Neutral Citation Number: [2022] EWHC 1171 (QB)

QB-2020-000119

IN THE HIGH COURT OF JUSTICE
QUEEN'S BENCH DIVISION

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 17 May 2022

Before:

MR JUSTICE RITCHIE

- -

BETWEEN

PHOEBE CHARMAINE PICKERING

Claimant

and

CAMBRIDGE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST

Defendant

Catherine Ewins instructed by **Ashtons Legal Solicitors** for the **Claimant**
Claire Toogood QC instructed by **Kennedys** for the **Defendant**

Hearing dates: 4, 5, 6 and 9 May 2022

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This judgment was handed down by the Judge remotely by circulation to the parties' representatives by email and release to The National Archives.
The date and time for hand-down is deemed to be Tuesday, 17 May 2022 at 10:00 am.

Mr Justice Ritchie:

The Parties

[1] The Claimant is a patient who attended Addenbrookes Hospital in Cambridge for treatment.

[2] The Defendant runs Addenbrookes Hospital and is responsible for the standards of clinical care provided there.

Bundles

[3] For the trial there were 10 paper bundles of documents together with written skeleton arguments.

The Issue

[4] By the end of the trial there was one issue for the Court to determine. That was and is whether, but for the negligence of the Defendant, the Claimant would have avoided suffering a stroke due to the beneficial effects of Heparin treatment, which the Defendant should have given her starting just before 02:00hrs on 25 September 2015 and continuing until she was provided with therapeutic anti-coagulation using Warfarin or alternative modern pills.

Terminology

AF: atrial fibrillation.
INR: international normalised ratio.
LA: left atrium.
LAA: left atrial appendage.
TE: thrombo embolism.
TEE: transeosophageal echocardiography.
PE: pulmonary embolism.
SEE: systemic embolic event.
MHV: mechanical heart value.
TIA: transient ischaemic attack.
P value: P over 0.05 is the probability that the null hypothesis is true. The null hypothesis states that there is no relationship between the two variables being studied (one variable does not affect the other). It states the results are due to chance and are not significant. A statistically significant test result is P equal to or less than 0.05.
Confidence Interval: this figure shows the range of results within the sample and hence the level of confidence that we can have that the stated result will be repeated in the whole population. The wider the CI, the wider the likely range of results in the population, the narrower the CI, the narrower the range of results.

The Evidence

[5] I heard evidence from the following witnesses: Dr. Jaffey, Mr. Saab, Dr. Michael, Professor Mehta and Dr. Patel.

[6] An expert report from Dr. Giallombardo was served by the Defendant but he was not called. The Claimant relies on some parts of it.

[7] No lay witnesses were called, however witness statements were provided by the Claimant, her husband and son. In addition witness statements were served by the

Defendant from the treating clinicians: Dr. Roderick MacKenzie and Dr. Omar Elsaka. Neither of them was called.

The Medical history

[8] In September 2015 the Claimant was 52 and a half years old. Her relevant medical history (with deletions for privacy) is set out below.

[9] 12 09 85 Diagnosis of muscular dystrophy.

[10] 12 05 97 Ambulatory electrocardiogram showed atrial fibrillation.

[11] 19 01 04 Cardiology clinic letter: "*In view of the significantly increased left atrial size, along with Mrs Pickering's history of atrial fibrillation, I do feel that she now needs to be considered for anti-coagulation, if pregnancies in the future are not an issue*."

[12] 01 12 04 Cardiology clinic letter: "*She and her husband have been concerned about long term anti-coagulation and also about the need for beta blockade. I spent some time explaining to them that both were advisable long term, the Warfarin to reduce the risk of stroke, and the beta blocker to protect her ventricles from rapid rates. But she is unhappy about taking anything more than just aspirin and since the decision is not urgent I thought the sensible plan was continuing follow up … If there is any evidence of deterioration such as increasing left atrial size then the case for anti-coagulation would be strengthened.*"

[13] 19 01 05 Cardiology clinic letter: "*The other more pressing issue is regarding anti-coagulation with Warfarin. Again Mrs Pickering has been averse to this although her echocardiogram did show that the longitudinal dimension of her left atrium was significantly increased. I do agree with her that … are more pressing at present but she is aware that in the long term anti-coagulation would be strongly suggested in view of her increased left atrial size and the increased risk of a cerebral vascular event. I have also spoken to her that if we did start anti-coagulation, then we would need to be aware should she wish a further pregnancy. She is not taking any form of contraception at present*."

[14] 10 08 05 Cardiology clinic letter: "*Echocardiogram demonstrated overall reasonable left ventricular function and the left ventricle was undilated. In keeping with her atrial fibrillation her left atrium was dilated at 4.9cm. A mild eccentric jet of mitral regurgitation was noted but otherwise she had no significant valvular lesions*."

[15] 10 10 05 Cardiology clinic letter: "*She is well and is asymptomatic from her atrial fibrillation. … She remains on aspirin 75mg od. … At present she is not keen for Warfarinisation and although she has a mildly dilated left atrium she has no other indicators to start formal anti-coagulation.*"

[16] 24 01 07 Cardiology clinic letter: "*Atrial fibrillation; moderate mitral regurgitation; muscular dystrophy. … she remains well with no real symptoms. In particular there is no shortness of breath, chest pain, dizzy spells or collapses. … It may be ultimately she will need a pacemaker. I have today recommended anti-coagulation for thromboembolic prophylaxis. She however was rather resistant to this idea and therefore we have agreed that we will re-review this at the next clinic …*"

[17] 01 02 07 Cardiology clinic letter: "*She takes just aspirin and is reluctant to take Warfarin.*"

[18] 02 04 07 Cardiology clinic letter: "*She feels unlimited as regards shortness of breath or chest pain and takes aspirin 75mg only. … I have discussed with Mrs Pickering her heart rate and the trends that this is in fact slowing and she may come to require permanent pacemaker insertion. As you are aware, her uncle who also suffered from myopathic problems, did suffer pacemaker problems, but in spite of this Mrs Pickering made it entirely clear that this is something she would consider if it was felt necessary. She is very keen to be closely monitored and she mentioned that she did not wish to take any risks whatsoever and would accept any advice regarding treatment.*"

[19] 19 07 07 Cardiology clinic letter: "*Although she does suffer from muscular dystrophy … she is fully mobile with a full and normal lifestyle. … is awaiting pacemaker implantation. Overall LV function is reasonable although she does have a degree of pulmonary hypertension. … she has been found this year to be significantly hypertensive …*"

[20] 29 09 07 Cardiology clinic letter: pacemaker implanted.

[21] 01 09 09 Cardiology clinic letter: "*The question is the indication … for Warfarin. Her echocardiogram at Papworth on 8 October of last year showed that the left atrial size was 4.5 and with normal heart function otherwise. A further echocardiogram on 29 June would seem to indicate that not much has changed at this point. She does have two leads in the ventricle and has a single chamber two lead pacemaker. My view has generally been that she could remain off Warfarin for the moment. She remains under 60 years of age with normal heart function and I don't think the [muscular dystrophy] Lamin mutation would cause me to be more pro-active in terms of initiating Warfarin in place of aspirin*."

[22] 11 01 10 Cardiology clinic letter: "*… we do have a very low threshold in these patients with Lamin A/C mutation for considering in particular ICD devices [implantable cardioverter defibrillator] in view of the risk of ventricular arrhythmias. Mrs Pickering … at present is being kept under close surveillance. … She is fully aware that should she develop symptoms in the interim period that she should seek urgent medical attention.*"

[23] 06 08 12 Cardiology to neurology referral: "*… over the years she has in fact been difficult to persuade regarding investigation and treatment for example with a permanent pacemaker for atrial fibrillation with block which was put in in September 2007. She has not been keen in the past to be on anti-coagulation with Warfarin for her underlying atrial fibrillation and currently continues on aspirin. … it has only been recently that she has appeared keen for further involvement [re the muscular dystrophy]*."

[24] 15 07 13 Cardiology clinic letter: "*… she is asymptomatic from the cardiac point of view and in particular denies any breathlessness, palpitations or syncope. … her other medication includes … aspirin although she comments that she takes her aspirin erratically. … 12 lead ECG showed paced rhythm with underlying atrial fibrillation.*

I have discussed with Mrs Pickering again the issue regarding Warfarinisation in view of her atrial fibrillation but this is still something that she does not feel she wishes to pursue at present. She did ask regarding the new oral anti-coagulant agent but again mentioned that she did not wish to commence at present but would consider this at a later date. I have mentioned to her regarding taking her aspirin on a regular basis."

[25] 17 02 14 Cardiology clinic letter: "*Recent episode of shortness of breath when boarding plane. ... but she has no ongoing symptoms. I will arrange update of her echocardiogram which in August last year showed satisfactory left ventricular function with ejection fracture of 60-65%. Right ventricular size was reported as normal although I note that tricuspid regurgitation was recorded. ... I have again discussed with her the possibility of anti-coagulation with Warfarin in view of her underlying atrial fibrillation but she does not wish to move forward to this as yet*."

[26] 18 08 14 Cardiology clinic letter: "*... her last echocardiogram suggested some increase in her level of tricuspic regurgitation with a degree of pulmonary hypertension. ... her holter monitor performed in March ... showed her ventricular paced rhythm with frequent ventricular ectopics occurring in singles and couplets and accounting for 12% of the recording. With this in mind I have recommended the introduction of beta blockers ... As you will be aware Mrs Pickering is reluctant regarding taking medication but in view of the risk of ventricular arrhythmias and Lamin ACT cardiomyopathies, undoubtedly her ventricular ectopy should be treated. ...we would advise Mrs Picking is on anti-coagulation with Warfarin. She is reluctant regarding this, as she has been in the past and mentions that she will discuss this with you further*."

[27] 19 02 15 Cardiology clinic letter: "*We discursively considered with her the idea of potentially replacing her pacemaker with an ICD. ... The outstanding issue of course remains risk stratification and ambulant ventricular ectopy does not map easily onto risk. Of course she remains reticent in respect of changes of medication and she continues just on aspirin, thyroxine and lisinopril despite the observation of the ectopy and underlying atrial arrhythmia*."

[28] 20 05 15 "*... In the past we have discussed with her anti-coagulation with Warfarin in view of her atrial fibrillation in the setting of a structurally abnormal heart, but she has always been reluctant regarding this. I did mention this again today but she reported that as her blood pressure was well controlled it was not felt necessary, but I have again reiterated to her that it is not for blood pressure but reduced stroke risk, given her atrial fibrillation. She will give this aspect some further thought and undoubtedly as she gets older her thromboembolic risk will increase*."

