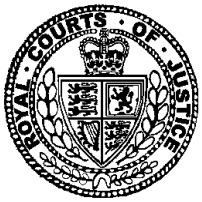

Neutral Citation Number: [2020] EWCA Crim 1628

Case No: 2016/03378/B3

IN THE COURT OF APPEAL (CRIMINAL DIVISION)
ON A REFERENCE BY THE CRIMINAL CASES REVIEW COMMISSION

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 04/12/2020

Before :

LADY JUSTICE MACUR
MR JUSTICE WILLIAM DAVIS
and
MRS JUSTICE McGOWAN

- -

Between :

DEBORAH KATRINA ANN WINZAR	**Appellant**
- and -	
REGINA	**Respondent**

Reference by the Criminal Cases Review Commission under S.9 of the Criminal Appeal Act

- -
- -

Mr Peter Wilcock QC and Mr Nick Brown (instructed by **Birnberg Peirce & Partners**) for the **Appellant**
Mr James Curtis QC and Ms Lucy Organ (instructed by the **Crown Prosecution Service Appeals Unit**) for the **Respondent**

Hearing dates : 2-4 November 2020

- -

Approved Judgment

Macur LJ:

1. Deborah Winzar ("the Appellant") was convicted on 19 July 2000 of the murder of her husband, Dominic McCarthy, who died on 9 February 1997. She was sentenced to life imprisonment, with a minimum term of 15 years, now served. The case comes before us, primarily, by reference of the Criminal Cases Review Commission ("CCRC") pursuant to s 9(2) of the Criminal Appeal Act 1995, who certified on 19 July 2016 that " [t]here is fresh evidence that the deceased may have died from natural causes ..[which]… goes to the heart of the Prosecution case. The jury might reasonably have acquitted had the evidence been available at trial." However, whilst the ambit of the s 9(1) appeal remains intact, part of the original case has been abandoned following the receipt of a Consultant Neuropathologist's report, confirming the nature of the brain injury sustained by the deceased, after which the medical expert consulted by the CCRC on the possibility of death arising from a specified natural cause became redundant to the appeal. So it is that we are asked to determine a different case to that originally predicated on the medical evidence considered by the CCRC, by granting leave to amend the grounds of appeal pursuant to s14 (4B) of the Criminal Appeal Act, 1995 and to hear 'new' medical evidence on issues which the CCRC declined to refer.

2. The Appellant concedes that the part of the reference that does remain, and which relates to the likelihood of an injection being administered to the deceased without his knowledge is, of itself, insufficient to undermine the safety of the conviction. Nevertheless, clearly it does provide the platform for an application for permission to appeal on other grounds which "are not related to any reason given by the [CCRC] for making the reference" pursuant to s 14(4B). The application to amend/vary the grounds of appeal which resurrects issues that the CCRC declined to refer, was initially listed for determination on submissions prior to the hearing of the appeal, but was ultimately adjourned for a 'rolled up' hearing to allow for exchange and consideration of further medical reports.

3. We were satisfied that there is nothing in section 14(4B) that precludes us from considering an application for permission to pursue grounds of appeal arising from reasons which have already been considered and rejected by the CCRC in deciding whether to refer the conviction to this court, and equally that there was nothing in either the statutory provision nor the authorities that requires the Appellant to demonstrate "substantial injustice" in order to succeed, as is required in 'change of law' cases. That said, we considered that the CCRC's inquisitorial role and its investigatory powers, demonstrably articulated in the comprehensive report before us, created a particularly high hurdle for the Appellant to clear when suggesting that there is 'fresh evidence' which provides a viable ground of appeal. Put shortly, the fresh grounds advanced would need to effectively establish an error in the analysis already undertaken. (See *R. v. James* [2018] EWCA Crim 285 @ [38 (vi), (vii)].) Nevertheless, in the somewhat unusual circumstances of this long running case, as will appear below, and with a view to accommodating the several medical experts who had been warned to attend the hearing fixed to consider the application to admit fresh evidence, it appeared to us that the most pragmatic course was to proceed to hear their evidence de bene esse, in much the same way as we would if the grounds of appeal had been based upon the CCRC reference, rather than attempt to determine the merits of the application to vary the grounds of appeal and call additional and different "fresh evidence" on the papers beforehand.

4. The appellant is represented by Mr Wilcock QC and Mr Brown. The Respondent is represented by Mr Curtis QC and Miss Organ.

Background Facts in Brief

5. Dominic McCarthy married the Appellant in 1985 after he had suffered a catastrophic injury in October 1984 which rendered him paralysed below mid chest. He has been described in this case as having been a "high performing" paraplegic, and evidence showed he was obviously determined to live an independent and active life. He engaged in upper body building and weightlifting and actively participated in the care of the couple's child, born in 1993 with the aid of assisted fertility technology. He worked as a social worker at a local centre catering for people with disabilities. Unfortunately, he was confined to a wheelchair, suffered frequent urinary tract infections resulting from catheterisation, had experienced cellulitis in his lower limbs and undergone removal of his gall bladder.

6. The Appellant was a hospital ward nursing sister. She assisted as necessary in her husband's personal care. The family relationship had adapted to Mr McCarthy's disabilities and was evidently strong.

7. In January 1997, the family holidayed in Ireland. Mr McCarthy became ill with flu like symptoms. He subsequently took time off from his employment but had been at work on 30 January 1997. He visited friends on his return from work, one of whom recounted that he was "not his usual self and could not keep his food down". He spoke to family members on the telephone later that evening and complained of feeling "extremely tired". He was discovered the next morning to be unconscious, his breathing was laboured, he appeared to have vomited and was suspected to have aspirated vomit into his lungs. The GP who attended made a preliminary diagnosis of pneumonia. He was taken to hospital and vomited twice en route and fitted. Mr McCarthy's white blood cell count was found to be markedly elevated on admission to hospital and remained high throughout. He received antibiotics, was intubated and ventilated, but his condition deteriorated, and life support was withdrawn. He died without regaining consciousness.

8. The Appellant had, by prior arrangement, spent the night away from the family home over the 30/31 January and had gone straight from there to work, arriving for the start of her 7 am shift. When she left the family home, just before 9 pm on 30 January, to attend a party at the hospital she was aware that her husband felt unwell, but spoke to him later in the evening when he said he was feeling slightly better. She had been unable to rouse him on the telephone the following morning and discovered that their son had not been taken to nursery and so asked the nursery manager to investigate. The nursery manager found Mr McCarthy as described above.

9. The results of an immunoassay test made of a blood sample taken on the day of Mr McCarthy's hospital admission were made known to the pathologist, who had conducted a routine post mortem on 11 February 1997, prior to delivery of his report to the Coroner. The results indicated an unusually high concentration of insulin and "undetectable" C-peptide, indicative of exogenous insulin. Consequently, at the request of the police, who hitherto had not been involved in the case, a second post-mortem was conducted by a forensic pathologist. Both pathologists agreed that the cause of

death was adult respiratory distress syndrome (ARDS) because of the aspiration of gastric contents attributable to hypoglycaemia. There was no indication of any endogenous condition to account for the insulin detected.

