Diagnosis and Management of Strokes in Emergency and Primary Care Settings

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The diagnosis and treatment of suspected strokes and transient ischaemic attacks (TIAs) is a very broad topic. Depending on the context, determination of the issue of breach of duty is likely to involve consideration of relevant NICE guidance and individual NHS Trust guidelines. It is invariably fact-sensitive and involves detailed expert evidence. Even when breach of duty is not in issue and/or is established in evidence, causation is likely to be contentious in all but the clearest of cases due to the absence of definitive evidence or trial data regarding the efficacy of anticoagulant treatment.

For the purpose of this blog, and by examining the case of *Pickering v Cambridge University Hospitals NHS Foundation Trust* [2022] EWHC 1171 (QB), the question of causation focusing on one very specific factual scenario will be explored, i.e. the efficacy of low molecular weight Heparin in the prevention of thromboembolism in patients with atrial fibrillation.

Before turning to the facts in *Pickering*, it is helpful to have definitions of the medical terminology used in this case.

Stroke

A stroke is a serious life-threatening medical condition that happens when the blood supply to part of the brain is cut off. Strokes are a medical emergency and urgent treatment is essential. The sooner a person receives treatment for a stroke, the less damage is likely to happen.

There are two main causes of strokes:

- ischaemic – where the blood supply is stopped because of a blood clot, accounting for 85% of all cases; and
- haemorrhagic – where a weakened blood vessel supplying the brain bursts.

Treatment depends on the type of stroke a patient has, including which part of the brain was affected and what caused it.

Patients at risk of suffering strokes (e.g. those with atrial fibrillation) are often treated with long-term prophylactic anticoagulants, including low-dose Aspirin, warfarin and newer types of medication such as apixaban and rivaroxaban. In cases of acute ischaemic events or thromboembolism, Heparin, which is a fast-acting anticoagulant treatment, is often used to treat and prevent (further) clot formation.

The Facts and Decision in *Pickering*

Mrs Pickering, who was 52 years old in September 2015, had a long-term history of atrial fibrillation for which anti-coagulation with Warfarin had been recommended by her treating consultants on numerous occasions. Mrs Pickering had rejected this recommendation in favour of Aspirin, which she took erratically, especially in the week leading up to her A&E attendance on 24 September 2015.

On 24 September 2015, Mrs Pickering started to experience symptoms of acute lower limb ischaemia which ultimately led to her attendance at A&E at the Defendant's Trust late on 24 September 2015. Breach of duty was denied right up to the trial. Following evidence of the Defendant's breach of duty expert, the Defendant admitted that Mrs Pickering should have been commenced on low molecular weight Heparin by injection in the Emergency Department at or before 01:44 on 25 September 2015. As it happened, Mrs Pickering did not receive such treatment, and went on to develop a major stroke 67 hours (2.79 days) later.

At the trial, the judge (Ritchie J) made the following findings of fact:

- As agreed by the haematology experts, in the lead up to 24 September 2015, Mrs Pickering developed an unstable

blood clot in her left atrial appendage as a result of her longstanding atrial fibrillation and her failure to take Aspirin for quite a few days.

- Mrs Pickering's acute intermittent right limb ischaemia was caused by the unstable 'mother clot' firing off an embolus which travelled to her leg, causing ischaemia in respect of which she sought hospital treatment.
- At the time of her discharge on 25 September 2015, she was at high risk of suffering further emboli (from the 'mother clot') causing either stroke or peripheral arterial ischaemia.
- The stroke that Mrs Pickering suffered on 27 September 2015 was caused by a blockage of a cerebral artery which was due to fragments being thrown off the same cardiac source, i.e. the 'mother clot', which had caused the earlier limb ischaemia.

The only question for the court, in the circumstances, was: "*Would Heparin given 67 hours earlier have prevented the stroke?*"

On this crucial issue, the court's determination turned on the evidence of the parties' haematology experts: Professor Mehta for the Claimant and Dr Raj Patel for the Defendant. Both experts referred extensively to published medical literature which they contended supported their respective positions. However, there was no literature or data that dealt specifically with the efficacy of low molecular weight Heparin in the prevention of stroke caused by left atrium thrombosis. As recognised by the judge, the absence of such evidence is explained by the impossibility of doing gold standard, randomised, peer reviewed research on whether Heparin has a front loaded or constant effect in such cases where the clot has already fired off an embolus. Heparin treatment is mandated in such circumstances. There is no placebo group for comparison, for obvious reasons.

