risk category, and having major surgery increases the risk further. Add this to immobility after major surgery and these are the three main factors that cause VTE.

60% of Patients who have this type of major surgery could develop VTE without prevention. So is increased decided upon by previous person history or close familial history? Unless Thrombophillia testing is going to be introduced before each operation, we cannot categorically be in a position to judge ‘increased risk’

Shouldn’t every patient who has had knee or hip surgery be treated with a non-evasive oral drug like Dabigatran Etexilate (Pradaxa®)? The dosage of Pradaxa® is a single capsule of 110mg (Which is the Half dose, the full dosage can be up to 220mg) is administered orally between 1-4 hours following surgery. This is continued with 2 capsules, one daily thereafter for a total of 10 days in total knee replacement patients and 28-35 days in total hip replacement. With a tablet there is more chance this will be taken once a patient is discharged from hospital

Pradaxa prevents thrombus formation by specifically and selectively inhibiting thrombin, the central and essential enzyme that enable the conversion of fibrinogen into fibrin during the coagulation cascade, and there for prevents the development of a thrombus, Pradaxa has a rapid onset and offset of action and predictable anticoagulation effect, avoiding the need for coagulation monitoring.

The only other option is Warfarin, which was approved by the FDA in 1954, making it a 54 year old drug. This is the first oral tablet for prevention of VTE since the launch of Warfarin. This requires continuous monitoring, which is a drain on NHS resources.

In my personal opinion, Pradaxa has much more benefits than anything else currently on the market, and is more cost effective than other options. If this oral tablet does not need continuous monitoring or does not need to be sub-cutaneously injected, it benefits the patient.

Most importantly it seems to be the best way forward to save lives, in a non – evasive manner.