SUDEN UNEXPECTED DEATH IN INFANCY (SUDI) –
THE ROLE OF THE PATHOLOGIST

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ABSTRACT

The involvement of a pathologist with forensic and pediatric training in all stages of the assessment of sudden and unexpected infant death (SUDI) is crucial as pathologists are among a limited group of medical practitioners who have been trained in evaluating the interaction of injuries, disease processes, and post-mortem changes. However, problems exist, with variations in the quality of pediatric autopsy practice and in diagnostic categories that are applied. While the development of standard definitions and protocols has improved this situation, use of the term SUDI as an umbrella term has also assisted in evaluating trends and reducing the impact of diagnostic shift. The following paper reviews the contributions that may be made by pathologists in cases of SUDI, from an initial evaluation of a death scene, through the autopsy process, discussions with families, research and participation in multidisciplinary death review committees.

Keywords: SUDI, pathology, death scene, autopsy, SIDS, infant death
INTRODUCTION

SUDI, or sudden unexpected death in infancy, is a general term that refers to all infant deaths that are sudden and unexpected, not just to those that are attributed to SIDS. A major advantage of this term is that all infant deaths will be available for study and analyses, without having the potential problems caused by differences in pathological diagnoses resulting in numerous subclassifications. For example, a case that may be attributed by different pathologists to asphyxia or SIDS, or that may be registered as ‘undetermined’, will still fall under the umbrella of SUDI.

A difficulty that has been encountered, however, is the variable use of the term SUDI, with, for example, cases due to inflicted or non-inflicted injury sometimes being excluded. Guidelines provided by the CESDI (Confidential Enquiry into Stillbirths and Deaths in Infancy) study in the United Kingdom have proved useful. Deaths were classified as SUDI if they occurred between 7 and 365 completed days of life and fulfilled the following criteria:

- deaths that were unexpected and unexplained at autopsy,
- deaths during an acute illness, not recognised as life-threatening,
- deaths due to an acute illness of less than 24 hours duration in a previously healthy infant (or death after this if life had only been prolonged by intensive medical care),
- deaths from a pre-existing occult condition, and
- deaths from any form of accident, trauma or poisoning [1].

Under this framework cases are graded from Grade Ia to Grade III based on the certainty with which a cause of death can be established. Unfortunately the importance of an adequate death scene examination is not
specified in this classification. To deal with practical considerations where investigations have not been completed it has recently been proposed to add a ‘zero’ classification to identify cases that belong within SUDI, but where critical information is missing that prevents them being classified as explained or unexplained deaths [2].

Efforts have also been made to standardize definitions of sudden infant death syndrome (SIDS). The San Diego definition of SIDS attempted to introduce a broad general definition, with more specific subcategories to enable delineation of how much information was available in arriving at the diagnosis [3]. Despite this however a disappointingly high number of papers in the literatures either fail to specify the definition of SIDS that has been used, or use an idiosyncratic version [4].

The issue of how to grade ‘sudden’ and ‘unexpected’ is one that is encountered in all of these definitions, with the limits of “sudden” death being zero, one, six and 24 hours from the time of onset of symptoms and signs to the time of death, depending on the reference source [5]. Over all infants have either been completely well or have been suffering from only apparently minor illnesses immediately prior to their deaths. Any major illness that was present was thought to be stable. Very often infants were found dead in bed, or suffered cardiopulmonary arrests during their usual activities. Death is called ‘unexpected’ when it occurs before it was anticipated.

Three broad groups of sudden and unexpected death are therefore encountered at autopsy: i) infants who were apparently well, who suffered an unexpected cardiac arrest/collapse and died within hours, or who were simply found dead in bed; ii) infants who were thought to be only mildly unwell and
who present in a similar manner to the first group. This includes those with minor illnesses completely coincidental to the underlying lethal process, those with only relatively minor symptoms and signs of a serious disease, and those in whom major symptoms and signs were either missed or deliberately ignored, and iii) infants with a known serious but stable condition who suddenly died.

THE INFANT AUTOPSY

The cornerstone of the pathologist’s contribution to this area is the autopsy. Infant autopsies are, however, complex and involve extensive dissections with appropriate tissue sampling and ancillary investigations including radiology, microbiology, metabolic screening and, on occasion, genetic analyses. Unfortunately these autopsies are not always performed to an appropriate standard with, for example, a recent study from the United States indicating that almost 10% of pathologists surveyed still did not order skeletal surveys, and that 30% favoured babygrams (single anteroposterior total body radiographs that are often taken on morgue equipment) in autopsies of infants and young children (≤ 36 months) [6].

