

# The continuing decline of autopsies in clinical trials: is there any way back?

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## Rehabilitation of the autopsy as a tool of audit, surveillance, teaching, and research

Despite continued advances in clinical and laboratory medicine and diagnostic imaging, there remains a significant divergence between clinical diagnosis and autopsy findings. Even in the intensive care unit, where some of the most advanced medical technology is to be found, diagnostic error rates of 6–40% are reported, with postmortem examinations regularly identifying previously unrecognised pathological processes.<sup>1</sup> Although these published figures may overestimate the current scale of the problem, it is beyond dispute that postmortem examinations sometimes reveal unsuspected pathological processes which may result in a change in death certification. Despite this, autopsy rates continue to fall, prompting concern about their diminished role in disease surveillance and medical audit.<sup>2</sup>

In this issue, Snowdon *et al* publish a series of articles in which they survey the attitudes of parents and medical professionals to perinatal autopsy.<sup>3–5</sup> Although the articles deal with the specific circumstances of an autopsy in a randomised control trial, the responses provide considerable insight into at least some of the reasons why the autopsy is in decline.

It is clear from a review of the articles that many of the neonatologists quoted are unfavourably disposed towards the autopsy. They find discussion of the procedure distasteful and distressing to relatives. Furthermore, it is apparent that recent recommendations about providing more detailed anatomical information and more explicit consent forms (see below) have added further to their discomfort. Many also feel that the examination is of limited value. With autopsy rates declining and physician attendance at the autopsy increasingly rare, clinical staff have less and less familiarity with the procedure they are describing and “advocating”.<sup>6,7</sup> As O’Grady<sup>6</sup> has succinctly observed, doctors cannot explain the purpose and benefits of the procedure if they do not understand it themselves. It is inevitable that these attitudes would manifest themselves in discussions with relatives

about an autopsy and may themselves contribute to a lower autopsy rate. Indeed, the reported comments of some of the bereaved families support this contention, implying that their decision was influenced one way or another by the emphasis placed on the procedure by the neonatologist who discussed it with them. Despite this, it is my experience that many parents do seek an opportunity to find something positive in the death of their child, either in the form of information for them and their extended family about what has caused their loss or by assisting medical staff in their efforts to treat other children in the future. An autopsy may represent just such an opportunity if presented to them in a positive light.

It is likely that pathologists have also contributed to the negative attitude of their medical colleagues. Lack of clinical correlation and delays in reporting autopsy findings conspire to reduce the relevance of the procedure to many clinical services. The absence of structured conferences to discuss autopsy results may also limit the vital feedback of information, which may explain the clinical course in one case and prompt a more rigorous pursuit of a post mortem in the next.<sup>8</sup> Furthermore, the structure of the pathology arm of randomised trials may also contribute to reduced participation, by necessitating the referral of tissue/organs for central pathology review. This centralisation has allowed standardisation of examination technique, ready comparison of cases, and the application of specialised techniques that may not be available in all centres.<sup>8</sup> There are therefore sound professional reasons for advocating such a process. However, preparation and delivery of these materials is difficult and tedious for the initial pathologist. More importantly, the dispersal of autopsy tissue and in particular organs from one location to another as an integral part of a research programme is likely to be a major obstacle to parental consent in the current climate, whatever the professional arguments in its favour. It seems sensible then to suggest that pathology review in such trials will, in

future, involve central coordination and analysis of pathology data collected on multiple sites rather than referral of formalin fixed or fresh tissue.

The decline in postmortem examinations is particularly disturbing in the setting of a randomised controlled trial. In addition to the normal uncertainties that surround clinical diagnosis and treatment, there are the superimposed uncertainties about the specific responses of a patient to a new treatment or new combinations of treatments. Many authors have argued that the absence of autopsy validation imposes critical limitations on the credibility of detailed and expensive clinical trials.<sup>9–11</sup> It is therefore even more disappointing to hear a neonatologist dismissing an autopsy in the setting of a randomised controlled trial as unnecessary because “you usually know why a baby has died”.<sup>5</sup> Such an observation is simply not borne out by published series.<sup>12–14</sup>

