Sudden Unexpected
Death in Infancy And The Dilemma of Defining The Sudden Infant Death Syndrome

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Abstract

Sudden unexpected death in infancy (SUDI) is an umbrella label that some employ to encompass all sudden unexpected infant deaths, whether or not explained, while others restrict its use to cases in which the cause of death is uncertain, but possibly due to asphyxia as may occur, for example, with sleeping prone, face down on a soft sleep surface, and/or being found with the head covered. Since sudden infant death syndrome (SIDS) is a diagnosis of exclusion, there is an inevitable interface between it and those cases whose deaths are potentially caused by unsafe sleep environments. This interface is especially blurred given the lack of definitive, easily identifiable postmortem marker(s) for SIDS. Therefore, present SIDS definitions are imprecise and its diagnosis remains one of exclusion. Improved death scene investigation has resulted in a diagnostic shift away from SIDS towards other causes of death such as positional asphyxia or undetermined. Unfortunately incomplete death scene investigation has hampered evaluation of the real circumstances of death in too many of the cases further contributing to confusion. In this report, the purposes for and primary definitions of SIDS are delineated. Subsequent discussion focuses on the increasing challenge to incorporate risk factors and the underlying pathology germane to the pathophysiology of SIDS into future definitions. This challenge is matched by the need to develop affordable and widely available testing that will identify pathology relevant to medical examiners and others charged with certifying the cause and manner of death.
Introduction

Sudden unexpected death in infancy (SUDI) is among the greatest tragedies of human existence. None of us is adequately prepared for the sudden and unexpected death of a seemingly healthy infant, even if the cause is subsequently explained. In these cases, forensic and pediatric pathologists are faced with the challenge of determining the cause and manner of death, a daunting responsibility given that the pathologist is called upon to serve not only as a diagnostician but also often as a grief counsellor for survivors. Other responsibilities include identification of unsafe infant care practices and products in order to notify treating physicians as well as appropriate authorities and agencies whose function it is to protect the public.

SUDI is an umbrella label that some employ to encompass all sudden unexpected infant deaths, whether or not explained, while others restrict its use to cases in which the cause of death is uncertain, but possibly due to asphyxia as may occur, for example, with sleeping prone, face down on a soft sleep surface, and/or being found with the head covered. Since sudden infant death syndrome (SIDS) is a diagnosis of exclusion, there is an inevitable interface between it and those cases whose deaths are potentially caused by unsafe sleep environments. This interface is especially blurred given the lack of definitive, easily identifiable postmortem marker(s) for SIDS. Therefore, present SIDS definitions are imprecise and its diagnosis remains one of exclusion.

Over the past decades, it has become increasingly apparent that assignment of the cause and manner of death in cases of SUDI is critically dependent upon careful investigation and reconstruction of death scenes and evaluation of the circumstances of death. With this recognition, it is not surprising that improved death scene investigations have added uncertainty and resulted in a diagnostic shift away from SIDS towards other causes of death, such as positional asphyxia or undetermined.1, 2 Nevertheless, death scene investigations are still all too often incomplete and lack of information continues to
hamper evaluation of the real circumstances of death further contributing to confusion. Historically, the cause of death in such cases was assigned to minor pathologic findings, exemplified, for example by interstitial pneumonitis, that today would not be accepted by most as valid. Thus, beginning with its original definition in 1969, sudden infant death syndrome (SIDS) became an increasingly common assigned cause of death, such that by the mid 1970s more than half of such deaths were ascribed to this cause. A recent study found that nearly two thirds of 546 cases presenting as sudden unexpected infant deaths at a single institution remained unexplained. The mandate of some SIDS definitions that the death scene and circumstances of death be evaluated has lead to recognition of potentially unsafe and even lethal sleep environments. In the past, the deaths of some infants in these sites inadequately investigated would have been ascribed to SIDS; the assigned cause of death is now shifting towards suffocation, positional asphyxia or undetermined.