[29] Thus it is clear that by her own choice the Claimant had refused therapeutic anti-coagulation, contrary to medical advice, for many years despite having left atrial fibrillation (AF). She was instead taking Aspirin.

The Clinical Negligence

[30] On 24 September 2015 the Claimant suffered symptoms at home in the evening. A call was made for an ambulance.

[31] 24 09 15 21:20hrs: Ambulance (111) report: "*Reported condition: right leg from knee down goes white. ... Has been sitting a lot last couple of days. Right leg below knee keeps going white, feels cold then goes pink again, started this evening, feels painful, refused ambulance will go to ED. … Encounter Disposition: attend Emergency Treatment Centre within 1 hour.*" The Claimant was taken to A&E at the Defendant's hospital.

[32] 24 09 15 Defendant's Triage notes at A&E: 22:04hrs: "*Was sitting on the sofa this evening and noticed that she has some pins and needles in her foot. She got up and walked around. She noticed that her Rt foot had gone very cold and white in appearance. This lasted for a few minutes and then it returned to normal. This keeps happening every so often but then returns to normal again. Some temperature difference in the toes but no swelling in the calf.*" After being triaged the Claimant was sent to the Out of Hours GP centre near A&E.

[33] 24 09 15 Defendant's Out of hours GP centre near A&E: 22:23hrs: "*Intermittent episodes of leg turning perishingly cold, paraesthesia and pain; episodes lasting about 5min and then seems to completely resolve; evidenced by RN in A&E; is on aspirin and took 300mg aspirin this evening; no hx of trauma; does suffer muscular dystrophy; no GP records available; no prev hx of vascular problems reported.*

"*Examination 36.6^{o} C; P 70; 130/66mmHg; RR 18; 95%; ECG reported as normal; near normal appearance of both legs; pedal pulses bilaterally present; feet slightly cold equally; normal power and sensation in knees and ankles; no evidence of abnormal discolouration. Diagnosis: ?intermittent claudication ?cause Outcome: returned to ED as requires further work up.*"

[34] 24 09 15 The Claimant was then sent back to A&E. A&E notes: Dr. Elsaka, specialist registrar, 01:35hrs: "*Rt leg problem. Leg went very cold and white in colour. Called 111 and then sent up here for assessment. HPC: Rt leg paraesthesia & pallor since this PM. Intermittent episodes with 5 minute intervals. Associated paraesthesia. No pain or weakness. Denies any other CVS [cardio vascular system], CNS [central nervous system] symptoms. Is normally on aspirin but had forgotten to take it for last 5/7 due to stress.*
Past medical history: AF (atrial fibrillation); pacemaker; muscular dystrophy, limb girdle; hypertension; thyroid disease…
Physical exam: BP 130/86mmHg; pulse 70; Temp (Src) 36.6^{o} C (Tympanic); Resp 18; SpO2 95%
Examination: both legs warm;
Buerger's test -ve;
Cannot palpate Rt DP[dorsalis pedis] & PT [posterior tibial] pulses, rest pulses up to femoral equally felt B/L;
Both Rt DP & PT heard strongly on Doppler & equal to Lt side
D/W Dr. Makenzie – he advised since symptoms have resolved can be referred to GP to continue management & advise on further FU.
Diagnosis: ? Resolved ischaemic event of Rt leg
Plan: D/C home; GP to FU in 5-7 days & advise on further management & FU if needed. Advised to return to ED if any pallor, coldness, pain or paraesthesia of Rt LL. Advised to restart aspirin." (End of note timed at 01:44hrs).

[35] By the end of the first day of the trial the Defendant had admitted that it had been negligent in failing to treat the Claimant with immediate low molecular weight Heparin by injection in A&E at or before 01.44 am on 25 September 2015.

The risk

[36] It was admitted that the Claimant was at high risk of suffering an embolus (part of the blood clot), breaking free from the blood clot which was most probably present in her left atrial appendage. The further embolus risk could lead to a stroke: a blockage in the arteries in the brain, or a blockage of the arteries to the gut or limbs. Where the embolus travels to is a matter of pure chance. It breaks off from the left atrial mother clot, travels into the left ventricle, is pumped up the arch of the aorta and may turn left to the brain or right to the body.

The stroke

[37] The Claimant was healthy between 25 and 27 September. She did what she was advised to do and called her GP, but she was not offered an urgent appointment.

[38] Events then took a turn for the worse in the evening of 27 September 2015. She suffered a stroke at home. The ambulance service was called.

[39] Returning to the medical notes:
27 09 15 Ambulance note: "*…20:42 sudden onset of R facial droop and slurred speech. … Remained the same en route to ED*."

[40] 27 09 15 The ambulance dropped the Claimant at the Defendant's A&E. "*Recognition of stroke in emergency room*": asymmetric facial weakness and speech disturbance.

[41] Specialist Nurse Practitioner: 21:43hrs "*Improved for 5 mins then came back again. No limb weakness pupils equal and reactive throughou*t."

[42] 21:45hrs "*Pt says not felt confused. No headache or pain. had recent DVT*"
Dr. Surendranathan, hospital practitioner: 23:31hrs: "*HPC: Since 8.40pm has noted difficulty expressing herself with associated right sided facial weakness. No limb symptoms. No sensory symptoms*.
Recent admission for ?ischaemic limb …
Working diagnosis: Left MCA territory infarct
Management plan: CT head/perfusion shows mismatch in flow and volume with large salvageable penumbra. D/W Dr. Manford agrees thrombolysis if no contra-indication. Discussed benefits and risks, difficult decision for family but together with Mrs Pickering have agreed."

[43] CT Brain perfusion with contrast: "*There is a short segment of hyperattenuating thrombus in the distal M1 segment of the <u>left middle cerebral artery</u> … delayed temporal parameters and reduced cerebral blood flow in the left insula and adjacent frontoparietoterriporal convexity territory of the left middle cerebral artery. The basal ganglia of the left MCA is spared. There are small areas of slightly reduced cerebral blood volume in some of the frontoparietal subcortical white matter but the appearances are almost entirely of potentially salvageable ischaemic penumbra. CTA images reconstructed from the volume perfusion data show occlusion of the <u>left internal carotid artery</u> from at least the level of the skull base. The left M1 MCA is supplied via*

the anterior communicating artery and contains thrombus in its distal M1 segment. There is good collateral opacification of the left MCA branches distal to the thrombus."

[44] Thrombolysis treatment: 23:15hrs bolus, infusion commenced 23:32hrs.

[45] 23:47hrs Nurse Practitioner: "*Pt became dysphasic again while in CT which became worse. She started writing down for us but this became worse. Since the bolus and commencement of infusion writing is becoming better again so far remains dysphasic*."

[46] 28 09 15 Specialist Registrar note: expressive and receptive dysphasia, worsening right arm weakness and right leg weakness. "*Explained to family that … there is increasing size of area of damage to brain from stroke*."

[47] 29 09 15 CT angiogram of the aortic arch and carotid (bilateral): "*Note is made of the recent CT head scan demonstrating hyper density within the proximal left MCA and distal left ICA. CT angiography demonstrates lack of opacification of the left internal carotid artery and the proximal left middle cerebral artery and proximal left anterior cerebral artery. These appearances are consistent with a T occlusion of the distal left ICA. There is good collateral filling of the middle cerebral artery to the distal left M1 segment. The rest of the extracranial and intracranial arterial circulation is within normal limits. Opacification of the right posterior communicating artery and anterior communicating artery are noted.*"

[48] CT of the head: "*Further interval evolution of the left MCA territory infarct compared with yesterday's CT. Ischaemic changes now include the left thalamus and basal ganglia, sub-insular grey matter, insular cortex and focal wedge of the left frontoparietal cortex. No new territory infarct. Conclusion: Further evolution of the left MCA territory infarct with extensive involvement of left thalamus, basal ganglia, insular and frontoparietal cortex.*"

[49] The Claimant had suffered a massive stroke. A blood clot or clots had travelled from her left atrial appendage to her brain and lodged in the left middle cerebral artery and the left internal carotid artery. The lack of blood flow resulting from the clot/s had caused initial damage but the damage worsened over the following two days despite the Defendant treating the clots with thrombolytic drugs (clot busters).

Pleadings and chronology of the action

[50] The claim was issued in January 2020. In the Particulars of Claim the Claimant alleged that the Defendant was negligent on 25 September. The Defendant failed to advise the Claimant that because she had suffered an embolus in her right leg on 24 September she was at real risk of suffering another embolus. The Defendant failed to treat the Claimant with Heparin and instead discharged her with advice to take Aspirin, which she had been on for a long time. She was advised to contact her GP in the next 5-7 days for follow up. The Claimant asserted that had she been advised that she needed treatment she would have accepted that advice. She also asserted that had she been treated immediately with Heparin and thereafter daily anti-coagulation she would have avoided the stroke. The time between the breach and the stroke was 67 hours or 2.79 days. It was asserted that the Claimant would have had a good long term prognosis.

[51] In its Amended Defence dated March 2022 the Defendant denied negligence and denied that it was bound to administer Heparin, but admitted that the clinicians should have advised the Claimant urgently to seek a decision regarding anti-coagulation from her treating physicians for her pre-existing heart conditions. The Defendant denied that its clinicians were required to advise the Claimant that she faced a future risk of further emboli, pleading that such advice was a matter for her treating clinicians. The Defendant denied that the Claimant would have accepted Heparin even if they had offered it. Finally on causation the Defendant denied that Heparin would have prevented the embolus breaking free of the atrial clot and travelling to the brain on 27 September.

The evidence on breach

[52] At trial, the evidence from Dr. Jaffey, a consultant in A&E medicine, which I found was persuasive, logical and clear, was that in his opinion no reasonable A&E clinician would have let the Claimant leave without offering her advice on the "*significant risk of further embolisation*" and advising her that she needed Heparin "*to reduce the risk of further embolic events*". He advised that:

> "*Given that she was known to be at risk of developing an atrial thrombus, and that this carried significant risk of causing embolic episodes, the only logical conclusion should have been that this is what had occurred. As such she was clearly at risk of further embolic episodes unless action was taken to reduce such risk and the only appropriate actions was to administer an anti-coagulant that would have an immediate effect. … Heparin.*"

[53] Mr Saab, the Defendant's A&E consultant, advised the Court that it was entirely reasonable not to treat the Claimant with Heparin because there was no evidence of ongoing leg ischaemia so no responsible body of A&E clinicians would have advised that the Claimant should have been started on anti-coagulation. However in his live evidence under cross examination, he was wholly unable to explain why he had failed to mention in his report that the Claimant had, on the balance of probabilities, a clot in her left atrium and that it had already "*fired off*" one embolus and created a very significant risk of firing off another with potentially fatal consequences. He had concentrated on the leg clot and ignored the mother clot. Whilst he did not wholly withdraw his opinion that no reasonable clinician would have advised the Claimant to take Heparin treatment immediately at A&E, he came so close as to be indicating to the Court that he was relenting. In any event he could not explain why it would be safe to make the Claimant wait for anti-coagulation when the Defendant's clinicians had Heparin in the fridge and a simple injection would start the protective process.