A number of national and international protocols have been developed, in addition to published practice guidelines from expert committees [7], to provide direction in this area. While a single protocol will obviously not be suited to every jurisdiction these documents are designed to provide a template that can be adapted for local use. The two most widely recognized are the Sudden Unexplained Infant Death Investigation Report Form (SUIDI) from the Centers for Disease Control in the United States (http://www.cdc.gov/SIDS), and the International Standardized Autopsy
Protocol. The latter was developed by a working group set up by SIDS International and the NICHD in the 1990s in an attempt to provide an international protocol aimed at standardizing autopsy practices and diagnoses [8]. The use of standardized protocols has resulted in an increase in the identification of certain types of deaths, such those due to mechanical asphyxia form unsafe sleeping environments [9].

Despite these guidelines, inadequacies in infant autopsies are still reported with problems including incomplete examinations and testing [10]. This occurred in the case of Sally Clark, an English lawyer who was sentenced to life imprisonment for the murder of her two sons, the conviction later quashed by a Court of Criminal Appeal. Essential steps such as routine dissection and histology had been omitted preventing verification of alleged autopsy findings [11-13]. It has been stated that ‘investigations into the pathology and circumstances of sudden infant death are often scanty and inexpert’ with omission of essential steps such as routine histology being noted [14,15]. An investigation into a series of pediatric autopsies in Toronto, Canada, recently concluded that serious inadequacies were present and that these had led to miscarriages of justice [16].

THE ROLE OF THE PATHOLOGIST AT THE DEATH SCENE

Although most would now agree that examination of the death scene should be undertaken in all cases of sudden and unexpected infant and toddler deaths, this idea has not achieved universal acceptance [17]. Ideally every scene should be evaluated by police officers with the support of medical personnel. The involvement of a pathologist with forensic training is crucial in this process as pathologists are among the few medical practitioners with
training in the assessment of injury patterns, post-mortem changes and time of death. If a pathologist does not attend the scene, communication by telephone and the taking of photographs and video recordings are required so that adequate information is available prior to commencement of the formal autopsy dissection. A doll can be used to simulate the position that the infant was put to sleep in and found. By obtaining information from the death scene a pathologist can determine whether there are any points of concern, and whether the bedding and crib should be brought in to the mortuary for examination, or for a re-enactment with photographs. This may help to support or refute the carer’s descriptions of events [17,18].

Careful examination of death scenes has resulted in the identification of a number of dangerous sleeping environments and situations for infants such as those involving the use of ‘U’ shaped pillows, overhead suspended rocking cradles, inflatable beds and certain types of strollers, prams and cribs. Thus, properly conducted death scene examinations may identify causes of death that would not be discernable after prolonged pathological dissection or sophisticated laboratory testing [19-21].

The pathologist can also be of assistance to the family at the scene by providing information about the process that is about to occur and also by allowing parents to hold their infant in non-suspicious cases. Although viewing an infant for some time at room temperatures may cause loss of tissue detail for histology, or bacterial overgrowth that may compromise postmortem microbiology, loss of trace evidence in a non-suspicious case, where the body has probably already been moved, is usually not significant [22].
THE ROLE OF THE PATHOLOGIST AT THE AUTOPSY

Important tasks for pathologists at autopsy are to determine the cause, mechanism and manner of death. In all autopsies there needs to be a careful examination of the body with an integration of clinical and laboratory data to determine what would be a reasonable explanation for the lethal event, and what should be considered in the differential diagnosis. This also includes the exclusion of other possibilities, and so negative as well as positive findings are of importance.

A danger for pathologists is mistaking what a person may have died with, for something that they have died from [23]. An example of this in infancy involves the significance that was once attributed to minor inflammatory infiltrates as a possible etiological factor in SIDS, with studies subsequently showing them to be also a common finding in control cases [24,25]. Variations in pathological diagnoses have occurred in the past and resulted in so-called “diagnostic shift” where changes in diagnostic practices have altered the numbers of fatalities being placed in particular categories, with no overall change in death rate. Application of standardized definitions and protocols should reduce this effect, as well as the institution of multidisciplinary death review committees where all aspects of an infant’s background and health can be reviewed.