Currently PubMed, the search engine for the National Library of Medicine in the United States, at the time of this writing has greater than 9200 scientific papers when “sudden infant death” is used as the keyword, greater than 9300 scientific papers with “SIDS”, and 99 when “definition” is added to SIDS. Nevertheless, no single SIDS definition is currently accepted or used universally. This report focuses upon and reviews the purposes for defining SIDS, delineates principal past and present SIDS definitions, discusses their limitations, and offers recommendations for the future.

**Purposes for Defining SIDS**

A universally accepted, widely used SIDS definition serves many purposes including:

- Certification of the cause and manner of death
- Guidelines to assist pathologists in the assessment of infant death
• A classification scheme that allows separation of cases based upon the degree of certainty of a SIDS diagnosis

• Reduction of diagnostic confusion by the establishment of uniform terms

• Vital statistics

• Research

• Funeral proceedings

• Insurance settlement

• Grief counseling and support

• Future pregnancy planning regarding recurrence risk of SIDS or other identified genetic disorders

• Development and implementation of SIDS legislation

The first and foremost purpose of a definition for any lethal disorder is to enable accurate certification of the cause and manner of death. Given that SIDS is a diagnosis of exclusion, other disorders capable of causing sudden infant death must be ruled out. As such, death scene investigation and reconstruction to evaluate the circumstances of death, and a thorough autopsy supplemented by ancillary studies must be addressed in any definition.

Scene investigation in cases of sudden infant death has led to recognition of potentially unsafe sleep environments, introducing the possibility of asphyxia in some infant deaths. Consequently, another purpose for a SIDS definition is to accommodate levels of uncertainty.

Death administration, including proceedings for funeral rituals, insurance settlement, and development of vital statistics data rely upon usable and widely accepted definitions of causes of death. Accurate vital statistics data are necessary for
optimal dispersal of limited resources from governmental agencies and foundations supporting public health activities and research.

The importance of accurate death certification, whether as SIDS or some other disorder, in ameliorating the grief of the survivors cannot be overstated. Parents are understandably reluctant to have an autopsy performed immediately following the death of their child, but their views change over time as the emotional pain engendered by their loss is increasingly replaced by questions of why their infant died. It has been my personal experience during the last three decades that parents of autopsied infants are invariably grateful that they were not left with an irresolvable uncertainty about the cause of their infant’s death.\(^9\)

Advancing research into conditions wherein the mechanisms of death are incompletely understood, as is the case with SIDS, is dependent upon accurate death certification which in turn rests upon clear definitions. It is important to have an accessible framework that delineates the characteristics of cases to allow evaluation of individual studies and to facilitate comparison of studies with one another. The present SIDS definitions (\emph{vida infra}) are broad, imprecise, and mandate a diagnosis by default. Therefore, given the limitations of the current definitions, accurate SIDS diagnosis is even more important in clarifying the interaction of its unique age distribution and its concomitant anatomic and physiologic development, external and intrinsic risk factors (e.g., prone sleep position, cigarette smoke exposure, soft bedding, head covered, and male gender), and underlying pathology in the mechanism(s) of death. Research is continually hampered by the lack of a universally accepted SIDS definition. Some jurisdictions have used classification schemes that allow a diagnosis of SIDS without death scene investigation\(^10\) despite the availability of the much earlier-published NICHD definition.\(^6\) A recent audit of 50 papers published in 2005 on SIDS found that 29 had either not specified any definition, or had used non-standard or idiosyncratic ones;\(^11\) 15
used the NICHD definition, 6 5 used the San Diego definition, 7 and 1 used the Seattle definition. 3

The failure to have a universally accepted and adequately delineated SIDS definition has led to numerous problems, including inconsistency in death certification, inappropriate inclusion or exclusion of cases, local trends in SIDS rates diverging from national rates, difficulties in comparing research findings, and denial or delay in survivors receiving grief support.

SIDS Definitions

Since originally defined, SIDS has been and continues to be a diagnosis of exclusion, i.e., if another diagnosis can not be made in a case of SUDI, then it defaults to SIDS. As such, ascribing the cause of death to SIDS necessarily rests upon comprehensive review of the medical record, death scene evaluation and the autopsy supplemented by ancillary studies. The thoroughness undertaken in each of these three efforts will increase or decrease the certainty of SIDS.