[54] Rightly, after Mr Saab's evidence, the Defendant conceded breach of duty. Had they not have done so I would have found breach of duty in this judgment and I would have rejected Mr Saab's evidence. The Defendant also conceded that the Claimant would have taken their advice to start Heparin.

Causation

[55] Four medical experts reported on causation.

[56] Dr. Michael is an eminent consultant neurologist who qualified in medicine at Oxford, is a fellow of the Royal College of Physicians and worked for 30 years as an NHS consultant in the South East Thames area and then at Kings College Hospital in South London. He reported on causation from a neurologist's point of view. He advised that both the leg clot and the stroke clot "*were attributable to the same mechanism, namely embolic fragments being thrown off from a common cardiac source.*" As to the risk he advised that: "*Given that she had the episode in the legs, the risks of other episodes was clearly extremely high.*" He advised that:

> "*At that stage, the only effective treatment was anti-coagulation, namely daily injections of Heparin for three days until a therapeutic level of oral anti-coagulant was achieved. Had such anti-coagulation been administered following the visit to A&E on 24 September 2015, on the balance of probabilities the stroke three days after the leg symptoms would have been prevented as would the extension of damage to the brain in the days thereafter.*"

[57] Dr. Giallombardo, a consultant in general medicine, geriatrics and strokes, who worked in Basingstoke General hospital until he retired in 2016, still does some locum consultant work in stroke and geriatrics. He was a principle investigator for various blood clotting multicentre NHS sponsored trials. He developed and ran a thrombolysis service from 2008 onwards. He advised that stroke physicians would have recommended the Claimant be treated with Apixaban. He advised that that drug did not itself dissolve blood clots but inhibited propagation. He advised that blood clots are slowly *"degraded"* by the same mechanism that normally prevents the blood from clotting within the circulation. He advised that oral anti-coagulants tipped the balance of action and reaction towards blood clot dissolution and away from blood clot formation. He produced and relied upon a paper by McBride et al published in 1991 called "*Stroke Prevention in Atrial Fibrillation*". This study showed that in patients with atrial fibrillation the rate of ishaemic stroke or systemic embolism was substantially reduced by taking Warfarin compared to those who did not. The risk reduction was 67% and the confidence quotient was high. The probability of the results being accurate was P = 0.01. One minus 0.01 is 99%.

[58] Dr. Giallombardo also produced a paper by Lee et al dated 2019 called: "*Left atrial or left atrial appendage thrombus resolution after adjustment of oral anti-coagulation treatment.*" In this study 41 patients were chosen and 22 underwent transoesophageal echocardiography to determine whether oral anti-coagulant of the modern type (NOACs) affected the blood clots in their left atrium or left atrial appendage.

[59] These were not all AF patients. Only 25 had long standing AF and 16 of those had paroxysmal AF. Patients with severe valvular regurgitation, severe valvular stenosis and mechanical valve disease were excluded. The cohort had suffered new onset ischaemic stroke or valvular heart disease. Only 22 agreed to TEE follow up, the other 19 refused. Of those, before the TEE scan to find their thrombi, 9 had received no anti-coagulation, 10 had been on Aspirin, 13 on NOACs and 9 were on Warfarin.

[60] In the introduction the authors asserted that atrial fibrillation is associated with the development of left atrial and left atrial appendage thrombi. Also that these are the main source of stroke and systemic embolisms. Approximately 90% of such blood

clots are found in the left atrial appendage. The reference for these assertions was an article by Al Saadi et al dated 1999. The authors advised that ineffective irregular contraction and dilation diminished the blood flow velocity in the left atrium and resulted in significant blood stasis in the atrial appendage which, when coupled with abnormal blood constituents or atrial wall abnormalities, could lead to clots. The authors summarised that transoesophageal echocardiogram (TEE) was the gold standard for evaluating the presence of left atrial clots and that if a left atrial or atrial appendage clot is detected during TEE current guidelines recommended treatment with vitamin K antagonists for three weeks using an INR range of between two and three. A follow up TEE assessment three to four weeks after therapy was recommended to ensure thrombus resolution before any cardioversion procedure should take place. The reference for that advice is a paper by Kirchhoff et al from 2016.

[61] Of the 41 patients in the cohort some had clots in the left atrium (29%) and others the left atrial appendage (71%).

[62] Of the 22 who had follow up TEEs, their clots resolved as a result of the administration of the oral anti-coagulant in the vast majority (86%). Resolution occurred over a mean of 165 days. In addition, during the process of taking modern anti-coagulants the ischaemic stroke rate of the patients was stated to be low at 4.9%, despite their many diseases including, obviously, atrial fibrillation, diabetes and other conditions.

[63] The anti-coagulation treatment offered after the thrombi were identified by TEE was as follows: 5 had none; 4 had Aspirin; 18 had NOACs and 14 had Warfarin. So it is apparent the cohort of 41 did not all get Heparin, therapeutic Warfarin or NOACs and the report does not clearly state which of the 41 were the final 22 who agreed to the later TEE scan to determine whether the clots had gone. The decisions not to give therapeutic anti-coagulants was related to the risk of bleeding as a result of the previous ischaemic strokes they had suffered. I consider that this report is therefore of minimal assistance to me in dealing with the issue I have before me.

[64] Dr. Giallombardo approached the Claimant's case on the basis that she would have been prescribed Apixaban on 25 September 2015, which is not the pleaded case. However he wrote that on causation and on the issue of whether, if the Claimant was treated with Apixaban or low molecular weight Heparin, the period of 67 hours would have been long enough to prevent a further embolic event, he advised as follows:

> "*There is strong evidence that Apixaban is as effective as Warfarin in preventing cardiac embolism. However, the evidence comes from patients who were stable at enrolment in the relevant studies and were followed up for several months.*
>
> "*It is plausible and supported by personal experience that the use of anti-coagulant medication is effective in preventing early recurrences when used in patients with TIA or minor stroke due to cardiac embolism. This is probably due to the small size of the blood clots in patients with TIA or minor stroke.*"

[65] I take note that this stroke physician has personal experience of anti-coagulants, including Heparin, preventing early recurrence of emboli generated in the heart causing

strokes. This is directly relevant to the issue. He went on to defer to Dr. Patel on causation thus:

> "*However, bearing in mind the mechanism of action of anti-coagulant medications, the short time scale and relying on Dr. Patel's expertise, I conclude that anti-coagulation with Apixaban or low molecular weight Heparin between 25 and 27 September would not have prevented the stroke on 27 September 2015 due to the large blood clot occluding the left internal carotid artery.*"

[66] In their joint report Dr. Michael and Dr. Giallombardo agreed that the Claimant was at significant risk of further emboli after she had suffered the first blood clot in her leg. They agreed that the benefits of administering Heparin to the Claimant outweighed the risks. They agreed that the stroke the Claimant eventually suffered was caused by an embolism from the clot in the heart. They could not decide whether it was the whole clot or merely part of it which travelled to the brain. On the key issue of causation Dr. Giallombardo deferred to the haematologists but thought that anti-coagulant would not have saved the Claimant. Dr. Michael repeated his opinion that on balance the Heparin would have prevented the stroke and relied on a paper by Weitz et al published in 1997 which, he asserted, supported the statement that the use of Heparin for over 48 hours reduced the stroke risks in patients with atrial fibrillation. He went on to advise in the joint report that the effect of Heparin is immediate and that after a few weeks of anti-coagulation the relative risk of embolisation is reduced by over 60% as a result of the anti-coagulation. They also both agreed that the thrombolysis given on 27 September is unlikely to be relevant to the decision on causation. They agreed that if the stroke had been avoided then the Claimant would have continued on oral anti-coagulation for life and would have avoided a stroke for life.

[67] In cross examination Dr Michael was criticised in three main ways. The first was that he had retired 22 years ago and so was not up to date. The second was that he was a general neurologist not a stroke physician or a haematologist and therefore was not properly qualified to advise on causation in relation to left atrial blood clots and their potential for embolization. The third was that he had relied on a paper by Weitz et al which, on the Defendant's submission, did not say what Dr Michael said it said.

[68] The paper by Weitz et al was published in 1997. The authors examined the actions of Heparin, in particular low molecular weight Heparin on venous thromboembolism. They advised that low molecular weight Heparins exert their anti-coagulant activity by activating anti thrombin. They advised that Heparin binding to anti thrombin causes a conformational change in anti-thrombin that accelerates its interaction with thrombin and activated factor X (factor Xa to be precise) by about 1000 times. They went on to say that "*when low molecular weight Heparin is given subcutaneously in low doses the recovery of antifactor Xa activity approaches 100%.*"

[69] Weitz et al advised that "*Heparins are safe and effective for the prevention and treatment of venous thromboembolism. They have also been used successfully in patients with unstable angina or acute thrombotic stroke*."

[70] The words "*acute thrombotic stroke*" are relevant to the Claimant's case. Weitz et al then summarised the use of Heparin against thromboembolism in various surgical

procedures. Firstly general surgery, in which they stated that low dose unfractionated Heparin given two hours before surgery and every eight to 12 hours post operatively provides safe and effective prophylaxis for patients undergoing general surgery reducing the risk of venous thromboembolism and fatal pulmonary embolism by 70% and 50% respectively. Secondly they summarised the same effect in orthopaedic surgery of the lower limb and gave the percentage reduction in the risk of thromboembolism in total hip replacement as a result of Heparin at between 31% and 79%. They summarised that in patients with stroke there is an overall incidence of deep vein thrombosis of 42% in the paretic or paralysed leg and low molecular weight Heparin was able to reduce the incidence of venous thrombosis. But for patients over 65 low molecular weight Heparin reduced the rate of thrombosis detected by fibrinogenic leg scanning from 9.1% to 3%, this study having a certainty ratio of P = 0.03. In relation to ischaemic stroke they summarised a study of 312 patients with acute ishaemic stroke, half of whom were given low molecular weight Heparin and the other half of whom were not. The Heparin was given for only 10 days and six months of follow up then took place. Those given Heparin suffered less adverse outcomes at between 45 and 52% of the cohort, whereas those not given Heparin suffered more adverse outcomes in 65% of the cohort.

[71] Weitz et al also advised that low molecular weight Heparin prevented thrombus growth and produced a reduction in thrombus size in 64% of patients treated.