10. The Appellant was arrested on 5 August 1997 and denied any wrongdoing. She was eventually charged on 30 January 1998, tried, and convicted in 2000. She maintained her innocence throughout and continues to do so.

The trial

11. The trial took place between 8 June to 19 July. The Prosecution case was that the Appellant had caused the death of her husband by deliberately injecting him with insulin; the evidence against her was circumstantial. The evidence, including that of treating clinicians and expert medical opinion were recited comprehensively in summing up by the trial judge, Owen J, over the course of five days. The transcript, excluding discussions between judge and Counsel in the absence of the jury, exceeds 325 pages.

12. A summary of what we regard to be the relevant evidence from the trial for the purpose of this appeal follows and is derived from the summing up.

Immunoassay tests

13. The evidence underpinning the Prosecution case was the results of two immunoassay tests carried out on the serum produced from a single sample of the deceased's blood shortly after he arrived in hospital. The first of these tests was carried out by Dr Teale at the Guildford Laboratory on 10 February 1997; the second by Mr Hiscutt at the Forensic Science Service laboratories on 21 March 1997. Whilst the quantitative results differed from each other, both independently found that the blood contained unusually high levels of insulin and, by contrast, undetectable or negligible levels of the enzyme C-peptide. In 'normal' circumstances the pancreas produces insulin and C-peptides in equal amounts as proinsulin, which then splits up. One of the two compounds cannot ordinarily be found without the other and C-peptides are usually expected to be recorded in higher numbers than insulin, because they stay longer in the body before excretion in urine.

14. Dr Teale had also applied a 'double dilution technique' on the immunoassay. This technique is said to reinforce the reliability of the results; if the substance being measured is insulin, the tests will record the same values for each of the dilutions. He said the results 'marched' in step with his primary conclusions. He recorded insulin at 887 picomoles per litre and C-peptide less than the level of measurability at <94 picomoles per litre. Dr Teale agreed that in a forensic examination he would have gone further than an immunoassay test. He explained that the discipline of clinical biochemistry is founded upon a compromise of producing results which are '*probably correct within a time frame which enables them to be of value to the patient'.*

15. Mr Hiscutt performed an immunoenzymometric test. He recorded insulin at 616 picamoles per litre and undetectable C-peptide.

16. The defence at trial understandably emphasized the different figures which emerged from the two immunoassay tests as an indication of the unreliability of the results.

Prosecution clinicians and experts dismissed this concern and maintained that despite minor numerical differences the two sets of results were compatible and mutually supportive of the conclusion that Mr McCarthy's hypoglycaemia was caused by administration of exogenous insulin.

17. Professor Forrest, a forensic toxicologist, had '*greater confidence'* that the immunoassay results were accurate and there had been no interference leading to a false insulin reading in the light of the double dilution technique used. He stated that *'[y]ou are going from being sure it [*insulin*] is there to being absolutely sure it is there*' and was 99% confident in the accuracy of the test results. In his opinion, absent rare exceptions, the high insulin recordings in the immunoassay test results combined with undetectable levels of C-peptide '*suggests one thing and one thing only, and that is that there has been the injection of insulin into the patient.'* He was not '*aware of any medical condition which could cause a person to produce within their own body an excess of insulin sufficient to cause hypoglycaemia and yet, at the same time to have an undetectable c-peptide reading'*.

18. Dr Ferner, a consultant physician with particular interest in Clinical Pharmacology, confirmed his conclusion that the cause of death was triggered by administration of insulin but conceded "*in fairness,* [he should] *add that the opinion is based on the assays and the idea that the assays are reliable.' However,* both sets of results were consistent with each other and *'right in the broad picture'* of Mr McCarthy's condition. He said that '*[a]ccuracy has a rather specific meaning in the context of assays'* and avoided using this term.

19. In his summing up relating to the reliability of the immunoassay tests, Owen J addressed the defence arguments in terms:

> *'It is very hard to see that there is any real criticism of the way in which the tests were carried out by Dr Teale. We had all the evidence of how the blood was treated, the serum obtained was sent on and the temperatures. None of that, as I understand it, is criticised as such. What is said, however, is that there are so many ways in which the system can go wrong.'*

<u>Alternative cause for the hypoglycaemia</u>.

20. Dr Ferner gave evidence on Mr McCarthy's medical presentation and tests carried out on arrival at hospital. The low blood glucose recording from the finger-prick test administered to him would be '*a quite exceptional finding in someone who is not treated with insulin'***.** Under 1 millimole – was '*very rare outside the context of patients who are known to be injecting themselves with insulin or taking some drug for diabetes.'* Mr McCarthy's blood was found to be of normal acidity which contraindicated septicaemia with shock**.** Where a low blood glucose concentration was recorded in patients with septicaemia, *'those patients often have, in addition to the infection, damage to the kidney; the kidney does not function properly or at all…Mr McCarthy's kidney function was absolutely normal when he was brought into hospital…. he did have a high white blood cell count…and there was a small number of pus cells seen in his phlegm. Subsequently he developed fever. At a later stage, an organism was actually grown from his urine, so it is possible that he had, it is even probable that he had, some*

inflammatory process of which infection, including infection in the lungs, is possible, but what he did not have was septic shock. He was not dying as a result of the infection.''

21. He found no evidence that the hypoglycaemia was caused by another condition rather than injection of insulin. He ruled out a malfunction of either the liver or the adrenal glands, as well as acidosis, or short-term protein malnutrition. The hypoglycaemia could not be attributed to insulin-secreting tumours in the pancreas for even when malfunctioning, it secretes insulin a *'pre-packaged molecule'* composed of both insulin and C-peptide, whereas manufactured insulin does not contain C-peptides at all . Insulin autoimmune syndrome could be ruled out because in such cases C-peptide can still be measured and very low blood glucose levels are '*absolutely exceptional'*. In his view, '*the only even reasonable explanation for what happened is low blood glucose concentration coma, aspiration of vomit, serious lung disease and then dying.'*

22. Dr Harris, a consultant microbiologist, carried out the first post-mortem. He specialises in the laboratory diagnosis of infection within samples received from patients. He considered the pus cells found in the sample of Mr McCarthy's sputum showed no significant growth because the bacteria in question were relatively harmless and found only in the upper respiratory tract as opposed to a lower respiratory infection, which is a recognised cause of pneumonia**.** The pus cells found in a sample of urine which produced a heavy growth of bacteria and high white blood cell count on admission was usually evidence of some response to injury**.** He dismissed the possibility that the hypoglycaemia might have resulted from infection with septicaemia since platelet levels were recorded as normal upon Mr McCarthy's admission to hospital and remained so throughout. In *'severe septic conditions …one of the common findings is that there is a reduction in the platelet level in the blood'.* There were other factors that also pointed against septicaemia being present, such as the absence of any abnormality in blood clotting and the fact that levels of fibrinogen – a substance involved in blood clotting – were not reduced. He agreed that with Dr Ferner that if Mr McCarthy had septicaemia to such an extent as could cause hypoglycaemia, he would expect to find evidence of impairment of the kidneys and liver, which was not this case.