Whilst the experts were agreed that Heparin prevents new clot growth and the propagation of an existing clot, they reached different conclusions regarding the effectiveness of Heparin in organising or stabilising the existing clot, thereby preventing further emboli, during the period of clot dissolution.

Professor Mehta, whose evidence the Judge ultimately preferred, opined that Heparin given over 67 hours would have, on balance, prevented the embolus from breaking free from the clot in the Claimant's left atrial appendage (LAA) and causing the stroke. He relied upon the following in support of his opinion:

- His vast academic and clinical experience.
- The immediate use of Heparin by clinicians worldwide, over decades, to treat acute Atrial Fibrillation and the significant risk of embolic stroke arising therefrom.
- UK and US guidelines recommending Heparin for similar situations.
- Similarities between the effects of Heparin and Warfarin on human blood clots.
- The agreed knowledge that Heparin tips the balance in the human blood stream against clotting and in favour of clot dissolution and organisation of the clot.
- Heparin's agreed 'fast on' effect.
- Published data (by extrapolation) relating to the beneficial and fast effects of Heparin on pulmonary embolism and DVT blood clots in the first 48 hours after commencement.

Dr Patel relied upon articles of bridging studies and asserted that Heparin did not reduce the risk of an atrial blood clot firing off an embolus during the first three to four weeks of anti-coagulation. He did not accept that as the clot got smaller, it was also becoming more organised, stable and adherent. He did not accept that it was less likely to fire off emboli. Whilst accepting that Heparin was better than 90% effective in preventing emboli from DVT and pulmonary embolism, he refused 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 was irrelevant to atrial clots.

In respect of the bridging trials (which involve the use of Heparin as a short-term therapy to bridge the peri- and post-operative periods when Warfarin treatment is stopped), the court found that they simply did not prove Dr Patel's contention that Heparin does not decrease the thromboembolic risk generally. In arriving at this conclusion, the judge relied upon Professor Mehta's view that these studies, which would have excluded patients (like Mrs Pickering) who had

suffered an embolus in the weeks before the operation, had little or no relevance to the issue in the case. Further, since the bridging studies were not randomised and Heparin treatment was given to higher risk patients in the first place, the published statistics do not show that Heparin has no effect in reducing the thromboembolic risks in patients.

Against the background of the experts' evidence, the judge found that on the balance of probabilities, had Heparin been given to Mrs Pickering over the days following her A&E attendance on 24 September 2015, it 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. During the process of dissolution, 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. In short, the judge rejected Dr Patel's contention that Heparin does not enable the body to reduce the embolic danger created by a blood clot and merely allows the body to dissolve the blood clot. Ultimately, the judge concluded that but for the Defendant's negligence, Mrs Pickering's stroke would have been avoided.

Takeaway Lessons

1. When finalising expert evidence, it is important to ensure that the medical/published literature, paper or data relied upon by your expert does in fact support their opinion or proposition. Credibility of medical experts can be quickly undermined if your expert is unable to substantiate or explain their conclusions by reference to the cited literature in cross-examination.
2. Make sure that the entirety of a particular paper/study is served with the expert's report and included in the trial bundle. In this case, one of the experts failed to include a detailed chart exhibited to a paper which contained four scans of a clot of a patient taking part in the study. The scans showed that the clot had dissolved by 50% to 75% in the first week and then disappeared by week 5.5.
3. Do not accept without question the conclusions of the published studies. Consider any caveat or proviso that may undermine that conclusion or enable the other side to argue that it should be distinguished from the facts of the present case.
4. From a practical point of view, this case turned upon the strengths of the expert evidence, which can be tested rigorously in conference. If properly prepared, the flaws in your own expert evidence should have been identified prior to trial or even exchange of expert evidence. There should be no major or fatal surprises in your own expert's oral evidence at trial. Whilst we cannot always accurately predict the likely quality of the opposing expert's oral evidence from written reports, adequate preparation can ensure that your own experts come up to proof at trial, thus maximising your chances of success.