Interestingly, the articles make no reference to a potential role for the coroner in the specific circumstances of a randomised controlled trial. Whereas the death of small and ill infants in special care baby units is an unfortunately regular and indeed expected occurrence, the possibility that participation in the trial could in some way have contributed to the child’s death could be viewed as an indication for referral to the coroner as a matter of course. Indeed, the possibility that participation in the trial may have played a role in the patient’s death is remarked on by one of the parents and is implicit in several of the quoted comments from pathologists.<sup>4,5</sup> Certainly, coroners in Ireland would feel that such a referral would be appropriate or indeed mandatory even if the particular circumstances of the child’s illness would mean that the coroner may not always direct a postmortem examination to be performed (D Cusack, B Farrell, personal communications). That this possibility is not acknowledged in the reported comments of the neonatologists suggests that practice varies substantially between jurisdictions.

It is easy to forget that the autopsy is performed primarily for the family, secondarily for the clinical staff caring for the patient, and, especially in the context of publicly funded research, for society at large. They are not sought for the benefit of the pathologist. Autopsies are difficult, time consuming, even unpleasant procedures. There are other less onerous tasks in the laboratory to which pathologists could turn their full attention if they were not burdened by postmortem examinations. However, many pathologists (not all) continue to recognise the potential value of

necropsy. One colleague has gone so far as to redefine a pathologist as “a medical practitioner who specialises in the diagnosis of disease on tissue samples and who is willing, in the public interest and for the benefit of his medical colleagues, to perform post-mortem examinations”. If pathologists remain willing to perform autopsies because they recognise this value, are they willing to take on an additional task to ensure that autopsy rates do not fall further?

At our institution, pathologists now meet the family before any proposed autopsy irrespective of whether the autopsy has been directed by the coroner.<sup>15</sup> The pathologist has therefore replaced the treating clinician as the principal source of information about the procedure. These meetings have resulted in benefits to both the pathologist and the parents. In particular, they have resulted in a clarity and consistency of information for relatives as well as removing any potential gap between families’ understanding of what has been proposed and the examination itself. Despite general satisfaction with the postmortem examination, one mother quoted in the articles from Snowdon *et al* expressed distress at the discrepancy between the procedure discussed and the procedure performed, specifically the examination of her infant’s head at autopsy.<sup>4</sup> Such perceived discrepancies have been at the heart of much of the public outcry surrounding past postmortem practices. If the procedure is explained to parents directly by the prosecutor, the potential for such miscommunication is reduced.

The pathologist should offer the family a more informed and critical assessment of both the benefits and limitations of the proposed procedure, hopefully from someone who is better disposed towards the examination. The direct discussion with the pathologist also facilitates discussions about the extent and timing of the examination as well as return of tissues and the timing of the funeral. The pathologist and family are both active participants in negotiations surrounding a set of terms under which the examination will be performed, a fundamental change from the former practice where information was delivered to the family and their passive consent documented.

The reaction of bereaved families and the media to revelations about postmortem practice described in the Bristol Royal Infirmary enquiry illustrate a significant discrepancy between the

postmortem procedure as understood by parents and that performed in good faith by pathologists. Already, recommendations from the enquiry have been incorporated into substantial changes in the procedures for conveying information and the documentation surrounding postmortem consent.<sup>16</sup> The Department of Health has taken the process a step further, publishing an extensive series of proposed consent and information documents and a lengthy consultation article, “Human bodies, human choices”.<sup>17, 18</sup> It is felt that these documents will form the basis of future human tissue legislation in the United Kingdom which should give legal clarity to the actions of medical and scientific staff in pathology, transplantation, and medical research. However, even a brief review of the published responses to this document indicates that there is no consensus in many aspects of this area.<sup>19</sup> One can only hope that the legislation will find an appropriate balance that will facilitate and nurture the work of the medical and scientific community as well as protect the rights of the public.

What is now beyond dispute is the necessity to provide detailed, sometimes distressing, information to families about the procedure that is proposed. However, although public confidence in the procedure has undoubtedly dropped in recent years, it has not been established in the literature nor has it been my experience that families are less likely to agree to such an examination simply because of the explicit nature of the consent procedure that now precedes it.<sup>20</sup> However, it is clear from the work of Snowdon *et al* that doctors are now less likely to ask about a postmortem examination, at least in part because of their discomfort with the subject.<sup>5</sup> Perhaps allowing the neonatologist to raise the topic and then defer the detailed discussion to the pathologist would encourage greater participation.