23. Dr Harris did not think it was possible on the evidence available to confirm whether Mr McCarthy was septicaemic at the time of his admission or whether he may have contracted an infection whilst in hospital. However, if he had become infected with septicaemia, he thought this was unlikely to have caused coma since, given the duration of presumed unconsciousness before Mr McCarthy was discovered, he would have expected to see more normal features of septicaemia if that were the case

24. He did not think that a urinary tract infection diagnosed from a sample of urine on 5th February could have led to septicaemia. It was '*very unusual to see sepsis arising from this source'* unless a catheter has been blocked and Mr McCarthy's catheter was 'full to bursting' when he was found. Also, if the urinary tract infection caused septicaemia, then this would have been untreated until at least the 2 February when the antibiotics were administered and it was '*extremely unlikely'* that Mr McCarthy would have been able to survive this long in such circumstances. The worsening of Mr McCarthy's septic condition would have been clear to medical staff. Moreover, since he had survived until 2 February when the blood sample was cultured, the bacteria in question (pseudomonas) would have been found in the bloodstream at that point and they were not). In these circumstances he also dismissed the possibility that Mr McCarthy had been suffering

from another bacterial infection. There are four species of bacteria capable of leading to grave illness and death within a matter of hours. If any of these bacteria had been present, there would be clear signs on the patient's body and in samples taken. Having reviewed some of the papers cited by Professor Marks, the defence expert, he concluded that '*hypoglycaemia resulting from sepsis or septicaemia is an uncommon condition'* which is *'only seen when there are certain well-defined medical conditions already existing in the patient'.* Most of these cases involved elderly patients, cirrhosis of the liver, alcoholism, and similar conditions. By contrast, Mr McCarthy was '*a previously relatively healthy man of 35'.*

25. Dr Cary, Forensic pathologist, carried out the second post-mortem. He considered the high white blood cell count could be attributed either to the aspiration of vomit or the subsequent development of sepsis in hospital. He accepted that there probably was an infection in the bladder when Mr McCarthy was admitted to hospital, but rejected the suggestion that septicaemia was the cause of his rapid degeneration from being 'OK' the night before to in a coma the following day as '*unreasonable',* He said there was no evidence of typical symptoms such as '*severe rigors, high fever or a complete collapse.'* If septicaemia did explain the hypoglycaemia, the levels of C-peptides would have been detectable. In his opinion there was no evidence of an endogenous upset which might have caused excessive insulin because *'there were no tumours and there was no septicaemia'***.**

26. Dr Park, a Director of Intensive Care and Consultant in Anaesthesia, said that in rare cases septicaemia can cause hypoglycaemia. However, in this case, only two of the three necessary findings for a diagnosis of septicaemia were present, namely a suspected source of infection (the pus) and a high white blood cell count. The third criterion was a body temperature of above 38.5 or below 35.5. In addition to these criterion, three out of six further conditions must be present for a diagnosis of septicaemia to be made. In this case there were only two -a very fast heart rate and rapid breathing. At no time following his admission to hospital was Mr McCarthy treated for septicaemia and whilst it was possible the treating doctors had made a mistake, there was no evidence of 'septic shock'**.**

27. Professor Marks was called on behalf of the Appellant and described by Owen J as a '*world renowned expert'* on both hypoglycaemia and on the development and application of immunoassays. Professor Marks said that several factors pointed towards hypoglycaemia caused by an underlying disease rather than insulin injection:

    i) An insulin injection may cause hypoglycaemia and eventually death, it is much more likely that the victim will recover;

    ii) Vomiting is '*exceedingly rare'* as a feature of insulin-induced hypoglycaemia;

    iii) Anxiety, palpitations, feeling ill and sweating are all results of insulin poisoning and were not present in this case;

    iv) Upon arrival at hospital, Mr McCarthy's body temperature had been normal and then elevated, rather than dropping to between 36.5 and 37.5 as is customary in cases of insulin induced hypoglycaemia;

v) The high white blood cell count is '*not usual in uncomplicated insulin hypoglycaemia cases…You can have it, but you would not immediately think of insulin.';*

vi) In cases of insulin-induced hypoglycaemia, it is usual to find '*very high plasma insulin levels, over 2000 picomoles per litre'.*

28. In his view there were many other ways in which hypoglycaemia might have been caused. Not all the evidence that could have been obtained was in fact obtained, and consequently there was no incontrovertible evidence that the condition had here resulted from insulin poisoning. 'The immunoassay tests *'fall short of the quality I would expect where everything depended on the result of the laboratory procedure… [T]he experts still do not know enough…New information is coming out all the time and you have to be very, very careful indeed before you rely on one test, namely the test which was as to the insulin and the test which was as to the C-peptides.'*

29. He disagreed with the level of confidence expressed about the double dilution test and that *'[I]f it doesn't double dilute then you are not measuring what you think you are, but the fact that it double dilutes does not mean that you are measuring the substance that you thought you were…They only rule things out. They don't rule them in. It does not tell you that you have got identity. If you have not got it, it rules it out.'*

30. He considered that Mr Hiscutt should have performed a different test *'to approach the problem from a forensic point of view rather than from a clinical point of view.'* The difference of 40% in the recorded insulin levels from the different tests was '*entirely consistent…with it being due to interference in two different assays.'* They should be treated with caution. The question which should have been asked was whether it could be proven that insulin was present in the serum samples, rather than *'other contaminants and interfering substances'.* He thought: **'***these are erroneous results which have led to the whole escalation of the idea that this man had insulin induced hypoglycaemia. I personally believe that he almost certainly died from natural causes which is what the doctors would, if the insulin result had come back anything other than inappropriately, they would have said 'We don't know the cause'… they would have said this was death from natural causes, but we cannot really say what it is due to.'*

31. Professor Marks, who set up the Guildford laboratory where the first set of immunoassay tests were done had agreed when first discussing the matter with Dr Teale, that this was a case of '*factitious hypoglycaemia'* caused by insulin injection but upon reading the clinical notes had changed his mind. He conceded that he could not prove that the hypoglycaemia had not been caused by insulin injection and that septicaemic hypoglycaemia '*does not fit very well'* with the evidence either and was equally '*unprovable'*.

<u>The previous appeal 2002</u>

32. The appeal is reported at [2002] EWCA Crim 2950. It was wide ranging, including the consideration of the asserted improbable scenario of the Appellant injecting her husband in the early hours of the morning without his knowledge, and admitted 'fresh' medical evidence. We refer, in brief, to that evidence they heard which was concerned

with the reliability of the immunoassay tests and the 'alternative cause' then being pursued.

33. Dr Ismael**,** a consultant in clinical biochemistry and chemical endocrinology, Dr Wood**,** a consultant clinical biochemist and Dr Clark a consultant clinical scientist gave evidence that the possibility of interference with the immunoassay tests could not be ruled out. The double dilution test did not provide a guarantee against interference and neither did the similar results obtained from the Guilford and FSS laboratories. Antibody tests which could eliminate interference had not been performed.

34. Dr Teale gave evidence to the Court of Appeal, maintaining that *'confidence in the reliability of the tests was further justified by the fact that (a) linear results were obtained following the application of the double dilution technique, and (b) the results of the two tests were broadly in line with each other.'* He accepted that no test was infallible but said that in the immunoassay tests carried out by himself and Mr Hiscutt**,** '*neutralising reagents'* had been added to reduce the possibility of interference.