Table 1 delineates the most commonly recognized and widely used definitions for SIDS, including those stratified into categories based upon availability of information and certainty of diagnosis. Other definitions exist, but have not gained widespread acceptance. 12, 13

The first formal definition was authored by Dr. J. Bruce Beckwith in Seattle in 1969 (published in 1972) and states that SIDS is “the sudden death of any infant or young child which is unexpected by history, and in which a thorough post-mortem examination fails to demonstrate an adequate cause of death.” 3 Twenty years later, the Seattle definition was refined by an expert panel convened by the NICHD; their definition published in 1992 restricted cases to sudden unexpected deaths occurring in the first year of life and with death scene investigation. 8 The European Society for the Study and
Prevention of Infant Deaths (ESPID) definition was introduced in 1993 and has been successfully used by Scandinavian countries\textsuperscript{14} to unify their analysis of cases of sudden unexpected infant death.\textsuperscript{15} In 1992\textsuperscript{16} and again in 2003\textsuperscript{17} Beckwith proposed a two-tiered approach: a general definition intended for case management and death administration and a restrictive one intended primarily for research purposes by distinguishing infant deaths closely fitting the classic SIDS profile from those with one or more atypical features. In response to his recommendation in 2003, an international panel of pediatric and forensic pathologists and pediatricians meeting in San Diego, CA in January 2004 again refined the definition to: 1. acknowledge the long-recognized apparent relationship of SIDS with sleep,\textsuperscript{18,19} 2. broaden the concept of death scene investigation to include evaluation of the circumstances of death, and 3. generate categories of cases for research purposes. Subsequently, the National Association of Medical Examiners issued a white paper in 2007 to establish a functional approach to the investigation of sudden unexplained infant deaths outlining "bare minimum" requirements for the scope of investigation as well as recommending methods and wording for certifying infant deaths.\textsuperscript{20} In 2009, Randall et al proposed a classification based upon the level of probability that an unsafe sleeping environment caused the infant to die of asphyxia (Table 1).\textsuperscript{21} Table 2 summarizes essential elements in the current SIDS definitions. Only the San Diego definition with its stratification incorporates all of the elements most closely associated with SIDS.

Others have proposed investigational schemes to provide support and information for bereaved families, investigate the circumstances of the death and identify potentially preventable factors or evidence of neglect or abuse, collect and collate information on patterns of causes of death, identify potentially significant epidemiological or environmental factors, and modify current practices in medical or social care to reduce the risk of such deaths in the future.\textsuperscript{22}
Discussion

The continuing controversy regarding SUDI and SIDS will remain until SIDS definitions become more precise, the causal relationship of intrinsic and extrinsic risk factors and underlying pathology in SIDS is further unraveled, scene investigation improves universally, and affordable diagnostic postmortem testing for SIDS and other disorders masquerading as SIDS becomes widely available. In the meantime, other disorders causing SUDI must be carefully considered and excluded. Ion channelopathies, exemplified by long QT syndrome (LQTS), is an important consideration and has been identified in a small but significant subset of sudden infant death cases.\textsuperscript{23, 24} A SIDS definition incorporating a mandate to exclude LQTS is particularly problematic given the current high cost of molecular analysis and the necessity of collecting DNA during the autopsy if diagnostic electrocardiograms are not available from the decedent or its parents. Unfortunately, such tissue is typically unavailable. A variety of other cardiac disorders, including myocarditis,\textsuperscript{25-29} congenital heart disease (especially obstructive left heart defects),\textsuperscript{30} arrhythmogenic right ventricular dysplasia,\textsuperscript{31, 32} anomalous coronary arteries,\textsuperscript{33} and cardiomyopathies\textsuperscript{34, 35} must also be considered in cases of sudden death.\textsuperscript{32} Metabolic disorders, mostly represented by defects in fatty acid oxidation, also account for a small percentage of sudden deaths of infants, but fortunately can be diagnosed inexpensively and effectively using tandem mass spectrometry to analyze blood obtained at autopsy or from the newborn screen.\textsuperscript{36} SUDI has been caused by a variety of neoplasms,\textsuperscript{37} intoxications, accidental and inflicted injuries, and electrolyte disorders that can be identified through thorough postmortem dissections, radiography, and ancillary testing.