Hill and Vance<sup>21</sup> have argued that the medical profession should “reject the possibility that the autopsy is an elective procedure. The autopsy is a professional obligation”.<sup>21</sup> It should be obvious therefore that diminished participation in the pathological arm of randomised controlled studies is a cause for concern. The first part of finding any solution involves characterising the problem. The articles by Snowdon *et al* support the contention that not just education of the public but re-education of the profession are necessary first steps to the rehabilitation of the autopsy as a

tool of audit, surveillance, teaching, and research.

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## REFERENCES

- 1 Pastores SM. Autopsies in the ICU: we still need them! *Crit Care Med* 1999;**27**:235.
- 2 Burton JL, Underwood JCE. Necropsy practice after the “organ retention scandal”: requests, performance and tissue retention. *J Clin Pathol* 2003;**56**:537–41.
- 3 Snowdon C, Elbourne DR, Garcia J. Perinatal pathology in the context of a clinical trial: a review of the literature. *Arch Dis Child Fetal Neonatal Ed* 2004;**89**:F200–3.
- 4 Snowdon C, Elbourne DR, Garcia J. Perinatal pathology in the context of a clinical trial: attitudes of bereaved parents. *Arch Dis Child Fetal Neonatal Ed* 2004;**89**:F208–11.
- 5 Snowdon C, Elbourne DR, Garcia J. Perinatal pathology in the context of a clinical trial: attitudes of neonatologists and pathologists. *Arch Dis Child Fetal Neonatal Ed* 2004;**89**:F204–7.
- 6 O’Grady G. Death of the teaching autopsy. *BMJ* 2003;**327**:802–3.
- 7 Underwood J. Resuscitating the teaching of autopsy. *BMJ* 2003;**327**:803–4.
- 8 Evans MJ, Keeling J. Histological changes in the hearts of non-survivors of the UK collaborative trial of neonatal ECMO (extracorporeal membrane oxygenation). *Arch Dis Child Fetal Neonatal Ed* 1999;**81**:F30–4.
- 9 McManus BM. The autopsy and public need: can medicine respond? *Arch Pathol Lab Med* 1994;**118**:870–2.
- 10 Benjamin DJ. New challenges to the autopsy in the United States. *Pediatr Dev Pathol* 1999;**2**:295.
- 11 Uretsky BF, Thygesen K, Armstrong PW, *et al*. Acute coronary findings at autopsy in heart failure patients with sudden death. Results from the assessment of treatment with lisinopril and survival (ATLAS) trial. *Circulation* 2000;**102**:611.
- 12 Sarode VR, Banerjee AK, Joshi K, *et al*. Autopsy findings and clinical diagnoses: a review of 1,000 cases. *Hum Pathol* 1993;**24**:194.
- 13 Harrison M, Hourihane DO. Quality assurance programme for necropsy. *J Clin Pathol* 1989;**42**:1190–3.
- 14 Vujanic GM, Cartilidge PHT, Stewart JH. Improving the quality of perinatal and infant necropsy examinations: a follow-up study. *J Clin Pathol* 1998;**51**:850–3.
- 15 McDermott MB. Obtaining consent for autopsy. *BMJ* 2003;**327**:804–6.
- 16 Royal College of Pathologists. *Guidelines for the retention of tissues and organs at post mortem examination*. London: Royal College of Pathologists, 2000.
- 17 Department of Health. *Human bodies, human choices. The law on human organs and tissues in England and Wales*. London: DoH, 2002.
- 18 Department of Health. *Families and post mortems: a code of practice*. London: DoH, 2003.
- 19 Department of Health. *Human bodies, human choices. Summary of responses to consultation report*. London: DoH, 2003.
- 20 Womack C, Jack AL. Family attitudes to research using samples taken at coroner’s post-mortem examinations: review of records. *BMJ* 2003;**327**:781–2.
- 21 Hill RB, Vance RP. The autopsy: a professional obligation dissected. *Hum Pathol* 1990;**21**:127.