35. Professor Bagshawe**, Emeritus** Professor of Medical Oncology at London University, gave evidence directed to the possibility of endogenous insulin production leading to Mr McCarthy's hypoglycaemia. He conceded that immunoassay tests are generally reliable but said that they are neither infallible nor conclusive. The evidence in the present case was equally consistent with the theory that the cause of the hypoglycaemia was endogenous as exogenous but agreed that alternative endogenous causes of Mr McCarthy's hypoglycaemia were undermined by the absence of certain conditions or symptoms which would have been expected in these scenarios. He accepted that *'the clinical features were consistent with insulin induced hypoglycaemia…. either endogenous or exogenous'.* He agreed with Professor Marks' evidence at trial that the features of the case were not consistent with septicaemia, or 'septic shock', and could therefore be ruled out.

36. The Prosecution called three of the expert witnesses who had given evidence at trial in rebuttal of this evidence, namely Dr Cary, Professor Forrest, and Dr Ferner**.** All maintained substantially the same position as below. In short, they considered that when the clinical features of the case were considered in the round, the existence of an insulin-producing tumour in the pancreas and insulin auto-immune syndrome ('IAS') could both be ruled out as causes of Mr McCarthy's hypoglycaemia.

37. The Court of Appeal found that if the insulin was endogenous then apart from IAS it could not have been caused by any of the other conditions canvassed by Professor Bagshawe**,** (namely the possibility of small insulinoma in the pancreas or other cancers; hyperplasia of the beta cells in the islets of the pancreas, and fatty changes in the liver indicating the possibility of failure to degrade insulin), who had had himself *'conceded that the evidence was consistent with exogenous insulin',* and neither Dr Ismael nor Dr Wood had ruled out this possibility. The Court of Appeal rejected IAS as a possible cause in [75] to [80] of the judgment.

38. The Court of Appeal acknowledged that in summing up, the judge had not summarised the evidence of Dr Teale entirely accurately, since he had said that double dilution technique shows that insulin is '*likely'* to be present (rather than conclusively) but that this '*modest inaccuracy'* did not endanger the safety of the conviction. In any event,

following the receipt of fresh evidence the Court of Appeal concluded that: "*On the evidence before us, it is indisputable that the hypoglycaemia was induced by insulin. Once this is recognised, the issue of the interference in the assays recedes into the background so far as concerns the insulin figures found on the two forms of test."* The court agreed that there were many cogent points to be made as regards what appeared to be an improbable scenario of the Appellant leaving her colleague's home sometime between 3.30 and 6 am on 31 January, and administering the injection intravenously in the dark without his co-operation but that "*it is important to bear in mind that none of these points is new. They were all canvassed in great detail at the trial…Moreover, the jury had the benefit (denied to us) of seeing the appellant give evidence for about 3 days. It is clear they did not believe her account…The jury must have been sure that the hypoglycaemia was caused by exogenous insulin. Having considered all the points made on behalf of the Appellant about lack of known motive and lack of ready opportunity, and having heard her give evidence, the jury were sure that she had injected the deceased with insulin."* They found no basis for concluding the verdict to be unsafe and dismissed the appeal.

Involvement of Criminal Case Review Commission

39. The Appellant applied to the CCRC for a review of her conviction in June 2005. The grounds in summary which reflect on medical issues were that, in light of the decision in *R v Cannings* [2004] 2 Cr. App. R 63 , the conflict of medical evidence was an unsafe basis to proceed; there was new expert evidence from Dr Ismail, concerning a similar case in 2002 in which a patient had died of natural causes, possibly as a result of IAS; Mr McCarthy's plasma albumin levels had fallen rapidly during his stay in hospital and this had not been addressed by experts at trial; criticism of the reliance placed by Prosecution expert witnesses upon the immunoassay tests and 'new' evidence from Professor Marks and Dr Ismail regarding the test's unreliability; the likelihood of death being caused by natural causes whether known or unknown was real and sufficient; the possibility of autonomic dysreflexia (AD), a condition to which spinal cord patients are prone to, leading to death; a case of sudden adult death caused by pneumonia in one of Mr McCarthy's cousins in the previous year.

40. These, and other issues, were investigated by the CCRC in depth over several years. At [26] in the 2016 Reference it is recorded that: " *In January 2013, the CCRC arrived at a provisional view that there were no grounds upon which the conviction should be referred to the Court of Appeal. [The Appellant] was offered the opportunity to make further representations in response. As a result of those further submissions, further inquiries were commenced, including an investigation by the Cambridgeshire police pursuant to s 19 of the Criminal Appeal Act 1995 and additional scientific enquiries, including submitting original exhibits for further forensic tests. None of these steps produced conclusive evidence, but the CCRC continued to consider the scientific aspects of the case."*

41. In 2015 serum samples submitted by the CCRC for Mass Spectrometric Immunoassay to the German Sports University in Cologne were inconclusive due to degradation or untimely blood sampling after the hypoglycaemic attack. Thereafter, two further expert reports were commissioned, one on hypoglycaemia and immunoassays of insulin and C-peptide, it being considered that the latter had been "relatively neglected" at trial, and the second on spinal cord injury. Professor Matthews, Professor of Diabetes, and Mr Thumbikat, Consultant in Spinal Cord Injury, were briefed accordingly. As a result, the

CCRC concluded that there were significant features which supported a referral. In brief, there was new evidence: of the profound metabolic, adrenal, autonomic and other changes caused by paraplegia and obesity which complicate the medical picture as it was understood at trial; that the concentrations of insulin might well have been the norm for Mr McCarthy; the dangers of relying on a single sample of serum to measure C-peptide; possible pituitary apoplexy as a cause of hypoglycaemia; atypical symptoms of a disease process affecting the body below the level of the injury; features of spinal cord injury which may have led to unconsciousness other than hypoglycaemia; shedding a new light on information available at trial and on the emergency, clinical and post mortem examinations.

42. On 19 July 2016, the CCRC referred the case on the grounds that, although exogenous insulin remains the most likely explanation for the events leading to Mr McCarthy's death, there is fresh evidence that the deceased may have died from natural causes, which is unsafe to exclude taking the evidence as a whole. Grounds of appeal were filed in October 2016 reflecting these reasons

This appeal

43. As indicated above, the Appellant has conceded that any argument based upon a significant part of the CCRC reasons for referral cannot succeed and has consequently abandoned any prospective argument based upon autonomic dysreflexia and hypertensive encephalopathy. However, this Court granted permission for the Appellant to obtain a further expert's report from Professor Grossman, an Emeritus Professor and Honorary Consultant Endocrinologist, an internationally recognised expert in spontaneous hypoglycaemia and, subsequent to its receipt, from Professor Gama, an Honorary Professor of Laboratory Medicine.

44. Accordingly, the Appellant seeks to amend her grounds of appeal to plead that: (i) the fresh evidence of Professors Gama and Grossman undermine the assumptions made at trial and former appeal in relation to the inappropriately high insulin levels, and establishes a potential natural cause for Mr McCarthy's hypoglycaemia and death; and, (ii) the fresh evidence of Mr Thumbikat undermines the assumptions made at trial that Mr McCarthy was a "perfect victim" because he had no feeling below his chest and would not feel if a needle was stuck into him."

