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Sudden Infant Death Syndrome and Unclassified Sudden Infant Deaths: A Definitional and Diagnostic Approach

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ABSTRACT. The definition of sudden infant death syndrome (SIDS) originally appeared in 1969 and was modified 2 decades later. During the following 15 years, an enormous amount of additional information has emerged, justifying additional refinement of the definition of SIDS to incorporate epidemiologic features, risk factors, pathologic features, and ancillary test findings. An expert panel of pediatric and forensic pathologists and pediatricians considered these issues and developed a new general definition of SIDS for administrative and vital statistics purposes. The new definition was then stratified to facilitate research into sudden infant death. Another category, defined as unclassified sudden infant deaths, was introduced for cases that do not meet the criteria for a diagnosis of SIDS and for which alternative diagnoses of natural or unnatural conditions were equivocal. It is anticipated that these new definitions will be modified in the future to accommodate new understanding of SIDS and sudden infant death. Pediatrics 2004;114: 234–238; SIDS, sudden infant death.

ABBREVIATION. SIDS, sudden infant death syndrome.

Sudden infant death syndrome (SIDS) is a term that has been used to describe unexpected deaths of infants or young children when subsequent investigations fail to demonstrate a definite cause of death.1,2 The concept, which was first proposed in 1969, has been controversial, and its use has been characterized by great variability in the consistency with which the requirements of standard definitions have been fulfilled.3–5 Specifically, the term has been overused and applied to cases in which there have been obvious natural or unnatural causes of death; also, the term has been underused in favor of imprecise terms such as undetermined or unascertained. A number of other definitions that have included quite different criteria have been proposed.6–8 The most widely used definitions have made SIDS a diagnosis of exclusion.

In 1969, at the Second International Conference on Causes of Sudden Death in Infants, it was proposed that SIDS was “the sudden death of any infant or young child which is unexpected by history, and in which a thorough postmortem examination fails to demonstrate an adequate cause of death.”1 In 1989, the National Institute of Child Health and Human Development convened an expert panel to reexamine the issue of definition. The panel proposed that SIDS was “the 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.”2(p681) This definition limited the age to <1 year and specified that a thorough examination should include examination of the death scene and review of the clinical history.

In 1992, at the SIDS International Meeting in Sydney, Australia, Bruce Beckwith proposed stratification of the definition to enable separation of cases into typical and atypical groups.9 The proposal was not accepted at the time, although others subsequently supported subclassification.10 In 2003, Beckwith again called for a reexamination of the definition of SIDS, with the possibility of including positive diagnostic criteria and stratification to delineate particular subsets.11 As a result of this proposal, a meeting was held in San Diego, California, in January 2004; it was sponsored by the CJ Foundation for SIDS and involved an invited panel of experts, including pediatric pathologists, forensic pathologists, and pediatricians, all of whom had extensive experience with sudden infant death. Delegates came from Europe, North America, and Australasia.

DISCUSSION POINTS

Presentations on a variety of topics were made first. Bruce Beckwith (Loma Linda University, Loma Linda, CA) discussed the history of SIDS definitions,
the present status, and possible proposals for the future. He indicated that the meeting represented an attempt to formulate an approach to sudden infant death that would clarify subsets and assist research but that it was a work in progress that would need to be revisited regularly. Data presented from Seattle in the 1960s and 1970s demonstrated that 95% of SIDS cases were within the age range of 1 to 6 months. Edwin Mitchell (University of Auckland, Auckland, New Zealand) also discussed the need for redefinition and the possible place of risk factors in a new definition. He pointed out that, although specific risk factors were consistent across studies, the prevalence varied among countries; therefore, he considered it better to leave risk factors out of definitions. Mitchell emphasized the importance of researchers defining their study populations carefully. Henry Krous (Children’s Hospital San Diego, San Diego, CA) presented data from the San Diego study on the frequency of risk factors and the changes that have occurred since the Back to Sleep campaigns, specifically the decrease in the winter peak and the proportionate increase in the number of cases <1 month of age. Torleiv Rognum (University of Oslo, Oslo, Norway) discussed the need for a new definition and particular problems with SIDS because of its uneasy position between the health system and the legal system. Data from Oslo in the 1980s showed an age distribution similar to the Seattle results; in later years, however, there was a decrease in the number of cases 2 to 4 months of age, with increases in the numbers of cases involving younger and older infants. When cases >360 days of age were excluded from the latter cohort, however, the distribution of cases was similar to data from Seattle before the Back to Sleep program. Randy Hanzlick (Fulton County Medical Examiner’s Center, Atlanta, GA) discussed the advantages and disadvantages of reporting on the death certificate, or in other SIDS databases, those risk factors that might have been operative in causing or contributing to death, emphasizing that reporting such conditions might enable better tracking through official documentation. Hanzlick suggested that the group discuss the merits of abandoning the term SIDS and replacing it with “sudden unexplained infant death.” Problems with the use and scope of the International Classification of Disease coding were reviewed, including sometimes-inadequate specificity, overlap, and variable application among coders. Roger Byard (Forensic Science Centre, Adelaide, Australia) discussed the use of the terms undetermined and unascertained in flagging cases in which significant parts of the investigation were lacking or in which there were questions regarding possible causes of death. Byard also warned against the indiscriminate use of these terms to cover inadequate autopsy and case investigations.