[72] It is clear from a close analysis of this paper that it does expressly not say what Dr. Michael asserted in the joint medical report with Dr. Giallombardo. It does of course deal with Heparin and shows the widespread use thereof to prevent thrombus peri-operatively. I regret to say that Dr. Michael admitted that he had misquoted this paper in the joint report. He said he was summarising a different paper which he could not recall the name of and which he had not brought to Court or produced to Dr. Giallombardo when the joint report was produced.

Expert Haematology evidence

[73] **Professor Mehta** reported for the Claimant. He has an impressive CV. His specialities are clinical and laboratory haematology. He is a consultant physician and haematologist and worked at the Royal Free Hospital between 1986 and 2019. He is now retired from the NHS but continues in private practice in London in haematology and coagulation. He has published more than 350 peer reviewed articles in research journals and written 40 chapters in five books. Those include standard undergraduate and postgraduate textbooks in haematology. He has particular specialisation in lysosomal storage diseases. In his report, which was admirably concise, he asked the simple question "*Would Heparin have prevented the stroke?*"

[74] In his opinion aft ether negligence the Claimant suffered left middle cerebral artery infarction. The Claimant was at high risk of that due to atrial fibrillation and having a CHA2D-V AS2C score over 2. He considered that once a diagnosis of acute thromboembolism had been made by the Defendant at A&E the correct treatment should have been to start anti-coagulation with low molecular weight Heparin and Warfarin therapy should have been simultaneously started. Alternatively the Heparin could have been continued for five days and then treatment with a new oral anti-coagulant started as the Heparin was discontinued. He advised in relation to the Claimant that:

"*These are serious events with high morbidity and mortality and treatment is mandatory.*"

[75] He relied on the NICE Guidance on the management of atrial fibrillation dated August 2014 which at paragraph 1.7.7 advised that in people with new onset atrial fibrillation, who are receiving no or subtherapeutic anti-coagulation, in the absence of contraindications, Heparin should be offered at initial presentation and continued until a full assessment has been made and appropriate anti-thrombotic therapy has been started, based on risk stratification.

[76] He advised in his report that the Guidance made it clear (by inference) that subjects who were not on anti-coagulation therapy but had AF, especially if they had suffered an embolism, should be anticoagulated without delay. He advised that the Claimant should have been given a clear explanation that she had likely suffered an embolism as a consequence of her atrial fibrillation and "… *that she was at extremely high risk of a further embolism, and that immediate anti-coagulation was therefore advised.*" He went on to advise that:

"*Heparin has a rapid onset of action and is fully active within an hour or so of commencement. Its major action is to prevent further blood clot formation, and this gives the body's own mechanisms time to breakdown existing blood clot.*"

[77] He also relied on the Heparin licence dated 2016 which states that the therapeutic indications for Heparin are prophylaxis of deep vein thrombosis and pulmonary embolism, treatment of deep vein thrombosis and pulmonary embolism and acute peripheral arterial occlusion. I note of course that the Claimant had suffered acute peripheral arterial occlusion on 24 September 2015. As to the pharmacodynamic properties of Heparin the licence states:

"*Heparin prevents the coagulations of blood in vivo and in vitro. It potentiates the inhibition of several activated coagulation factors, including thrombin and factor X.*"

[78] He advised that institution of Heparin therapy on 25 September would have prevented clot formation such that on balance of probability the stroke that occurred on 27 September would have been avoided. He went on to advise in paragraph 9 of his report as follows:

"*Anti-coagulation with Heparin instituted on 25 September would have prevented further clot propagation in the left atrium allowing the body's thrombolytic mechanisms to lyse the clot and prevent the embolisation which caused the stroke on 27 September.*

"*The key issue is whether Heparin would have prevented the stroke and since it would have been started while the clot was still in the left atrium, 67 hours before the stroke and over 70 hours before the thrombolysis on balance of probability it would have prevented the stroke.*"

[79] **Dr. Raj Patel,** a consultant haematologist practising at Kings College hospital thrombosis centre in South London reported in February 2021 for the Defendant. He has worked in haematology since 1997 and currently works in an NHS national Exemplar Centre for thrombosis. He runs a large local anti-coagulation service and organises regular network anti-coagulation training courses for primary care. He has carried out research and published original papers on venous thromboembolism, modern anti-coagulation drugs, computational analysis of anti-coagulation use in atrial fibrillation, thrombosis management and many other topics.

[80] He advised the Court that atrial fibrillation is the most common abnormality of heart rhythm in the population affecting 1 to 2% generally and 25% by the age of 55. Stroke is the leading consequence of atrial fibrillation affecting 5% per annum without therapy. Individual risk of course varies but the factors affecting individual risk are: prior stroke, TIA, increased age, hypertension, diabetes, heart failure and gender. The risk can rise to 18% per annum. He advised that oral anti-coagulation with either Warfarin or the newer pills has been shown in large studies to reduce the risk of stroke by approximately 66% whereas Aspirin only reduces the risk of stroke by around 19%.

[81] He advised that about 2/3rds of strokes in atrial fibrillation patients are thought to be cardioembolic with the thrombus generally occurring in the left atrium and embolising from there. He accepted, based on a paper by Evans et al from 2001, that the risk of cardioembolic stroke is significantly reduced by Warfarin. He advised that the mechanism of Warfarin is to allow the thrombus to become "*organised and adherent*" or to "*resolve*". Those were his words. He advised that this probably occurs in the majority of patients after three to four weeks of stable anti-coagulation therapy and based that on a paper by Collins et al published in 1995.

[82] Dr. Patel produced and relied on a substantial number of published papers relating to the use of Heparin as a bridging therapy for patients who need elective surgery. He advised that Warfarin is highly effective in reducing the tendency of the blood to clot and is used to treat deep vein thrombosis and pulmonary embolism, to prevent strokes in atrial fibrillation cases and in patients with mechanical heart valves. However Warfarin has a slow onset and a slow offset, whereas Heparin has a fast onset and fast offset and therefore Heparin is used as a short term therapy to bridge between ceasing Warfarin before an operation and restarting Warfarin after an operation. Warfarin is usually stopped five days before an operation because of the risk of bleeding intra operatively. What he did not say was that Heparin is used to treat new onset atrial fibrillation and was mandated for this Claimant with her new atrial blot clot which had embolised. I shall return to this below.

[83] Dr. Patel advised that there is little evidence from published papers that Heparin is effective in the prevention of arterial thromboembolism in patients with mechanical heart valves or atrial fibrillation. He relied on a paper summarising figures from The United States Registry of Outpatients. He summarised that as stating that there was a two fold increase in cardiovascular events, heart attack, stroke, embolism and death at 30 days after operations where Heparin had been used as a bridging anti-coagulant. He relied on a paper by Siegal et al published in 2012 which was a meta-analysis of bridging studies which showed that using Heparin to bridge between the stopping and

starting of Warfarin before and after an operation led to a fivefold increase in bleeding but produced "*no difference*" in the incidence of arterial or venous thrombo embolisms.

[84] He also relied on a paper published in 2015 in the New England Journal of medicine (again with no author names given in the report) which he stated showed that Heparin did not reduce the thromboembolic risk when used as a bridge perioperatively but did increase the risk of bleeding.

[85] Therefore Dr. Patel used these bridging studies in his report to advise that Heparin does not decrease the thromboembolic risk generally. He also relied on the Guidance issued in 2016 by the BCSH which recommended that no Heparin should be used in bridging where the patient has atrial fibrillation unless the CHADS 2 score is above 4.

[86] On causation Dr. Patel advised the Court in his report that the Claimant's stroke was probably caused by embolism of the thrombus in the left atrium due to atrial fibrillation. He advised that long term anti-coagulation would have reduced the risk of stroke by around 66%. Once the anti-coagulation is started he advised that:

> "*There is some evidence for a reduction of the risk beginning three to four weeks after therapeutic levels have been achieved.*"

[87] I shall return to this assertion below. The words "*some evidence*" are not in my judgment a fair or accurate representation of the evidence before this Court and in particular the paper by Collins et al.

[88] He said therapeutic levels are generally achieved on Warfarin within one to two weeks. He advised that the reduction in risk occurred probably because it takes three to four weeks for the body to lyse (dissolve) the existing clots and based that advice on the Collins et al paper published in 1995 a copy of which he produced (missing a vital part, a matter to which I shall return below). He also relied on a paper published in 2013 by Guyatt et al which he stated showed that the reduction in stroke risk did not occur until 30 days after the Warfarin was started. Therefore, overall he advised that if anti-coagulation with Heparin had started on 24 September it would not, on the balance of probabilities, have prevented the stroke or materially reduced the risk of stroke for the Claimant.

[89] In their joint report, which was required to set out areas of agreement and of disagreement, the haematologists stuck to their original opinions. They agreed that:

(1) The Claimant suffered acute intermittent right limb ischemia on 24 September 2015 caused by arterial occlusion due to an embolism which had originated in her left atrium. The mother clot (my words) was likely to have been in the left atrial appendage. That on 25 September 2015 the Claimant was at risk of suffering further emboli causing either stroke or peripheral arterial ischaemia.

(2) Professor Mehta described how the Claimant was suffering an emergency in medical terms with potentially life threatening consequences which required urgent action.

(3) They agreed that the stroke on 27 September was caused by a blockage of a cerebral artery which was due to embolic fragments being thrown off from the same cardiac source as the embolus which had caused the limb ischaemia earlier.

(4) In the paragraph in relation to the key question of causation Professor Mehta stated that the Claimant had an unstable blood clot in the left atrium. He advised that it was difficult to do any clinical trials relating to acute emergency situations because they were impossible to conduct. However the lack of papers on the direct short term effects of Heparin in such acute situations did not mean that Heparin lacked effect in such situations. He pointed out that Heparin is still recommended for high risk patients who require bridging in the peri-operative period. He distinguished the other bridging papers as relating to patients with a lower risk of embolisation because their clots in their Atria were abolished, prevented or already dissolved by the preoperative anti-coagulant therapy that they had been given before the elective surgery was started. Therefore Professor Mehta did not consider those bridging studies to be of any relevance to the Claimant's case. He relied on:

- the fact that Heparin is recommended for the treatment of acute presentation with a systemic embolic event relying on a paper by Bekwelem et al published in 2015.
- The fact that Heparin is the recommended treatment for acute new onset atrial fibrillation by NICE.
- The fact that Heparin is recommended treatment for acute onset atrial fibrillation by the American Heart Association and the American Academy of family physicians.
- The fact that Heparin is recommended by the American College of Chest Physicians in their evidence based clinical practice guidelines for situations where there is acute onset atrial fibrillation or acute thrombosis, relying on the paper published in 2012 by Guyatt et al.
- He also relied on the American College's recommendation of the use of Heparin in DVT and pulmonary embolism cases for the prevention of venous thrombo embolism in non-surgical patients; for patients who require bridging anti-coagulation in the peri operative period; for patients with atrial fibrillation undergoing cardioversion, especially if urgent, and in patients who are hemodynamically unstable, and for patients with acute limb ischemia due to arterial emboli or thrombosis.