45. We heard the 'fresh' evidence called on behalf of the Appellant and that called in rebuttal on behalf of the Prosecution de bene esse over three days. Before doing so we had the opportunity to digest the contents of comprehensive, and sometimes lengthy, expert reports and the papers which have been referred to in support of expert opinion expressed therein. The reports demonstrate the considerable expertise of their authors and contain a level of detail which, it has become apparent to us, is superfluous to record for the purpose of a judgment such as this. Consequently, we only set out the thrust of the evidence which focuses on the issues which are relevant to our decision, and encompasses the professional disagreement between the witnesses, as made clear during the oral evidence of the experts who were cross examined on the relevant parts of their reports. The authors of two reports, Professor Forrest and Professor El Masri, were not ultimately required for cross examination in so far as their evidence was either confirmatory or available for appropriate comment without need of cross examination. We have taken the contents of their reports into account.

46. We heard from Mr Thumbikat, a specialist in spinal cord injuries, in respect of Mr McCarthy's likely physical response to an injection but, predominantly, the evidence was concerned with 'immunoassay results' and 'possible alternative cause of hypoglycaemia'. We heard the evidence of the expert witnesses immediately consecutively in their respective disciplines. It became abundantly clear from the evidence of all witnesses, however, that the subject matter could not be treated discretely save for the evidence from Mr Thumbikat and Professor El Masri.

Immunoassay results

47. The technique employed in the immunoassay tests is to raise an antibody to the compound of antigen that it is sought to find and measure in the human sample. The immunoassay tests that were obtained in 1997 were interpreted to show "inappropriately high" readings of insulin and negligible levels of C-peptide occurring in the presence of hypoglycaemia, and therefore to be indicative of exogenously introduced insulin. There is no doubt that Mr McCarthy had developed hypoglycaemia. The issue is whether the results were accurate or subject to interference (taint) which created a false reading; specifically, was the substance identified as 'insulin' genuine or faux.

48. Professor Gama, a consultant chemical pathologist and Professor of Laboratory and Metabolic Medicine, was called on behalf of the Appellant, Dr Morley, a consultant in clinical biochemistry specialising in toxicology, was called on behalf of the Respondent. Both participated in a joint expert conference in October 2019 and gave oral evidence in which common ground was revealed, as follows.

    i) Immunoassay testing is not generically capable of producing sufficiently accurate and reliable results to enable a sound finding to be made upon them without reference to the clinical scenario;

    ii) The published interference (something that causes false results in the assay) for all assays is in the region of 0.5 to 8%, dependent upon patient cohort, assay, and methodology. There is no reported data on interference specific to insulin assay interference in those who have never been treated with insulin;

    iii) Further 'insulin' testing on samples taken from Mr McCarthy later in the day of his admission to hospital would have been useful in investigating the possibility of interference;

    iv) Antibodies raised during the infective process can cause interference to a degree that would negate the findings of the immunoassay tests;

    v) The potential causes of antibody interference in immunoassays in this case are heterophile antibodies, human anti-animal antibodies and anti-analyte antibodies.

49. The significant area of disagreement between the two doctors was the degree of confidence they expressed in terms of the immunoassay testing in this case, and whether

there had been a sufficiently robust challenge to investigate the possibility of interference .

50. Dr Morley was satisfied that the testing was sufficient and showed no evidence of immunoassay interference. Accepting that no immunoassay test was "a hundred per cent perfect", he believed that by doing numerous tests the probability of an interference was reduced with proportionate probability. There had been three tests conducted in this case. The first Guildford test showed the assay to have an inappropriately raised insulin and undetectable C-peptide. The serial dilution technique then conducted showed no evidence for an interference. The data he obtained from the Guildford laboratory indicated that insulin-like peptides, or insulin pro-forming and proinsulin molecules which may mimic insulin, would not give a positive result in the Guildford assay test, so excluding these substances that would result in a false positive outcome. They had tested the aliquot using a non-immune serum. The FSS completed a different test, which confirmed a high insulin and a decreased C-peptide. The FSS test has an inbuilt mechanism reducing the antibody interference. From a clinical perspective, Mr McCarthy has never had any tests where there had been evidence of assay interferences in the past, despite numerous infections of his bladder and probably with E. coli present in his urine long term.

51. Professor Gama disagreed. There was no repetition or reproducibility in test results, as shown by the significant differing figures between assay tests in Guildford and FSS. There were unknowns. There had been no antibody investigation, although current guidelines suggested measurement of insulin antibodies to be first line in the investigation of spontaneous hypoglycaemia. It was unknown whether a non-immune serum had been used in the assays. There was no recorded measurement of ketones which could have indicated insulin induced hypoglycaemia. The general recommendation is to do three or four tests.

52. Professor Gama considered the marked difference in the results in competitive assay 'RIA' test carried out in Guildford, and a non-competitive assay 'IEMA' carried out by the FSS laboratory indicative of an immunoassay interference. It was unlikely to be because of deterioration of the aliquot in the five or six weeks that elapsed between the Guildford and the FSS tests since they were both frozen and insulin is stable when frozen. Whilst it could have been the result of 'method bias' to endogenous and exogenous insulin there is no way of knowing whether it existed in relation to either the Guildford tests or the FSS tests unless head-to-head studies were carried out. Dr Morley was more inclined to regard the difference in terms of method bias. He produced a paper by Manley showing a difference between the RIA and an IEMA competitive assay, but it was dismissed by Professor Gama as not providing a meaningful comparison, and our impression was that the difference between the two experts was not assisted either way by its contents.

53. In Professor Gama's view, even if the court did conclude that the Guildford results and the FSS results were comparable it would not necessarily exclude the possibility of there being interference in either test. Insulin antibodies can, but not necessarily will, give false positives in both competitive and non-competitive assays and heterophilic antibodies and human anti-animal antibodies could have caused interference with the immunoassay results.

54. Dr Morley considered the dilution technique adopted by the Guilford laboratory should dilute out interference and, if there had been interference, a 'non-linear' response would be anticipated which had not occurred in this case. Professor Gama disagreed that this would always happen. He was aware of cases of known immunoassay interference in which erroneous results were linear in dilution. He referred to reports on how common linearity on dilution in the presence of immunoassay interference can be as high as 44 per cent.

55. Professor Gama accepted that the immunoassay results could be consistent with exogenous insulin-induced hypoglycaemia. However, in his view, consideration should have been given to other possible reasons for the results which would include immunoassay interference. So, if as postulated by Professor Grossman this was possibly a sepsis-induced hypoglycaemia, it would not be expected to find insulin or C-peptide present, and the likeliest explanation, and perhaps the only explanation for the high insulin and undetectable C-peptide, is an immunoassay interference. The 'insulin' detected would, in other words, be faux.

56. He referred to two issues apparent on clinical testing of the blood that supported a differential diagnosis: the first a normal potassium level, and the second a comparatively low reading of insulin in terms of a mortal insulin overdose.