SIDS is no longer the mystery that faced early investigators. Beginning in the late 1960s, pathologists, especially, and other physicians began to recognize that the
majority of seemingly unexplained SUDI cases shared a characteristic epidemiologic and demographic profile despite the absence of pathologic findings that could explain their deaths. Nevertheless, the repetitive occurrence of characteristic age distribution, intrathoracic petechiae, liquid heart blood, empty bladder, minor microscopic inflammatory infiltrates, and absence of stress responses in the thymus and adrenals, allowed designation of a syndrome, though it’s underlying mechanism(s) of death are not understood.\textsuperscript{19, 38} Subsequent epidemiologic studies expanded the SIDS profile by identifying that certain factors, including prone sleep position, cigarette smoke exposure, and potentially unsafe sleep environments, enhanced the risk for sudden unexpected death.\textsuperscript{39-41} Recognition of these risk factors also provided clues to the underlying mechanism(s) of death which began in the early 1990s with identification of subtle underlying pathologic abnormalities, especially in the brainstem.\textsuperscript{42-45, 42, 46-53}

In 1994, Filiano and Kinney proposed the “triple risk” hypothesis that “sudden death in SIDS results from the catastrophic intersection of three overlapping factors: (1) critical, but unstable developmental period in homeostatic control, (2) exogenous stressor(s), and (3) an infant rendered vulnerable by underlying pathology.”\textsuperscript{54} This hypothesis has undergone progressive refinement with accrual of additional epidemiologic and pathologic data especially regarding the importance of medullary serotonergic system defects that are found in a high proportion of cases. The current hypothesis posits that SIDS, or an important subset of SIDS, may be due to abnormal brainstem mechanisms in the control of respiration, chemosensitivity, autonomic regulation, and/or arousal which impairs the infant's response to potentially life-threatening, and frequent, hypoxic, hypercarbic, asphyxial, hyperthermic stressors during sleep.\textsuperscript{50, 51, 53, 55, 56}

The earlier SIDS definitions do not adequately address the potential for an unsafe sleep environment resulting in an infant's sudden death and are thus
problematic. The spectrum of an infant’s sleep environment extends from completely safe where so-called “pristine” or SIDS IA cases are found alone and supine on a firm mattress with their heads uncovered. At the opposite end, there are cases of wedging or overlaying observed by a reliable witness that clearly explain the infant’s death. But between these two extremes, the determination of a potentially lethal asphyxial environment can be very difficult, if not impossible. The practice of bed sharing (which seems to be increasing in prevalence), is now established as an important risk factor for SIDS, and has compounded this problem. In the San Diego SIDS Research Project; only 8% of greater than 400 SIDS cases in the database were found in a completely safe sleep environment (defined as alone, supine, on a firm surface, and without the head covered).