(5) Professor Mehta asserted in the joint report that in all of the above situations there are supportive clinical, pharmacological and trial data. Finally, he asserted that it was his experience as a haematologist that Heparin is an effective anti-coagulant in the emergency setting which the Claimant was presented with on 24 September. He advised it was not appropriate to compare: (1) the study reports of outcomes from the peri-operative anti-coagulation, or bridging of chronic atrial fibrillation patients, with (2) the emergency scenario presented to the Claimant.

(6) Professor Mehta advised that Heparin commences its action within minutes of its administration and that within 24 to 36 hours Heparin has been shown to reduce the risk of pulmonary embolism in subjects with DVT. He asserted that the Claimant presented with an analogous situation. He advised that Heparin reduces blood clot formation and allows time for the body's own natural processes to dissolve the clot. He relied on the guidelines published by Baglin et al in 2006 from the British Society for Haematology in support of the effectiveness of Heparin in the prevention and treatment of venous and arterial thromboembolism.

[90] Both Professor Mehta and Dr. Patel agreed that after three to four weeks of therapeutic oral anti-coagulation the Claimant's risk of stroke would have been reduced by around 66%.

[91] In contrast Dr. Patel, in the joint report, stated that the evidence for the effectiveness of Heparin is "*lacking*". He summarised his reliance on the Heparin bridging reports stating that Heparin "*does not prevent stroke*". Whilst accepting that the bridging studies had relatively few "*high risk*" patients, he pointed out that one of the studies had 40% of the patients with a CHADS score of at least 3 and that 20% had mechanical heart valves. He asserted that Heparin had "*no effect in reducing stroke*" even in the higher risk atrial fibrillation and mechanical valve groups. He accepted that Heparin is commonly used in a variety of emergency situations for acute arterial and venous diseases but argued that it does not follow that the effectiveness of Heparin is equal in all these conditions. He was not prepared to extrapolate from one condition to another without clear research evidence. He fully accepted the effectiveness of Heparin was better than 90% for preventing emboli from deep vein thrombosis and pulmonary embolism, which he called "*venous thrombosis*", however he repeated that Heparin had a failure rate in cases involving mechanical heart valves in that it did not prevent stroke when Warfarin is stopped and likewise for atrial fibrillation cases when Heparin is used to bridge for elective surgery. So Dr. Patel advised that it was wrong to extrapolate Heparin's success in dealing with venous thrombosis to its ability to deal with left atrium thrombosis. He stated that the type of thrombus in the left atrium that the Claimant had suffered would not have been fundamentally different in her acute setting compared to the chronic peri-operative setting where thrombus forms in the left atrium and then embolises to the brain. Overall his opinion was:

> "*In my opinion Heparin would have been ineffective in preventing the Claimant's stroke, similar to the lack of effectiveness demonstrated in high risk AF patients in the two high quality phase three AF trials (where the mechanism of stroke and nature of embolising atrial thrombus would have been identical).*"

[92] When I go through the papers on bridging it will become apparent that I do not accept Dr. Patel's assertions that those situations are identical to the Claimant's situation or that the papers show Heparin has no effect in reducing stroke.

[93] He explained that with anti-coagulation the body's natural thrombolysis system results in "*clot organisation and resolution*" (his words) over time but advised that it takes three to four weeks for thrombi in the atrium to organise or resolve during the anti-coagulation treatment. Once again he relied on the paper published by Collins et al in

1995 for that opinion. He advised that during the initial three to four weeks the stroke potential still exists, despite anti-coagulation, probably because the pre-existing, fresh left atrial thrombus has not yet "*organised or resolved*". Stopping there it was clear to me that Dr. Patel was advising the Court that despite atrial clots reducing in size and resolving over 3-4 weeks of anti-coagulation, they do not become "*organised*" over that period so that their potential to fire off emboli remains the same as they decrease in size. I struggled to understand the logic of that in the face of his own evidence that with anti-coagulation the body's natural thrombolysis system results in "*clot organisation and resolution*" (his words) over time.

Anatomy

[94] The heart has four chambers. The left atrium receives oxygenated blood from the lungs and pumps it through a valve into the left ventricle which is bigger. Then the valve closes and the left ventricle pumps the blood through the arteries around the body. There is a large arched artery (the aorta) coming out of the left ventricle which has various branches, which go to the brain and others going to the whole body. Once the blood has fed the body it returns through the venous system to the right atrium which pumps it into the right ventricle. The right ventricle then pumps the blood to the lungs and it returns to the left atrium with oxygen.

[95] The left atrium has an appendage (or auricle). It is the shape of an oval sac. It is a bit of a backwater and the experts agree that most atrial clots form there in patients with AF.

The medical literature

[96] Because both experts relied on medical literature I must now descend into the papers and consider what they do to assist the Court on the issue which is to be determined. I will do so chronologically and I do so reminding myself that the issue is whether Heparin given properly over 67 hours would have prevented the embolus breaking off from the mother clot in the Claimant's LAA and causing the stroke. The experts agree that, on the balance of probabilities, this is what occurred on 27 September 2015 to the Claimant.

[97] Collins et al 1995 reported on TEE scans of the hearts of patients with AF (nonrheumatic) and with blood clots therein, who were treated with Warfarin for weeks after the scans with a view to making them safer for a cardioversion operations to resolve their irregular heart rhythms. Collins et al reported that previously it had been thought that Warfarin helped to "*organise*" clots and to help them adhere it to the walls of the Atrium, but their scans had shown that the clots resolved (dissolved) over a median time of four weeks. Of the 14 patients in the study (some had more than 1 clot): 14 had a clot in the LAA, 2 had a clot in the LA and 1 had a clot in the right atrium. The clot sizes ranged from a half centimetre to 2 centimetres. The patients were about half women and half men. They were all older than 53 and all had had AF for between 1 and 14 weeks. I note with interest that none suffered an embolic event during the study. This is relevant to the issue I have to decide. All were scanned at the start to show the size of their clots and then once or more thereafter. Most of the clots resolved in four weeks, two took 12-14 weeks, 1 took only three weeks. Of the clots which resolved in four weeks the sizes varied enormously: 1.5 cm; 0.8 cm, 1.3 cm, 2 cm, 1 cm, 1.5 cm, 1.5 cm. Of the clots which took 12-14 weeks to dissolve the sizes were: 0.8 cm and 1 cm. Most of the atrial clots were adherent (12) and some were mobile (6).

[98] A detailed chart was provided by Collins et al which Dr. Patel, who produced and relied on the paper, had not provided to the Defendant or Professor Mehta or the Court, was not in the trial bundle and was not referred to in his written evidence. I asked for it to be found during the evidence. Inter alia it showed 4 scans of the clot in patient five's LA as it dissolved by between 50% and 75% in the first week (on rough visual representation) and dissolved further by week 3 (by roughly 90%) and then disappeared by week 5.5.

[99] Dr. Patel relied on this paper to advise the Court that the Claimant's clot would not have been dissolved in 67 hours. He also interpreted it to advise that the risk of emboli being fired off from the mother clot stayed wholly unaffected throughout the existence of the mother clot whatever its size throughout the 3-4 week period. His first point it seems to me is correct. His second is not logical. No embolic events were recorded during the study so it does not show what Dr. Patel asserts it shows on whether Warfarin treatment reduces the risk of embolisation from the mother clot as it gets dissolved by the body's dissolving function. Quite the opposite.

[100] King et al 2002. This group reported in a journal for US family physicians that Heparin is recommended for initial anti-coagulation for AF which has endured for over 48 hours and it reduces the risk of thrombosis formation *and embolisation* until Warfarin INR is achieved. They cross referred to a paper by Falk et al published in 2001.

[101] The Defendant criticised Professor Mehta for producing and relying on this paper alleging that because it is for family physicians it has little weight and further criticising Professor Mehta for accepting the statement in the paper that the recommendations made therein were consistent with the guidelines of the American Heart Association and others. I shall return to this below.

[102] Konstantinides et al 2002. Professor Mehta relied on this paper to make the assertion in his live evidence that the Heparin would have dissolved and organised/stabilised the Claimant's LAA clot and, as it did so, would have reduced the risk of embolisation during the 67 hours gap such that the Claimant would not have suffered the stroke on the balance of probabilities. Konstantinides et al studied 256 patients who were haemodynamically stable but had pulmonary embolisms. 118 were given Heparin and Alteplase (a clot buster) and those were compared with 138 patients just given Heparin. The main conclusion was that the combined treatment was more effective than Heparin alone. However the results also disclosed the early effects of Heparin on adverse events. The table at Figure 1 in the paper shows that for those just on Heparin acute adverse events occurred in the first day to around 8% of the total number of patients, and in the second day to another 10% of the patients, but by the third day adverse events reduced to only 3% of the patients. From day 4 onwards there were hardly any adverse events at all so that the remaining 75% of patients were well protected going forwards. Professor Mehta extrapolated these results, which related to the body dissolving and organising the blood clots causing DVT and PE, to how the body would dissolve and stabilise the Claimant's LAA thrombus. He explained that the Claimant's thrombus was recent in genesis, was unstable, having already fired off one embolus and was amenable to Heparin treatment. He gave evidence as to the consistency of the clot being more jelly like and less organised than clots which had been in the system for

longer time periods. He compared the pressure in the pulmonary system with that in the LA and asserted it was similar. He specifically advised that:

"*As the clot gets smaller less adverse events and embolisations occur.*"

[103] Dr. Patel advised that this study could not be extrapolated to LAA clots because the results for Heparin/Warfarin on arterial clots in bridging studies were different from the results in venous clots, so the paper could not assist at all. However, he gave evidence in chief that Heparin does prevent venous clots from growing or propagating and that after 24-48 hours of Heparin treatment the risk of embolisation is much reduced and the patient is safer. He advised that due to the effects of Heparin/Warfarin on the venous blood stream the clot becomes organised and sticks to the venous wall. The blood lyses the fibrin strands and dissolves them slowly. As the clot becomes organised and sticks to the wall the embolic ability reduces. But he asserted that arterial clots are "*completely different*". He asserted that anti-coagulants "*do not affect the clots*" in arteries, they only prevent recurrence of clots. He advised that the body takes longer to get rid of the arterial clots: 3-4 weeks, as opposed to reaching safety in 48 hours in venous clots. He explained that Heparin worked against factors 10 (x) and 2 and others in the clotting cascade and Warfarin worked also against factor 10.