57. The potassium levels were, unusually, within normal bounds. He makes the point that in an insulin-induced hypoglycaemia of this profound extent, the deceased would be expected to have had much lower potassium levels, which at least militates against the possibility of, if not excludes, insulin-induced hypoglycaemia. In a recent book on forensic hypoglycaemia by Marks, 23 patients with insulin-induced hypoglycaemia intending suicide who had potassium measured before and after treatment had a potassium reading of less than four. His conclusion was that hypokalaemia with hypoglycaemia, is indicative of insulin-induced hypoglycaemia. Dr Morley had not seen the recent Marks study but referred to a paper by Kang in 2015 that showed that in cases of induced hypoglycaemia, approximately 41 patients in a study of 219 had normal potassium readings. He therefore considered that 'normal' potassium with profound hypoglycaemia is not pathognomonic.

58. Professor Gama identified that Dr Teale himself had described the insulin levels as "inappropriately high", but not as high as he would have expected in cases of exogenous insulin administration. In comparison to a 1999 study co-authored by Marks and Teale, results in Mr McCarthy's case were 700 per cent lower than the median. It is possible that Mr McCarthy had insulin resistance, by reason of his weight and the spinal cord injury. In that case a large dose of insulin would be necessary to overcome the insulin resistance and to produce profound hypoglycaemia; consequently, the insulin levels would be expected to be higher than the ones recorded. Dr Morley thought it significant that Mr McCarthy had at least a sixfold greater amount of insulin present than would be expected even an obese person with a spinal cord injury who is hypoglycaemic. He also raised the possibility that the insulin could have been higher, but both assays measured lower results if there had been a breakdown in the insulin before the samples were frozen.

Alternative cause

59. Professor Grossman, honorary consultant physician and Emeritus Professor at the Department of Endocrinology and consultant NET Endocrinologist and Professor of Neuroendocrinology with specific expertise in spontaneous hypoglycaemia was called on behalf of the Appellant. The Prosecution called Professor Heller, Professor of Clinical Diabetes and with ongoing research into pathophysiological responses to hypoglycaemia, and Dr Cowling, consultant microbiologist and infection control doctor, with a principal interest in bacterial sepsis.

60. All participated in a joint expert conference in October 2019, together with Dr Morley and gave oral evidence in which common ground was revealed, as follows:

(a) Sepsis is the only effective alternative candidate as a natural cause for the hypoglycaemia which was present in this case;

(b) Sepsis induced hypoglycaemia is rare and usually occurs in patients who are elderly, very ill with organ (particularly liver) failure and/or infected with virulent pathogen. When it occurs, it is associated with low insulin and C-peptide concentrations;

(c) There was evidence of infection on admission to hospital, but it was not severe and there was no evidence of kidney or liver failure. Some of the clinical data supports a diagnosis of sepsis;

(d) If there was severe sepsis, this could have been reversed and glucose metabolism stabilised as a response to antibiotic treatment and fluid replacement. It was extremely unlikely that if there was sepsis induced hypoglycaemia this would have been corrected so rapidly.

(e) Mr McCarthy was prone to recurrent urinary tract infections because of his paraplegia but had no known predispositions to sepsis-induced hypoglycaemia;

(f) If the insulin levels depicted in the immunoassay tests are assumed to be reliable, this would be incompatible with sepsis-induced hypoglycaemia and no other cause after than exogenous administration of insulin;

(g) The 'normal' potassium reading did not exclude exogenous administration of insulin

61. Professor Grossman said that, as a practising clinician, if Mr McCarthy had been admitted under his care, and he had subsequently died, putting aside the 'insulin' results, he "would not have been uncomfortable in saying: this is a very unfortunate septic illness that was lethal." He would have challenged the immunoassay tests. He thought a clinician would/should be very hesitant immediately to jump to the conclusion that somebody had injected Mr McCarthy with insulin. He would think:

"Have I got the diagnosis wrong? Is the assay wrong?" His first assumption would be that there was an error.

62. There were several features of the case that were rare in his experience of hypoglycaemia. There were two common aspects of hypoglycaemia: the first, a change in consciousness, confusion, cerebral changes; and the second an increase in heart rate, palpitations, and sweating. Vomiting was unusual and the high white blood count that was recorded at the hospital would usually lead a clinician to consider an infective process. The 'normal' potassium reading was unusual if this was due to external insulin administration.

63. He proposed a possible scenario to explain Mr McCarthy's death by natural causes, on the assumption that the immunoassay results were wrong, although he considered it highly improbable. That is, a paraplegic, who has had frequent urinary tract infections, was relatively immobile, and who reported to various members of his family he wasn't quite himself on the evening before his admission, underwent some form of septic illness either from a urinary tract or, possibly, chest infection. He then became unconscious, aspirated some of his own gastric contents, which in turn led to a septic process in the blood leading to hypoglycaemia and unconsciousness, further organ breakdown and disruption, and then death. This would be compatible with the high white count and the high temperature, which although not present on admission to hospital was subsequently in evidence.

64. Professor Grossman did not suggest that Mr McCarthy fulfilled the criteria for septic shock at the time of his admission to hospital, but there was indication of sepsis. There is a continuum from septicaemia, to sepsis, to septic shock. Septicaemia means there was an infective organism within the blood, causing problems; sepsis is the effect it is beginning to have on the body; septic shock occurs when blood pressure catastrophically falls and other organs begin to fail. The fact that Mr McCarthy did not meet the formal NICE criteria for sepsis at the time of admission did not mean that he was not suffering from sepsis. The raised white blood count and the neutrophil count indicated an infection, and the state of unconsciousness would have at least suggested the presence of an illness that could have been sepsis. Mr McCarthy would probably be categorised as having mild sepsis at the time of his admission to ITU at 1400 hours. Subsequently, in Intensive Care, he did appear to be increasingly unwell. For example, on 3rd February, at 11.45, he had a high temperature, a high heart rate; the upper half of his body was cold, and he was shivering, although he had warm feet. He became more unwell and it was more compatible with septic shock, but not necessarily diagnostic. Normally, you would expect very low blood pressure if someone was in septic shock, but the autonomic disfunction in terms of spinal cord injury plus the intense pressure on his bladder could have given him a falsely high level of blood pressure.

65. Professor Heller agreed that a natural cause of death was not impossible but in his opinion it was "extremely unlikely" that the clinical features in this case were consistent with sepsis and death. Mr McCarthy had retired to bed at around 10pm, and during the night he became profoundly unconscious, and was found the next morning with an extremely low glucose and signs of vomiting. If this was caused by an infection, he must have developed a very severe infection. He thought it extremely surprising that somebody who went to bed, "tired" and a "bit under the weather", would vomit and remain asleep, and his glucose level fall to such extremely low levels for two, three, possibly four hours, such that he sustained significant cerebral damage from

hypoglycaemia as was the case here. His reading of the literature suggested that hypoglycaemia due to infection could be corrected fairly easily, and it is unclear to what extent it contributes to the eventual mortality. Also, at the time of his discovery and admission into hospital, there was no evidence of overwhelming sepsis.