Ascertaining the extent of the asphyxial risk at the death scene is certainly hampered when an infant is discovered dead while bed sharing with another person. When a bed sharer awakens and discovers an unresponsive infant, s/he is overwrought and may not be a reliable witness as to whether an infant was overlain. This has led to a drift toward labels such as “undetermined”, “unascertained”, and more recently “unclassified sudden infant death” or USID and away from a diagnosis of SIDS. While not specifically acknowledged in the NICHD definition, asphyxial risk is explicitly addressed in the San Diego and Randall definitions, both of which provide a spectrum that accommodates whether death caused by asphyxia is possible, probable, or confirmed. That said, entirely reliable evaluations of the death scene and circumstances of death may not be possible and/or are not always made available to the prosecting pathologist. Therefore, determination of the cause and manner of death in such cases rests upon the experience and judgment of the certifying pathologist or coroner. And yet, consensus of opinion among multiple forensic pathologists is made even more unlikely when definitions used for establishing a cause of sudden unexpected infant death are nebulous.
Aside from requirements to broaden the scope of investigation and evaluation of the circumstances of death (Tables 1 and 2), it is noteworthy that successive iterations of the SIDS definition have not substantially changed from the first definition. While it is true that SIDS IA or “classic” or “pristine” cases have decreased disproportionately over the years with incomplete implementation of the Back to Sleep recommendations, important demographic and pathologic characteristics of most of the infants dying of SIDS have not varied dramatically. Although the median age appears to be declining, the vast majority of deaths continue to occur during the first half of infancy with sparing of the first month of life. Males continue to be disproportionately represented. With rare exceptions (e.g., infants who were awake before suddenly becoming unresponsive but were otherwise similar to SIDS cases), the association of SIDS with sleep remains nearly universal. Cigarette smoke exposure is becoming an increasingly important risk factor as the prevalence of prone sleep position is declining. A recent history of minor upper respiratory infections remains common. Lower socioeconomic groups are at greater risk. Intrathoracic petechiae, minor pulmonary inflammatory infiltrates, liquid heart blood, and an empty urinary bladder are seen in the majority of cases. Pulmonary hemorrhage and intra-alveolar siderophages are frequent, but not more so than in cases of infants who have died of accidental or inflicted suffocation. However, the postmortem examination is still noteworthy for the absence of lethal pathologic changes recognized by routine forensic examination. Therefore, it is not surprising that the most current iterations have retained many of the elements of the initial definition, and have undergone changes that easily and exactly incorporate important knowledge accrued over the last 20 years.

With this in mind, the potential asphyxial dangers imposed by the sleep environment and the presence of subtle pathologic changes, primarily in the central nervous system, that render the infant vulnerable to asphyxial risks represent the most
important issues to be incorporated into an even more precise definition. It is becoming increasingly clear that subtle asphyxial challenges during sleep, such as induced by prone position on soft porous surfaces, and/or being found with the head covered can unmask abnormalities in the medullary serotonergic system, the absence of which would otherwise allow the infant to rescue itself from these challenges. While the San Diego and Randall definitions acknowledge asphyxial risk in their scale of certainty of SIDS or non-SIDS, each leaves a slippery slope that is not easily scaled. On the other hand, progress will surely be made in creating affordable testing identifying important underlying pathology that can be widely applied by many jurisdictions in a fashion similar to tandem mass spectrometry with metabolic disease.

The practicability and applicability of the newer definitions is of particular interest. Although we found the San Diego SIDS and Randall definitions easy to apply to hundreds of cases in the San Diego SIDS Research Project database, but their effectiveness is dependent upon information made available from the death scene investigation. It also became apparent that there were few cases fulfilling criteria for SIDS IA, given that metabolic testing was rarely done prior to the availability of relatively inexpensive tandem mass spectrometry to identify metabolic disorders. The inconsistent recording of whether there was a family history of sudden infant death accounted for the paucity of SIDS IA cases between the time when the CDC Guidelines were released and their replacement by the newer protocol issued by the CDC. Using the German Sudden Infant Death (GeSID) classification, Bajanowski et al found that cases fulfilling SIDS IA criteria were uncommon, given that metabolic screening and vitreous chemistry are not required in their investigational scheme. Nevertheless, the German group recommended the universal acceptance and use of the San Diego SIDS definition.

Although helpful for tracking epidemiology and demography, the present definitions may not afford enough information for research into the mechanisms of death.
For example, identifying correlations between subtle pathologic findings and mechanisms of death, as has been undertaken with investigations into the medullary serotonergic system in SIDS as well as pulmonary intra-alveolar siderophages and hemorrhage, require accurate and comprehensive collection of clinical and death scene data.\textsuperscript{47-49, 52, 69} Since definitions have limitations, databases allowing searches based on keywords in narrative reports regarding cases of sudden infant death would be helpful and should be developed.