[104] Two papers in 2006 were relied upon by Professor Mehta. The NICE Guidelines: in these guidance is given for the treatment of permanent atrial fibrillation by the administration of Warfarin at an INR of 2.5. In addition the recommendation for acute atrial fibrillation was to provide anti-thrombotics, and if the patients were not receiving anti-coagulants at the time of the emergence of acute atrial fibrillation then the recommendation was to start the patients on Heparin and then risk assess for anti-coagulants.

[105] In the 2006 Guidelines for the British Society for Haematology, Baglin et al set out some interesting information that Heparin is obtained from porcine mucosa. The recommendation for the treatment of venous thromboembolism and pulmonary embolism was to use Heparin, which had been shown to reduce the risk of fatal recurrence and non-fatal recurrence of embolism. This was a Grade A recommendation.

[106] In contrast, in relation to arterial thromboembolism the Society pointed out that in acute limb ischemia there was "*no evidence to date of a definitive beneficial effect from Heparin*". However, it went on to say that Heparin is frequently given and so the recommendation was that when given it should be at a therapeutic dose. Dr. Patel relied on this paper to support what he had been advising; that there was no definitive evidence of any beneficial effect of Heparin in arterial thrombo embolism cases. It seems to me that the lack of definitive evidence is explained by the impossibility of doing gold standard, randomised, peer reviewed research on acute patients at high risk of death due to AF and atrial clots which have fired off emboli being mandated for Heparin treatment immediately. To fail to provide such is negligent. So no "*placebo*" group could be used for the trials.

[107] In 2012 Guyatt et al published a paper in the journal called "*Chest*". This contained the American College of Chest Physicians' Guidelines on anti-thrombotic therapy and the prevention of thrombosis. Advice was given on therapeutic levels for unfractionated

Heparin together with other anti-coagulants. Advice was given to prevent venous thromboembolism in non-surgical patients by the use of low molecular weight Heparin. In relation to patients with atrial fibrillation managed by some rhythm control strategy who were to undergo elective cardioversion the Society recommended at least three weeks of Heparin or other anti-coagulation treatment before the operation and the same for at least four weeks after the operation. In addition for patients with atrial fibrillation of 48 hours or less undergoing cardioversion Heparin was recommended. The grade of that recommendation was only 2C compared to the grading of the recommendation for elective cardioversion being 1B.

[108] Professor Mehta relied on this guidance to show that Heparin is effective. Although it must be said that the paper did not directly address the issue of whether Heparin is effective in the first few days of the recommended periods.

[109] In 2012 Siegel et al published an article in the journal called "*Circulation*". This was one of the bridging articles relied upon by Dr. Patel. The study related to US Medline, EMBASE and Cochrane database patients who had received Heparin bridging during interruptions of vitamin K anti-coagulant antagonists (Warfarin and more modern pills) because they were undergoing elective surgical procedures. This meta-analysis of 34 studies reached the conclusion that patients who received Heparin bridging had an increased risk of major bleeding events in the peri operative period, but these patients faced a similar risk of thromboembolic events compared with patients who received no Heparin bridging. The total results were: 73 out of 7118 bridged patients (0.9%) had thromboembolitic events and 32 out of 5160 non-bridged patients (0.6%) had such events. However the results paper by paper were varied because the confidence intervals were as follows: bridged (0-3.4); not bridged (0-1.2). However, Seigel et al were clearly slightly uncomfortable with their own conclusion because they stated:

> "*It is possible that with a majority of bridged patients considered high risk for thromboembolic events (57% in 19 studies) such high thromboembolic risk patients may have preferentially received bridging therapy whereas low thromboembolic risk patients did not. Thus bridging may have reduced a very high thromboembolic rate in the high risk, bridged group to that of the lower thromboembolic risk, non-bridged patients.*"

[110] Dr. Patel relied upon this study to show it supported his assertion that the bridging studies did not prove that Heparin had any worthwhile short term anti-embolic force.

[111] Professor Mehta asserted that this study had no relevance. He pointed out the patients were not randomised therefore higher risk patients would have been given Heparin. He relied on the caveat paragraph set out above to show that Heparin may well have been reducing the thromboembolic risks suffered by high risk patients and that the Claimant fell into a high risk category because she had already suffered one embolus from the mother clot which must therefore have been friable. In addition those entering the operations in the study would have been anticoagulated for 3-4 weeks before their operations so they would probably not have had friable or unstable LAA clots. Professor Mehta's final blow to the relevance of these studies was that all the patients would have been excluded had they suffered an embolus in the weeks before the operation, like the Claimant had suffered on 24 September 2015.

[112] In 2013 Azoulay et al published a paper in the European Heart Journal upon which Dr. Patel initially relied. The study was of the effects of transferring from NOACs to Warfarin on AF patients in the first 30 days of Warfarin treatment. No Heparin was involved. 70,766 patients on a UK clinical practice database were studied. Patients with MHVs were excluded. The mean age was 74. In one group patients were transferred from a new anti-coagulant: Rivaroxaban, to Warfarin. In another from Apixaban to Warfarin. In both studies there was an increased level of stroke during the first 30 days after the transfer so the conclusion drawn was that there was an increased risk of stroke in the first 30 days on transfer to Warfarin but also that there was a reduced risk after 30 days. The discussion postulated a hypercoagulation state during the initial transfer to Warfarin treatment. They advised that although Warfarin blocks activation of clotting factors 2, 7, 9 and 10 it also blocks two proteins which are anti-coagulants (C and S). Azoulay et al postulated that Heparin bridging between the change might have assisted. This paper examines the effects of transferring from one medication to another. It is not directly to point on the issue I have to decide.

[113] Dr. Patel could not explain how this paper which he relied upon could sit alongside the Collins et al paper he relied upon which showed that Warfarin treatment enabled the body to dissolve LAA clots over the first 3-4 weeks after treatment started. It cannot, on the balance of probabilities, be right that Warfarin (in cases not involving a treatment transfer) increases the risk of thromboembolism until day 30 and at the same time enables the body to dissolve the clots by day 28 as a median and that it prevents new clot formation.

[114] Dr. Patel did try to explain this conflict in his produced papers by asserting that more careful modern titration of Warfarin had abolished this "*so called*" increased risk period. In evidence he shied away from relying on the Azoulay et al paper. In any event Professor Mehta pointed out that Warfarin is different to Heparin. It acts differently to achieve the same results. It does not act on Vitamin K or proteins C and S. It has a powerful effect on factor 10 in the clotting cascade and a range of actions on platelets and thrombin. I do not find that the Azoulay et al paper assists me in determining the issue at all.

[115] In 2014 NICE updated its Guidance on the management of AF. The 2006 recommendations to treat with Heparin were maintained for acute new onset AF.

[116] In 2014 Violi et al published a paper in the Journal of Atrial Fibrillation. They advised that atrial fibrillation fulfils the criteria of Wirchow's triad, which are necessary for thrombus formation: blood stasis, endothelial dysfunction and clotting activation. Blood stasis is most evident in the left atrium of AF patients where flow velocity is markedly reduced, concomitantly with impaired contractility of left atrial appendage. They stated that:

> "*Management of AF have (sic) been addressed essentially in lowering thrombo-embolic stroke by anticoagulants and/or by antiplatelet drugs.*"

[117] They concluded that NOACs are likely to be a step forward for the treatment of AF. This paper does not take the issues I have to decide much further.

[118] In March 2015 Douketis et al published a short paper in "*Cardiology*" referring to papers published by himself in 2012 and by Siegel et al (above) and Steinberg et al and others. He summarised the evidential issues relating to bridging anti-coagulation with Heparin for patients with atrial fibrillation who needed elective surgery. He postulated that one unifying explanation may be that bridging anti-coagulation does not mitigate the risk of peri operative stroke or other thromboembolic outcomes because the pathophysiological mechanism for these events might be intra operative hemodynamic changes or hypercoagulability effects which are not affected by the use of bridging anti-coagulation before and after the operation. I find this logic to be persuasive. Dr. Patel accepted in his evidence that Douketis is a leader in this field and has an impressive reputation and knowledge of bridging and bridging studies. Despite this Dr. Patel would not be swayed by Douketis' reasoning from his firm position that Heparin does not reduce the thromboembolic risk in AF patients with LAA clots. I find Dr. Patel's approach here to be overly rigid and less than impressive.

[119] The logic of Douketis et al in this paper is apparent. If a patient with atrial fibrillation is treated in accordance with the guidelines the patient will have anti-coagulation for three to four weeks before the elective surgery. That will be stopped about five days before the surgery. The operation will take place and then the anti-coagulation treatment will be started a number of days after the operation. Without bridging there is an 8 to 10 day gap involving surgery. Surgery inevitably creates bleeding and blood clots and other vascular events. Whether the first bridging with Heparin between the stopping of the Warfarin (day 5 before the operation) and (day 1 before the operation) and then the second bridging after the operation (on day 1 after) up to the starting of Warfarin or therapeutic Warfarin would actually be addressing the sources of the blood clot, is inherently open to uncertainty. Particularly if the operation itself is the source of the blood clots. In addition and I consider importantly, these patients will have been provided with anti-coagulant treatment for 3-4 weeks before the operation, which should have resolved most of the LA clots they might have had and prevented new ones.

[120] In August 2015 Douketis et al published another paper in the New England Journal of Medicine. This again concerned peri operative bridging anti-coagulation in patients with atrial fibrillation. A total of 1884 patients were enrolled. 950 received no bridging therapy and 934 received bridging therapy with Heparin. All had been on Warfarin before which was stopped 5 days before the operation. Heparin was administered to the bridge group 3 days before the operation and stopped 24 hours before and restarted after for 5-10 days as the Warfarin was increased to therapeutic levels. The follow up end point was 30 days. The incidence of arterial thromboembolism was 0.4% in the non-bridged group and 0.3% in the bridged group. The risk difference was 0.1 (or 25% less in the Heparin group than the non-Heparin group). The P value was 0.01 showing the results to be significant. In straight forward terms Heparin had reduced the incidents of arterial thrombotic embolus by one quarter. However the incidence of bleeding in those who had taken Heparin was nearly three times as high and so the conclusion was that forgoing bridging would be sensible. Both Professor Mehta and Dr. Patel carried out fairly detailed analyses of the eligibility of patients for this study. Patients were not eligible if they had one or more of the following: a mechanical heart valve stroke, SEE or TIA within the previous 12 weeks; a low platelet count; planned cardiac or spinal surgery. In an appendix the nature of the operations that were to be carried out was

explained. 1539 were regarded as minor and involved orthopaedic, cardiothoracic, gastrointestinal, dental general, gynaecological, ENT or vascular surgery. 183 were regarded as major and included orthopaedic, cardiothoracic, gastrointestinal, general, gynaecological and vascular. Another conclusion was that overall the rate of arterial thromboembolism was lower than the expected 1%.