66. Professor Heller noted that Mr McCarthy had received three very large glucose corrections. He was deeply unconscious, and his glucose was found to be extremely low, at a level almost never seen in clinical practice. The first dose did correct it, but then shortly afterwards his glucose fell to less than one again, which suggested extremely high insulin levels, or something driving the glucose down that would be inconsistent with infection. The glucose level of those suffering with very severe sepsis and who are mortally ill does not fall that quickly. After the third dose, Mr McCarthy was then started on a 20 per cent glucose infusion and, thereafter, his glucose remained at normal levels. When sepsis supervenes thereafter, his glucose rose to levels above normal, which shows that the stress hormones which push the glucose up in people who have sepsis were working, as one often sees in cases of sepsis. The suggestion that sepsis had produced a very major dysfunction in his glucose metabolism, which had been largely resolved by three doses of antibiotics was extremely unlikely.

67. Professor Grossman acknowledged this argument but suggested that the data on hypoglycaemia in severe sepsis was limited. The great majority of patients in Intensive Care Units who have septic illness have problems with sugar control. Often it is high, but a minority of about five per cent in one study, had hypoglycaemia and a low blood sugar, and the evidence as to when that occurs and in what degree of septic illness and how it responds to glucose, are generally absent. There was evidence that the pre-morbid state does interact with whether a patient will become hypoglycaemic with sepsis. In Mr McCarthy's case he was relatively immobile, he has had very frequent urinary tract infections in the past, and there was some degree of obesity which were factors that would lead him to say that the scenario was still a possibility.

68. Dr Cowling's view was that the hypoglycaemia was "most unlikely" to have be caused by sepsis. He accepted that sepsis, but not severe sepsis, was a possibility in this case. The 2016 NICE guidelines were published with the intention to raise awareness to the possible diagnosis of sepsis. They are alerting, rather than diagnostic, guidelines. He accepted that there was objective evidence that Mr McCarthy fell within the high risk criteria in that he had objective evidence of a new, altered mental state; he needed 40 per cent or more oxygen to maintain 92 per cent or more saturation levels and Dr Roberts (GP) described Mr McCarthy as "grey" (ashen skin). Hospital records recorded a respiratory rate of 21 to 24 breaths per minute, and a heart rate of between 91 and 130 beats per minute as further indicators. This would alert the clinicians attending him to consider the possibility of sepsis, but does not exclude other reasons for these criteria being met All of the criteria that the deceased met on admission to hospital were explainable by his aspiration of stomach contents, without the need to invoke serious sepsis. Although he did observe that the treating team had delayed in administering antibiotics, one of the highly persuasive factors as pointing away from Mr McCarthy suffering from sepsis, so far as Dr Cowling was concerned, was the observation that the physicians who dealt with Mr McCarthy in hospital did not make such a diagnosis, even though he was unconscious. Dr Parks, the hospital treating physician, was emphatic and made a positive affirmation, that the deceased did not have sepsis on presentation in the A & E.

69. Dr Cowling agreed that, taken in isolation, the high white cell and neutrophil count is supportive of sepsis, but that there were other possible causes. He recalled that the deceased's blood pressure was normal, following the administration of one litre of fluid and it remained normal after that, which is not consistent with severe sepsis that would lead to septic shock and organ failure.

The administration of injection

70. Mr Thumbikat, consultant in spinal injuries, was called on behalf of the Appellant. Professor El Masri was available, but not required for cross examination subject to submissions on the contents of his report. Both experts contributed to a "joint statement" which revealed some disagreement between them.

71. The medical records revealed that as a result of a motor cycle accident in 1984, Mr McCarthy was a T6 paraplegic; he had no power or sensation from his lower chest downwards, and he also had associated bladder and bowel dysfunction and some autonomic problems associated with that, which would include blood problems, bowel problems, control of blood pressure and, to some extent, control of heart rate.

72. Mr Thumbikat considered Mr McCarthy's medical notes indicated he had significant spasticity affecting his body below the level of the injury, as fairly commonly encountered following spinal cord injury and brain injury and manifesting as an increase in the tone of the muscles. The effects of spasticity can manifest as increased resistance to passive movement and involuntary jerking, and he came across multiple references to increase in spasticity. Shortly after he had the spinal cord injury, there are references to him requiring a general anaesthetic for a relatively small procedure involving removal of the toe nails, at a time when Mr McCarthy's symptoms of spasticity were under greater control than they appeared to be at the time of death. There were references to an increase in spasticity, becoming increasingly stiff and that he required medications to control spasticity. Mr McCarthy did raise spasticity as a particular problem which he brought to the attention of both his GP and the Spinal Injuries Unit. Spasticity is not isolated to an individual muscle but tends to be a spread of contraction which then tends to affect all the muscles below the level of injury, and which individuals often find more difficult to tolerate.

73. Mr Thumbikat agreed it would be possible to inject Mr McCarthy in a paralysed area, without there being significant associated jerking and movement, but it was unlikely. Shortly before his death, he had been feeling unwell, and it is generally well recognised that whenever a person with spasticity is unwell, the levels of spasticity tend to increase, and it becomes more troublesome. If he had been asleep he wouldn't have been able to feel the needle if administered in the paralysed portion of his body but that would have triggered a set of spasms which in the normal course would have woken him up. His review of the notes suggested that Mr McCarthy was a 'highly performing paraplegic' so if there was no other reason to affect his general levels of consciousness and awareness, there is no reason why he would not have been able to resist if he had seen something happening and, subject to the opinion of diabetic experts, there would have been a window of opportunity for him to respond if he had become aware of it.

74. Professor El Masri did not agree that Mr McCarthy had significant spasticity and thought an injection could have been administered without his knowledge or co-operation. It is possible that he would have experienced some jerking of the legs, but

this would not necessarily have been significant if a high dose of insulin had been injected into a muscle.

Submissions

75. Mr Wilcock QC, conscious of the considerable overlap of the evidence that has been called before us and that heard at trial and, in part, by the Court of Appeal in 2002, nevertheless submits that there are exceptional circumstances to persuade us: (i) to exercise our discretion in granting leave to amend/vary the grounds of appeal; and, (ii) admitting 'fresh' evidence pursuant to s 23 of the Criminal Appeal Act 1968. He points to the "increased awareness" of sepsis hypoglycaemia; the decision of the Court of Appeal not to address the question of the reliability of immunoassay testing in the light of the 'alternative cause' argument then being pursued, and substantive content of the evidence we have heard which he says demonstrates a different medical panorama to that which was before the jury.

76. He asks that we consider the forensic evidence in the non-medical context, stressing the Appellant's previous good character, lack of apparent motive and determination by the Court of Appeal that the injection was administered between 3.30 and 6.30 am. He relies on Mr Thumbikat's evidence as capable of countering the impression given to the jury that Mr McCarthy was a "perfect victim" by reason of his disability. This evidence taken with the dosage required to give the resultant insulin levels and the window of opportunity for Mr McCarthy to summon help militates against insulin poisoning.

77. He argues that Dr Teale, who had given evidence at trial as to the near certain reliability of immunoassay tests in this case in identifying insulin, backtracked in 2002 by referring to them as 'consistent with' presence of insulin ; this Court now has evidence, including from Dr Morley, of their fallibility and their true identification as a screening rather than diagnostic test. There is a small error rate, but if there is a clinical reason to suspect interference then there is empirical evidence which demonstrates that the chances of interference are as high as 60%. The Guilford and FSS tests show discrepancies which is not readily explained by method bias that is unexplored. The dilution test is itself subject to the same professional and reasonable view that its results may be controvertible. They are to be seen in the light of the clinical picture and possible differential diagnosis postulated by Professor Grossman.