A major problem in infant autopsies is the subtlety of some conditions, and the non-specificity of findings in other situations. For example, the pathological findings in deaths due to SIDS and accidental or deliberate suffocation are often identical, which may make differentiating among them
difficult [26,27]. There is also a wide range of conditions that may cause sudden infant death with minimal preceding symptoms and signs.

Natural diseases involving all systems may cause sudden and unexpected infant deaths [5]. Given that these conditions may only be identified at autopsy, the danger in jurisdictions where autopsies are not mandatory for unexpected infant deaths is that all deaths of infants in cots will be classified as “cot deaths”. This may make subsequent research data uninterpretable.

Examples of unusual conditions involving the cardiovascular system that cause sudden infant death, and that may be first identified by a pathologist at autopsy, include pulmonary thromboembolism, anomalous coronary arteries, congenital cardiac defects, total anomalous pulmonary venous drainage, Kawasaki disease and idiopathic arterial calcification [28-37]. Intrinsic lesions of the upper aerodigestive tract that may cause lethal airway obstruction will also only be identified if careful dissection of the area is performed. This may identify thyroglossal duct or duplication cysts of the tongue, or mandibular hypoplasia [38-40]. Gastrointestinal lesions resulting in unexpected infant death include intussusception and volvulus and herniation through mesenteric or diaphragmatic defects [41-44]. Occult infections may prove lethal if there is involvement of the heart as in myocarditis, or the upper airway with critical stenosis [45,46]. Rarer conditions include leukemic infiltrates and connective tissue disorders such as Ehlers-Danlos and Marfan syndromes [47-48]. The heritable nature and genetic basis of some of these entities makes accurate identification at autopsy extremely important to ensure adequate family follow up.
Accidental deaths may involve sleeping accidents where infants become wedged between mattresses and crib sides, or between adult mattresses and a bedroom wall. Older infants and toddlers are also predisposed to hanging if clothing becomes caught on projections inside cribs or if they become entangled in curtain cords. It may be worthwhile in such cases to either visit the scene, or to bring furniture or items that were allegedly involved in the death into the mortuary with the body, so that a reconstruction can be performed [49]. In the latter cases the pathologist should readily identify parchmented ligature marks around the neck, although facial and conjunctival petechiae may be less obvious than at older ages [50,51]. Inhaled or impacted swallowed foreign bodies may also cause lethal airway obstruction, although this may not be an immediate effect [52]. Delayed deaths may follow iatrogenic injuries in hospital, for example from cardiac tamponade following central line insertion [53].

Testing the plausibility of the alleged sequence of events and providing evidence at autopsy that either corroborates or conflicts with a carer’s history is another important role for the pathologist. For example, it has been noted in recent years that there are cases of SIDS with fixed lividity on the front of the body, despite carer’s or parents insistence that the infant had been placed to sleep, and been found, on the back [54,55]. Despite this history the autopsy findings indicate that the infant was, in fact, lying face down for a significant period of time. The discrepancy with the history is most likely due to parental guilt at having allowed an infant to sleep prone, and is understandable in that context. The issue is however, that pathologists have demonstrated that parental histories may not always to be relied upon to
provide an accurate description of sleeping position, a factor which may skew future epidemiological studies.

Other issues arise with the identification of inflicted injury, which may be quite obvious in the case of a typical “battered baby”, or quite subtle with inflicted suffocation [56]. Unusual lesions such as retropharyngeal abscesses may be encountered that should raise concern about the possibility of inflicted injury, and there are often difficulties in determining the cause of death when inflicted but non-lethal injuries are present [57].

SIDS is, by definition, a diagnosis of exclusion [1,58] that now appears to be a common end point for a variety of different cardiovascular and neural mechanisms [59,60]. The “triple risk” or “fatal triangle” models hypothesize that the inter-relation of individual susceptibilities, developmental stage and environmental factors all have an additive effect that may in certain infants result in death [61-63]. Others would favor emphasizing the multifactorial nature of SIDS, giving variable probabilities for a range of risk factors [64].

Whatever the underlying mechanisms, the role of the pathologist is to determine whether there is any evidence of underlying occult organic disease or injury and how, or if, this may have contributed to death [65,66]. Every investigative step in the standard pediatric forensic autopsy has been shown to yield significant information, with improvements in protocols and autopsy practice increasing the number of alternative diagnoses being made [67-69].