[121] Dr. Patel relied upon this bridging study to support his argument that Heparin does not temporarily reduce the risk of embolism. Professor Mehta responded by relying on the 25% decrease in arterial thromboembolism in the group that was given Heparin before and after the operation. It seems to me that this paper was more properly analysed by Professor Mehta because the figures were 25% lower for those who were given short term Heparin. The Professor also made it clear that this study was not looking at the effects of Heparin generally but instead only when used in two separate short blocks either side of an operation. The Professor gave evidence that the Claimant is in a completely different category to those in these studies. Those in the studies would have had three to four weeks of anti-coagulation before the operation resolving most of the patients' atrial clots. The Professor pointed out that the Claimant would have been excluded from the study as a result of her recent leg thrombus. I accept those views from Professor Mehta.

[122] In 2015 Steinberg et al published a paper in *Circulation*. This was also on bridging patients who had atrial fibrillation and needed operations. His conclusion was that bridging was associated with a higher risk of bleeding so that his data did not support the use of routine bridging. In discussion he stated that bridging for low risk of thromboembolism patients should be avoided but that it should be considered for moderate to high risk patients.

[123] In 2015 Bekwelem et al published a paper in *Circulation*. It concerned extracranial systemic embolic events (SEEs) in patients with non-valvular atrial fibrillation. The investigation was to determine how many SEEs occurred in comparison to strokes as a result of blood clots caused by atrial fibrillation. The conclusion was that SEEs constituted 11.5% of clinically recognised thromboembolic events in patients with atrial fibrillation.

[124] This paper does not take the evidence any further in relation to the issue I have to decide.

[125] In 2016 the European Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology issued their guidelines. Kirchof et al advised at paragraph 9.4 that:

> "*The highest risk of recurrent stroke is in the early phase after a first stroke or TIA.*"

Two references were given for that assertion, one by Grau et al in 2001, and the other by Giles et al in 2007. This may be an important point because it directly relates to the Claimant's case. In relation to starting anti-coagulation after a TIA or ischaemic stroke the authors stated that data on the optimal use of anti-coagulants including Heparin, Warfarin and NOACs, in the first days after a stroke are scarce. Having considered and discussed using anti-coagulants directly after a serious stroke, which involved a

significant risk of additional bleeding in the brain at the site of the stroke, they went on to say:

> " *… whereas patients with a TIA or small stroke may benefit from early (immediate) initiation or continuation of the coagulation. Therefore we propose to initiate anti-coagulation in AF patients between one and 12 days after ischaemic stroke, depending on stroke severity.*"

[126] The conclusions in this paper seems to me to be only peripherally relevant to the issue before me because once a stroke has occurred in the brain, bleeding around the site of the brain tissues affected by the ischaemia becomes a real risk and anti-coagulants may increase that risk. I do not know if it is possible to equate the Claimant's position, she had a blood clot in her left atrial appendage, which had already fired off an embolus which stuck in her leg, to a patient with atrial fibrillation who has suffered a TIA or minor stroke. In the latter case the advice was for "*immediate*" coagulation within one to 12 days after ischaemic stroke.

[127] In 2021 Kovacs et al published a paper in the British Medical Journal. They considered Heparin bridging for patients at high risk of arterial thromboembolism. They did a double blind, randomised, controlled trial. The results came from Canada and India. 1471 patients were examined and they all had atrial fibrillation or mechanical heart valves and required temporary interruption of Warfarin for a surgical procedure. The conclusion was that no significant benefit was found for post-operative bridging with low molecular weight Heparin. The initial paper set out the thromboembolism rates at 90 days post operation. In the non-bridged group were higher at 1.2% than for the bridged group (who were given Heparin) in which the rate was lower at 1%. Another finding was that the major bleeding rates were not significantly different between the groups. Patients were excluded if they had a low platelet count, were undergoing spinal or neurosurgery, they had multiple mechanical heart valves or had a mechanical valve with a history of stroke or TIA. The results were published for the period of 90 days after the operations. At the request of a peer reviewer a second analysis was performed for the results at 30 days after the operation and set out in Table 4. At 30 days the data were: without Heparin bridging: 8 of 650 patients had major thromboembolism (1.2%). With Heparin bridging: 3 out of 820 patients had major thromboembolism (0.4%). The significance of that difference, between 1.2% for those who did not have Heparin and 0.4% for those that did have Heparin had a P value of 0.06 so it was just outside the range of significant results. Professor Mehta advised that the results may be significant in the early post-operative phase.

[128] It should be noted that this study did not include bridging before the operation. Furthermore, Kovacs et al expressly disavowed drawing any conclusions about patients with high risk atrial fibrillation, given that the elderly patients received direct oral anti-coagulation before the operations up until the usual stopping point.

[129] In relation to this study Dr. Patel asserted that this showed that Heparin bridging had no worthwhile effect in higher risk groups. He gave evidence that the bridging studies were entirely relevant and that they reflected what happened to the Claimant. He asserted that the risk of stroke arose when the Warfarin was stopped for the patients in the studies and they then developed clots in their left Atria when they were awaiting operations and these were not eradicated despite the Heparin given post operatively.

He asserted Heparin did not stop the clots forming or embolising. That is why, he asserted, Heparin has no effect when being used to bridge operations.

[130] Professor Mehta gave evidence that this paper adds nothing. Patients with a history of stroke and TIA were excluded. In addition the studied patients had been on Warfarin before their operations and so were unlikely to have had atrial clots before the operations. Professor Mehta stated that the Claimant was quite different. She had a friable clot which had different mechanical factors, it was dispersing actively. The patients in the studies did not or probably did not.

[131] I cannot avoid noticing that numerically the patients in the Kovacs et al studies who were given no post-operative Heparin suffered 300% more thromboemboli than those who were given Heparin. In addition I note that factually the post-operative Heparin use was only for those few days in which it takes Warfarin (or NOACS) to reach therapeutic levels.

Witness credibility

[132] Both Professor Mehta and Dr. Patel were cross examined in detail by senior and experienced counsel. Both showed stylistic differences in the way they approached the issues.

[133] Professor Mehta had a tendency under cross examination to descend into lectures.

[134] Dr. Patel had a tendency to be rigid and then to produce rather extreme opinions. So, for instance, Dr. Patel asserted in cross examination that the TEE scans which were displayed in the Collins et al paper upon which he relied, (which were only produced at my request during the hearing because they had not been produced by him either for the joint meeting or the trial bundle and were hidden behind a link in the body of the published paper) were unrepresentative because the clinician who chose them may have been t*rying to prove his point* rather than being fair by choosing the appropriate slides which accurately showed the reduction in size of the atrial clot over the course of the four separate scans carried out. This assertion was unworthy of him and when pressed upon it he pretty much withdrew it.

[135] At the root of the issue in this case is the lack of clinical trials to show whether Heparin has a front loaded or constant effect in acute cases involving atrial fibrillation with a clot in the left atrium or LAA which has already fired off an embolus. Or whether the beneficial effect only kicks in after 30 days as Dr. Patel advises. The lack of trial studies was not a surprise to either medical expert. Proposing such trials, as Professor Mehta explained, would not have been professionally allowed. If a researcher suggested carrying out a study in which half the patients in acute danger of death or serious stroke were given the recommended treatment, namely Heparin, and the other half were not, that would be a breach of the Hippocratic oath for the placebo patients. In any event no patient with capacity who was facing an acute and significant risk of death or serious stroke by thromboembolism would consent to enter such a study and accept the placebo.

[136] So at the root of the difference between the two experts was the matter of how each approached his analysis of the issue. Both accepted that Heparin prevents new clot growth and the propagation (growth) of existing clots.

[137] The Defendant questioned Professor Mehta on his cv and experience. It is clear to me that he had vast experience on thrombosis and AF, lectures and writes learned texts upon these areas and haematology and his published papers cover thrombosis. He was involved in writing the British Society of Haematologists guidelines on Warfarin. The Defendant challenged him on the proper definition of the but for test and he summarised it well.

[138] Professor Mehta advised in his evidence in chief that the Claimant faced a very substantial risk of further embolism of over "*50%*" in the very near future in the early hours of the morning of 25 September 2015. He considered the Claimant's clot to have been younger, probably more jelly like and less concentrated, less dense than long established or organised clots. He advised that Heparin given over 67 hours would on balance have prevented the embolus/emboli from breaking free from the clot in the Claimant's LAA and causing the stroke. He did so based on his vast academic and clinical experience. He also relied on the immediate use of Heparin by clinicians worldwide, over decades, to treat acute AF and the significant risk of embolic stroke arising therefrom. He relied on UK and US guidelines recommending Heparin for similar situations. He relied on the similarities between the effects of Heparin and Warfarin on human blood clots. He relied on the agreed knowledge that Heparin tips the balance in the human blood stream against clotting and in favour of clot dissolution and organisation/stabilisation/adherence. He relied on Heparin's agreed "*fast on*" effect. He relied, by extrapolation, on published data relating to the beneficial and fast effects of Heparin on pulmonary embolism and DVT blood clots in the first 48 hours after commencement. He agreed with Dr. Giallombardo that clinical experience showed that Heparin is effective in preventing early recurrence of stroke due to cardiac embolism. He relied on parts of the bridging studies which were of some relevance to the effectiveness of Heparin as set out above. Professor Mehta advised in his evidence in chief that the bridging studies did not really help to determine the issue before this court. Blood clots after surgery may be created by reasons other than Heparin not working to contain or prevent emboli breaking free from an unstable left atrial clot, for instance intra operative haemodynamic changes, IV fluids, blood transfusions, reduced or increased blood pressure, drugs and more.

[139] Dr. Patel was more troubled by the paucity of direct trial evidence on the issue. He chose to extrapolate his understanding of the data produced by bridging studies in atrial fibrillation patients who needed elective surgery. At the root of Dr. Patel's evidence was his firm assertion that Heparin does not reduce the risk of an atrial blood clot firing off an embolus during the first three or four weeks of anti-coagulation. He accepted that anti-coagulation in acute AF would usually start with Heparin by injection in the hospital and then transform a few days later into therapeutic Warfarin or new anti-coagulant drugs. Whilst he fully accepted, as he had to, as a result of the Collins et al paper, that Heparin and then therapeutic anti-coagulation tipped the balance in the blood stream so that the body's natural processes dissolved the atrial clot over that time; and he accepted that in the majority of cases the clot disappeared by week four; he was not prepared to accept that as the clot got smaller and became dissolved it was also becoming more organised or stabilised or adherent, and would not accept that it was less likely to fire off emboli. He was not prepared during his live evidence to enter into any consideration of the pathology or physiology or anatomy of the blood clot in the atrium over that three to four week period of dissolution. He eschewed answering questions put to him on friability, stability or organisation until the very end of his

evidence under cross examination when he did use the term "*friable*". Then he accepted that Heparin took 2-3 days to stop emboli being thrown off in DVT/PE cases due to "*walling off*". He accepted that Heparin prevents recurrent venous thrombosis and asserted that the body prevents clots in the leg causing further emboli. I find that it is Dr. Patel's fixed thinking and questionable logic on these matters which undermines the credibility of his evidence.