78. There were features which did not sit easily with the diagnosis of exogenous application of insulin including a new feature, namely the 'normal' potassium reading. What is more, each of the medical experts called by the Prosecution had accepted that it was at least 'possible' that Mr McCarthy died by reason of an infection rather than insulin induced hypoglycaemia.

79. In these circumstance, Mr Wilcock QC reminds us that "*particular caution is needed where the scientific knowledge of the process or processes involved is or may be incomplete. As knowledge increases, today's orthodoxy may become tomorrow's outdated learning. Special caution is also needed where expert opinion evidence is not just relied upon as additional material to support a prosecution but is fundamental to it.".* See Holdsworth [2008] EWCA Crim 971. [57]

80. Mr Curtis QC submits that the question we must answer is not whether the experts accept the possibility of an alternative cause, but whether the purported 'new' evidence renders the conviction unsafe. In short, the evidence of Professor Gama and Professor Grossman does not give a clear view and does not "come close to justifying a fundamental re-appraisal". The Court of Appeal in 2002 had not needed to determine whether the immunoassay tests were reliable on the new evidence called in order to determine the impact of the alternative cause then postulated, but equally had decided that it was open to the jury to conclude that the test results were reliable on the evidence that they, the jury had heard. The results of the immunoassay tests are not in "genuine conflict with the clinical picture", which Professor Gama accepted was key. Professor Grossman's postulated alternative hypothesis of the physiological processes leading to Mr McCarthy's death was 'diffidently' expressed and accepted by him to be "highly improbable". The alternative cause advanced ignored the chronology of events both pre and post admission to hospital and was dependent upon the immunoassay test results being "very wrong".

Determination

81. We are left in no doubt as to the high level of expertise of each of the expert witnesses, nor doubt the genuine and reasonable professional debate that has played out in the evidence. Obviously, each witness called by the Appellant is capable of belief and their evidence would have been admissible at trial. The question for us is whether it provides a ground of appeal. In answering that question, we remind ourselves of the test we must apply by reference to R v Pendleton 2001 UKHL 66, [17] – [19] and specifically:

"The Court of Appeal is entrusted with a power of review to guard against the possibility of injustice but it is a power to be exercised with caution, mindful that the Court of Appeal is not privy to the jury's deliberations and must not intrude into territory which properly belongs to the jury."

82. On that basis, where fresh evidence is admitted, the question on appeal remains whether the conviction is unsafe. As to the approach to be adopted, at para 19 Lord Bingham continued:

"…First, it reminds the Court of Appeal that it is not and should never become the primary decision-maker. Secondly, it reminds the Court of Appeal that it has an imperfect and incomplete understanding of the full processes which led the jury to convict. The Court of Appeal can make its assessment of the fresh evidence that it has heard, but save in a clear case is at a disadvantage in seeking to relate that evidence to the rest of the evidence that the jury heard. For these reasons, it will usually be wise for the Court of Appeal, in a case of any difficulty, to test their own provisional view by asking whether the evidence, if given at trial, might reasonably have affected the decision of the trial jury to convict. If it might, the conviction must be thought to be unsafe."

83. We bear in mind the concessions that Mr Wilcock's skilful advocacy has secured in relation to "possible" alternative causes leading to Mr McCarthy's death. Aware of the necessary caution urged by this Court in Pendleton (above) we have given anxious scrutiny to the evidence we have read and heard de bene esse.

84. However, ultimately, we are in no doubt that most of the evidence that we have heard is a re-package of the evidence that was before the jury in 2000 as is amply demonstrated by comparison of [11]-[31], [34]-[35] and [47] – [69] above. Nevertheless, in recognition that there may be rare exceptions to the principle that the court will not *"permit a repetition, or near repetition of evidence of the same effect by some other expert to provide the basis for a successful appeal*," (See R v ***Kai Whitewind*** [2005] EWCA Crim 1092, [97]), we have asked ourselves whether the evidence of Mr Thumbikat and that relating to sepsis and the 'normal' potassium reading presents a compelling new perspective.

85. We accept the evidence of Mr Thumbikat, which we consider is well grounded in Mr McCarthy's medical records and cogently articulated, that the administration of an injection would cause significant jerking that would likely have roused him. However, we are unable to deduce from that likely physical response, that he would have realised why he was in spasm nor necessarily have appreciated the need to 'seek assistance'.

86. Equally, we are satisfied that the 'normal' potassium reading obtained was 'unusual' in the context of insulin induced hypoglycaemia. Nevertheless, every one of the medical witnesses in this case has resisted any opportunity to describe this feature as pathognomonic of insulin overdose, and have referred to the relatively high incidence (nearly 25%) of cases in one study that did not exhibit this feature either .

87. Professor Heller and Dr Cowling conceded the possibility of natural causes leading to hypoglycaemia, in terms of it being "not impossible" and "foolish to deny as a possibility" but have countered it with their certain opinion that the totality of the evidence points to exogenous administration of insulin. Professor Grossman, on the other hand is more diffident. He accepts his hypothesis is highly improbable on the clinical presentation, which is consistent with exogenous insulin, and depends on the immunoassay tests being "very wrong".

88. Having evaluated all the evidence we conclude that Professor Grossman rightly describes his alternative hypothesis as "highly improbable". It does not create a realistic differential diagnosis. We accept Professor Heller's assessment that, absent exogenous insulin, for Mr McCarthy to have vomited whilst remaining unconscious, and then to develop such significant hypoglycaemia, would indicate a very severe infection taking hold, but which all experts agree was not apparent on admission to hospital. That assessment is corroborated by the extremely low glucose levels which were revealed on early hospital testing, indicative of high insulin, and the necessity to infuse three large boluses of glucose to stabilise glucose production. We agree with Professor Heller that Professor Grossman's posited case, that stabilisation of Mr McCarthy's production of endogenous insulin as a result of the limited infusion of broad spectrum antibiotics in the context of what would have to be such profound infective/sepsis induced hypoglycaemia to lead to the brain injury seen at post mortem is unrealistic. Dr Cowling's evidence which we regarded to be balanced and considered, supports this view.

89. Professor Gama's cautious approach to the immunoassay tests is not unwarranted in general terms and is acknowledged by all the experts who gave evidence before us. His evidence that the tests that were performed by Guilford and FSS would be incapable of conclusively excluding the possibility of interference in an uncertain clinical picture mirrors that of Professor Marks at trial. However, in accordance with his evidence

before us, once we are satisfied that the immunoassay test results are entirely congruent with the clinical picture of exogenous insulin, and there is no alternative natural cause that has been identified, this is capable of verifying the results obtained by Guilford Laboratories and FSS.

90. In summary, we do not see how the 'fresh' evidence, so called, can be said to dilute the medical case against the Appellant, or transform its perspective. The 'new' evidence does not provide any ground for allowing the appeal. Consequently, (i) we refuse permission to appeal on the amended/varied grounds and, (ii) we dismiss the appeal on the extant ground referred by the CCRC.