**Conclusions and Future Directions**

Given the ability of asphyxial challenges during sleep to apparently unmask defects in the medullary serotonergic system thereby causing sudden infant death,\textsuperscript{53, 56} meaningful inclusion of asphyxial risk imposed by the sleep environment into increasingly precise SIDS definitions is a particularly difficult challenge for the future and one faced especially by those responsible for death scene investigation and reconstruction. Its importance has already been acknowledged by creation of definitions that are stratified for certification and administration on the one hand and for research purposes on the other.\textsuperscript{7, 21} Factoring more precise quantification of other risk factors into newer definitions will be critical to delineating their role in the mechanism(s) of death in SIDS. For example, considerable efforts have been undertaken regarding the correlation of the extent of prenatal and postnatal tobacco smoke exposure with an increased risk of SIDS as well as hypoplasia of one or more brainstem nuclei in the rostral and caudal raphe groups.\textsuperscript{70-73}

Consistency in assignment of cause of death in cases of sudden infant death is a second important challenge and has yet to be achieved by nosologists, certifiers or researchers nationally and internationally. Greatly improved death scene investigations and evaluations of the circumstances of death, including by multidisciplinary pediatric
death review committees, have contributed to a diagnostic shift away from SIDS toward other causes of death.\textsuperscript{1, 2, 8} Nevertheless, this trend is further confounded by the resistance of some medical examiners to the very concept and application of a SIDS diagnosis who may opt instead to assign a cause of death to minor pathologic findings, such as mild focal inflammatory infiltrates in the pulmonary interstitium or leptomeninges, despite the lack of clinical support.

If consistency in assigning SIDS as a cause of death is to be achieved, it will depend upon the accuracy, applicability, and acceptance of the definition, as well as its widespread dissemination to users. Future definitions should focus on the triple risk model for SIDS wherein demographic profiles, risk factors and underlying pathology intersect to help explain mechanisms of death. This can be problematic, however, given that identification of subtle pathologic findings requires sophisticated technology currently available only in research laboratories. Thus, another future challenge is the development of cost-effective, easily available kits that will identify these abnormalities.

SIDS definitions developed by internationally respected panels can be disseminated through several venues, beginning with publications in peer-reviewed medical journals. Endorsements by and presentation at professional societies, such as National Association of Medical Examiners (NAME), Society for Pediatric Pathology (SPP), International Society for the Prevention of Infant Death (ISPID), American Academy of Pediatrics (AAP), and the College of American Pathologists (CAP) would also contribute to widespread publicity of definitions. Research publications must identify which, if any, definition of SIDS was used for case assignment. Finally, as recommended previously,\textsuperscript{7} every SIDS definition must be constantly reevaluated and reformulated as knowledge and understanding continue to accrue.
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Definitions</th>
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<tr>
<td>Beckwith, 1970³</td>
<td>General Definition: Sudden death of any infant or young child which is unexpected by history, and in which a thorough post-mortem examination fails to demonstrate an adequate cause of death</td>
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<td>Willinger et al, 1991⁶</td>
<td>General Definition: Sudden death of an infant under one year of age which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history</td>
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| Gilbert et al, 1992⁷⁴ | IA: No abnormal findings  
IB: Non-contributory findings  
IIA: Associated findings which may have contributed to death  
IIB: Extensive/sever associated findings but not a complete explanation for death  
III: Death fully explained by findings |
| Kerbl et al, 1992⁷⁵  | Classic SIDS: No other findings than those typical for SIDS  
Borderline SIDS: Minor findings not explaining the occurrence of death  
Non-autopsied SIDS; Explained Death |
| Gregersen et al, 1995¹⁴ | Pure SIDS: Autopsy and clinical information do not reveal any cause of death.  
Borderline SIDS: Pre-existing congenital disorders, clinical symptoms and/or post-mortem findings are not severe enough to cause death.  
Non-SIDS: Explained death.  
Pathological changes identified (or not) in the lungs, cardiac system, and brain are also stratified according to the categories above. |
| Beckwith, 2003¹⁷     | General Definition: The sudden and unexpected death of an infant younger than 1 year and usually beyond the immediate perinatal period, which remains unexplained after a thorough case investigation, including performance of a complete autopsy and review of the circumstances of death and of the clinical history. Onset of the lethal episode was presumably during sleep (i.e., the infant was not known to be awake). Minor inflammatory infiltrates or other abnormalities insufficient to explain the death are acceptable.  
Category I SIDS: An infant death that meets the generic criteria and also meets all of the following standards: Age between 3 weeks and 8 months. No similar deaths in siblings, close genetic relatives, or other infants in custody of same caregiver. No evidence indicative of significant trauma, abuse, neglect, or accident. No evidence of unexplained moderate or severe stress in thymus, adrenals, or other organs and tissues. Intrathoracic petechiae are a supportive but not an obligatory or diagnostic finding.  
Category II SIDS: An infant death that meets the criteria for Category I SIDS except for 1 or more of the following features: Age younger than 1 year but outside the 3-week to 8-month range. Similar deaths in
siblings or other close genetic relatives that are not considered suspicious for infanticide (genetic consultation indicated). Inflammatory changes or other abnormalities somewhat greater than usual for Category I but not sufficient to be an unequivocal cause of death. Cases in which accidental asphyxia is considered possible but not certain: Depending on specific features of each case and the preference of the certifying pathologist, such cases can be designated as Category I or II SIDS, or as undetermined cause. A diagnosis of suffocation or asphyxia in a case that would otherwise fit Category I SIDS should be made only with strong supporting evidence. Sometimes infants may, during a death struggle, get into situations that falsely suggest mechanical asphyxia.