[140] I was struck by Dr Patel's reliance on the bridging papers to prove something that I consider they just do not prove. What they do prove is that bridging with Heparin increases the risk of bleeding with elective surgery. In patients who need an elective operation and who have been properly anticoagulated for 4 weeks before the operation, thereby dissolving the majority of blood clots that they might have in their left atria or elsewhere, some of the bridging studies show that Heparin does not decrease the risk of a further blood clots occurring by a significant amount. These were generally low risk patients, but not always. The studies showed that the risk of bleeding was much increased by Heparin and so advised against routine bridging due to that risk in low risk patients. Others, including the most recent one by Kovacs et al, showed that post-operative treatment with Heparin before resumption of anti-coagulation reduced the incidence of emboli by 300% at 30 days. Even Dr. Patel accepted that in patients with a high risk of embolism Heparin bridging is recommended in the guidance. Further, as said above, it is clear that anti-coagulant therapy starting with Heparin and moving onto Warfarin or a newer anti-coagulant is highly effective in reducing the risk of further emboli in patients who have already suffered a blood clot causing deep vein thrombosis and pulmonary embolus. Dr. Patel accepted that the effectiveness of Heparin for DVT and PE was better than 90% and that such effect is shown in the first 24 to 48 hours. Dr. Patel simply refused in his live evidence to descend into the detail as to why and how Heparin's great success in abolishing the risk of emboli from blood clots in DVT and PE should be occurring so quickly and why it is irrelevant to atrial clots. This was odd considering that he had used the word "*organised*" to describe the effect of anti-coagulation on clots in the joint report.

[141] It seems to me that there are likely to have been three processes going on for Heparin to be so quickly effective on DVT and PE clots (blood clots in a vein or in the lung). The first is that the Heparin prevents new clots forming and prevents the mother clot growing more (propagating). The second is that the Heparin very quickly allows the body's natural process to start dissolving the blood clots. The third is that the body's natural defences organise and/or solidify and/or stabilise and/or "*wall off*" the blood clot. Indeed during cross examination when Dr. Patel was considering the Konstantinides et al table, he used the term "*walling off*" the clot for the effects of Heparin over the two to three days after the start of treatment and he used that in the context of Heparin preventing further embolisation of those clots. He gave evidence that Heparin prevents recurrent thrombosis and the body prevents the clot in the leg from causing further embolisation. In these circumstances he accepts that Heparin works quickly.

[142] Defence counsel criticised Professor Mehta for his evidence that Heparin treatment would not be recommended unless it was effective by more than 50% on the balance of probabilities. It was asserted that this is wrong in principle because many treatments are recommended that have limited effectiveness, for instance say only 15 to 20% in reducing adverse outcomes. This is certainly true for Aspirin in preventing clots in AF

patients. Defence counsel also criticised Professor Mehta for mis-summarising various papers to support the logic of his argument. For instance he relied on the Violi et al paper to suggest that it recommended patients suffering TIA and stroke who have AF should be treated with anti-coagulation, whereas in fact it states that patients with AF and a CHADS2 score greater than 2 should be treated with anti-coagulation. Whilst these criticisms have some factual validity I am not convinced that they really affected the main thrust of Professor Mehta's evidence or indeed his logic.

[143] In addition the Professor was criticised for relying on the NICE guidelines which the Defendant asserted only related to new onset AF and therefore did not relate to the Claimant because she had chronic AF for 18 years. Professor Mehta disagreed giving evidence that they obviously covered by analogy the Claimant who had just suffered a clot due to her AF, the failure to take her Aspirin and her heart conditions. She needed urgent Heparin as the Defendant finally admitted on day 1 of the trial. I find that the Defendant's criticism on this issue does not have merit. This Claimant's circumstances radically changed when she developed a blood clot in her left atrial appendage which embolised and occluded an artery in her leg. From then on both experts agree she was at very significant risk of a further embolus. Therefore the NICE Guidelines on new onset AF would obviously have been interpreted as requiring her to be treated with anti-coagulants even though that precise set of factual circumstances was not expressly set out. Guidelines can only be so long and cannot cover every factual circumstance in every case. I do not see anything of substance in that criticism of Professor Mehta.

[144] The Defendant criticised Professor Mehta for relying on the Heparin product licence. Professor Mehta had stated in his report that Heparin was licenced to prevent arterial thrombosis and embolisation. In fact the licence was *inter alia* to treat "*acute peripheral arterial*" occlusion. I consider that the difference complained about is peripheral and does not have substance. Acute peripheral arterial occlusion is a clot for instance in the leg which is precisely what the Claimant suffered. It came from her heart. The Guidance does not define where it came from. Arterial thrombosis and embolisation covers a clot for instance in the leg which came from an cardiac clot which gives rise to a risk of embolisation.

[145] The Defendant criticised Professor Mehta for relying on the article by King et al commenting rather scathingly in questioning that it was "*just for general practitioners*" as if GPs are some lesser sort of doctor. Again I do not see substance in that criticism because in my judgment GPs, and in the USA, family physicians, are fully qualified doctors who work hard at the frontline of dealing with chronic and acute symptoms. The advice given to them must be accurate in relation to the treatment of atrial fibrillation and acute atrial fibrillation.

[146] Taking all of the above into account and taking into account my assessment of the experts whilst they were giving evidence, and on the balance of probabilities, I consider that Professor Mehta's evidence was more logical and better reasoned than Dr. Patel's evidence. Where the evidence of the two conflict I accept Professor Mehta's evidence.

Findings of fact on the disputed issues

[147] On the balance of probabilities I find the following facts based on the evidence of the experts as analysed and summarised above and in particular of Professor Mehta.

[148] In the lead up to 24 September 2015 the Claimant developed an unstable blood clot in her left atrial appendage as a result of her longstanding atrial fibrillation and as a result of her failure to take Aspirin for quite a few days because she was suffering considerable personal stress due to the ill health of somebody very close to her.

[149] That friable or unstable clot fired off an embolus, a small part of it, which travelled through the left ventricle and round her aortic arch and down into her leg. It caused ischemia of her leg and she went into hospital that evening.

[150] The Defendant's hospital breached its duty of care to the Claimant, as it admits, in failing to start the Claimant on injected Heparin at just before 2:00 AM on the morning of 25 September 2015. The duty of care in relation to how the Claimant was to be treated focussed and fixed on how the Defendant could best protect the Claimant from suffering a stroke or SEE caused by an embolus or blood clot leaving the LAA and exiting the heart to cause death or serious ischaemia in the Claimant's body. That was the foreseeable mischief the duty of care aimed to avoid or ameliorate.

[151] The Claimant was at high risk of her unstable or friable clot firing off another embolus, another small part of it, which could either travel up the aortic arch and into the brain or down the aortic arch and into the limbs.

[152] Had Heparin been administered to her over the next three days, as it should have been, the Heparin would have started working within one to three hours and the effect would have been to start the body's natural processes of dissolving the friable or unstable clot and working towards stabilising it and/or organising it and/or "*walling it off*" to use Dr. Patel's phrase and/or adhering it to the atrial wall.

[153] In reliance on the evidence of Professor Mehta and the Collins et al study from 1995 and the Konstantinides et al paper I find as a fact that had the Defendant administered Heparin and then therapeutic Warfarin or modern anti-coagulation it would probably have taken between three and four weeks (roughly 25 days) to dissolve the Claimant's left atrial appendage clot.

[154] I find that during that 25 day period the Claimant would have been on Heparin for the first three to seven days and she would then have transferred to either Warfarin or a more modern anti-coagulant drug and the Heparin would have been ceased at the appropriate time.

[155] Taking into account the TEE studies carried out by Collins et al the effect of the Heparin on the Claimant's atrial clot, in the 67 hours (2.79 days), would have been that the clot would have reduced in size considerably and probably by over 50% in size. Taking into account that it takes a few days for Warfarin to reach therapeutic levels, the TEEs taken on patient 5 in the Collins et al paper showed really significant reduction in the LA clot size after 1 week from the start of Warfarin treatment so perhaps only 3 days of therapeutic levels of Warfarin. This generally and roughly matches the DVT/PE dissolution and resolution times in the Konstantinides et al paper which were relating to smaller clots and I consider that the studied DVT clots are likely to have been considerably smaller than the Claimant's LAA clot as Dr Giallombardo advised.

[156] At the same time as the thrombus was being dissolved and reduced in size by the body's natural mechanisms, encouraged and assisted by Heparin's effects on the blood, I find that the structure of the Claimant's LAA thrombus would have been becoming more organised, less friable, more stable and more attached to the atrial wall.

[157] I take into account that the effects of Heparin on blood clots in DVT and PE cases after the first 48 hours are very beneficial in preventing emboli breaking away from the blood clots in the venous system.

[158] I take into account the agreed evidence that Heparin prevents the formation of new clots in the LA and the LAA and prevents propagation of the mother clot and I find that Heparin would have done so in the Claimant over the 67 hours. This would therefore probably have prevented new clot formation on the surface of the Claimant's mother clot from embolising and causing the stroke.

[159] I take into account that it is the agreed medical evidence of the experts that if the Heparin had managed to prevent the embolus breaking away on 27 September 2015 the Claimant would have had a 66% chance of being stroke free for the rest of her life.

[160] Having carefully considered Dr. Patel's opinion that Heparin does not enable the body to reduce the embolic danger created by a blood clot and it merely allows the body to dissolve the blood clot, I reject that evidence and prefer the evidence of Professor Mehta to the effect that Heparin stabilises or organises or makes atrial clots less friable and/or more adherent.

[161] I take into account that Dr. Patel in his evidence accepted that "*Clinicians believe Heparin is going to have an effect. Most give it because they believe it works straight away.*" I take into account that Dr. Patel advised that Heparin reaches peak effect in 3-4 hours.

[162] I find that Heparin would have prevented new clot formation, prevented mother clot propagation (of the existing clot) and would have enabled the Claimant's body not only to reduce the size of the mother clot in the Claimant's LAA but also to make it less friable, more stable and more organised, so that on the balance of probability no embolus would have been fired off on 27 September 2015 and the Claimant would not have suffered a stroke.

Conclusion

[163] I enter judgment for the Claimant.