RESEARCH IN PATHOLOGY

Another of the difficulties facing pathologists in the investigation of SUDI is the static nature of the material that they are dealing with. Samples have begun to undergo post-mortem changes by the time of autopsy, with variable
degrees of autolysis and putrefaction that may preclude accurate assessment of the function of tissues and organs during life. Research is still, however, possible with elegant studies on the role of brainstem neurotransmitters and receptors currently shedding light on the possible role of the serotonergic system in the pathogenesis of unexpected infant death [70-72].

Pathological research may also be useful in providing possible explanations for epidemiological observations. For example the suggestion that the risk of SIDS may be decreased by breast feeding may have some basis in the reduced levels of decosohexanoic acid (DHA) found in brain samples from formula-fed infants. DHA is a polyunsaturated fatty acid related to cerebral maturation [73].

Tissue and autopsy research can also be useful in clarifying postulated lethal mechanisms. For example, the finding of more cytomegalovirus (CMV) inclusions in controls than in SIDS cases does not support a possible causal relationship [74]. Similarly a 10-year prospective autopsy study of 248 SIDS infants screening small and large intestinal contents for Clostridium botulinum failed to reveal one positive case, indicating that in the study population CI botulinum was not a significant pathogen in SIDS, as had been previously suggested [75,76].

Certain entities such as shaken infant syndrome have engendered considerable controversy [77] and both autopsy and animal research involving pathologists can be used to clarify questions of underlying mechanisms of injury and the speed with which symptoms and signs may develop [78,79]. Other studies utilizing histology can be undertaken on autopsy material to
assist with issues around the dating of bruises and the possibility of previous episodes of trauma [80,81].

In recent years there have been instances where research and teaching were conducted using tissues and organs obtained without specific parental consent. This has resulted in the institution of much stricter guidelines, however although organ retention is an extremely sensitive issue it can still be handled in a manner that enables material for research and teaching to be retained. By working with families and legislators, in the way that those seeking organ donations for transplantation have, families are often only too pleased to assist with medical education and research. Approaching families in an open manner with explanations of what is intended and institutional ethics committee approval will only serve to facilitate this type of tissue research. In addition, provision of a printed autopsy information pamphlet may assist in helping families to understand what is involved.

INTERACTION WITH FAMILIES

Terminology

It is sometimes forgotten by pathologists engaged in pediatric practice that the foundation of their daily case work is family loss, and that routine pathological terminology may, therefore, have significant and sometimes devastating effects on already traumatized families. An example of this is the use of terms “undetermined” or “unascertained” rather than SIDS. These terms are usually used to indicate that no specific diagnosis has been, or can be, made. Pathologists may also favor these terms due to concerns about i) attributing death to an entity when there are no diagnostic findings present, and ii) the
possibility that the death may subsequently be shown to be due to inflicted suffocation [82].

Unfortunately these terms can have an extremely negative impact, with parent organizations calling them “stigmatizing”, and families feeling that this means that their infant’s death has been left unclassified [83]. One solution to this issue would be to use ‘SUDI’ as an umbrella term in such cases. This would provide parents with a term that has a definition and is therefore more acceptable to them, but pathologists would still be able to discuss possibilities without being locked into a more specific diagnosis [83].

The use of the term “SIDS for parents” should also be discouraged. This has involved using “SIDS” as a term for parents who have lost an infant due to accidental asphyxia, the aim being to protect parents from extra feelings of guilt. Unfortunately this misuse of terminology may mask dangerous sleeping environments and result in subsequent infants being put at risk.

Counselling
Parents may sometimes want to meet with the pathologist who performed the autopsy on their infant to discuss the findings and to have any questions answered. More specifically, there is often also a desire to meet the person who looked after their infant, and to be reassured that their baby was always treated with the utmost care and respect. Although these meetings are never easy, they serve as a reminder of the burden of responsibility that performing such autopsies carries, and the loss associated with these deaths.
Preventative pathology

Finally, the involvement of pathologists in unexpected infant deaths may also include helping to disseminate information on preventive measures to the community [84]. Identification of unsafe practices may include the assessment of specific types of sleeping environments, feeding patterns, or household activities such as bathing [85-89]. Publicizing such deaths may lead to the recall or modification of defective products. Another area involves parental practices such as shared sleeping and breast feeding in bed. The recognition of the dangers of these situations and the reporting of fatalities may be useful in drawing parental attention to potentially hazardous situations that they were not previously aware of [90-94].
REFERENCES