Category III SIDS: While performance of a complete autopsy is a mandatory prerequisite to a diagnosis of SIDS, in some developing nations, religious groups, or economic settings, the performance of autopsies is difficult or impossible. Category III SIDS is suggested solely for purposes of developing statistical data from such situations and is intended to apply to those cases that seem to fit the generic criteria for SIDS but in which no autopsy is performed. It should not be considered an acceptable alternative to autopsy in most developed societies.

| Krous et al, 2004 | General SIDS: Definition: Sudden unexpected death of an infant <1 year of age, with onset of the fatal episode apparently occurring during sleep, that remains unexplained after a thorough investigation, including performance of a complete autopsy and review of the circumstances of death and the clinical history.

SIDS IA: >21 days and <9 months, normal clinical history, term pregnancy, normal growth and development, absence of similar deaths among siblings, close genetic relatives, or other infants in the custody of same caregiver, investigation of the various scenes do not explain, safe sleep environment, potentially fatal pathologic findings at autopsy, No evidence of unexplained trauma, abuse, neglect or unintentional injury. toxicologic, microbiologic, radiologic, vitreous chemistry, and metabolic screening studies negative

SIDS IB: General definition and category IA criteria met except investigation of various scenes not performed and/or ≥1 of following analyses not performed: toxicology, microbiology, radiology, vitreous chemistry, or metabolic screening

SIDS II: Age 0–21 days or >270 days [9 months, similar deaths among siblings, close relatives, or other infants in custody of same caregiver not considered suspect for infanticide or recognized genetic disorders, Neonatal or perinatal conditions resolved by time of death, Mechanical asphyxia or suffocation caused by overlaying not determined with certainty, autopsy may show abnormal growth and development not contributing to death, inflammation or abnormalities not considered sufficient to be unequivocal causes of death may be present

Unclassified Sudden Infant Death: Criteria for category I or II SIDS not met but alternative diagnoses are
equivocal, including cases for which autopsies were not performed

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<th>Source</th>
<th>SIDS: Only a trivial potential for an overt asphyxial event existed</th>
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<td>Randall et al, 2009</td>
<td>Unclassified: Possibly asphyxial-related; When any potential for an asphyxial death existed</td>
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<td>Unclassified-non-asphyxial-related: e.g., hyperthermia</td>
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<td>Unclassified: No autopsy and/or death scene investigation; No known cause of death</td>
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<td>Randall</td>
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