A group discussion followed, during which the advantages of formulating and promulgating a redefinition of SIDS were actively debated. It was agreed that creating and supporting a more inclusive SIDS definition would facilitate uniformity in diagnosis, with a resultant increase in information on current cases. It would also enable accumulated data to be better used and would provide opportunities to propose and evaluate new theories, particularly regarding possible SIDS subsets. Existing SIDS definitions were considered inadequate, often being applied too generally or too restrictively, and were exclusionary, failing to incorporate known features of the syndrome (such as sleep and age range). The conclusions of the group were based on assessments of current trends and data and were intended to be fully reevaluated in the future, when they will likely need to be modified to accommodate new developments.

The redefinition was also considered a useful step to enable more precise monitoring of changing epidemiologic patterns in sudden infant deaths and to allow more valid international comparisons. By more clearly defining subsets of sudden infant deaths, monitoring of the effects of public health recommendations and alterations in infant care practices can be facilitated. Finally, more precise definitions of subsets of sudden infant deaths, with specification of requirements for diagnosis, should help standardize investigative protocol development, by improving examinations of the circumstances of death and autopsy investigations and bringing investigations more in line with recommended guidelines. Providing more information and more rigorous subclassification of cases should also facilitate integrated multiagency approaches to such cases.

RESULTS

Definitional Approach to Sudden Infant Death

The following definition and subclassification were agreed upon.

General Definition of SIDS

SIDS is defined as the 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.

Category IA SIDS: Classic Features of SIDS Present and Completely Documented

Category IA includes infant deaths that meet the requirements of the general definition and also all of the following requirements.

Clinical
- More than 21 days and <9 months of age.
- Normal clinical history, including term pregnancy (gestational age of ≥37 weeks).
- Normal growth and development.
- No similar deaths among siblings, close genetic relatives (uncles, aunts, or first-degree cousins), or other infants in the custody of the same caregiver.

Circumstances of Death
- Investigation of the various scenes where incidents leading to death might have occurred and determination that they do not provide an explanation for the death.
• Found in a safe sleeping environment, with no evidence of accidental death.

Autopsy

• Absence of potentially fatal pathologic findings. Minor respiratory system inflammatory infiltrates are acceptable; intrathoracic petechial hemorrhage is a supportive but not obligatory or diagnostic finding.
• No evidence of unexplained trauma, abuse, neglect, or unintentional injury.
• No evidence of substantial thymic stress effect (thymic weight of <15 g and/or moderate/severe cortical lymphocyte depletion). Occasional “starry sky” macrophages or minor cortical depletion is acceptable.
• Negative results of toxicologic, microbiologic, radiologic, vitreous chemistry, and metabolic screening studies.

Category IB SIDS: Classic Features of SIDS Present but Incompletely Documented

Category IB includes infant deaths that meet the requirements of the general definition and also meet all of the criteria for category IA except that investigation of the various scenes where incidents leading to death might have occurred was not performed and/or ≥1 of the following analyses was not performed: toxicologic, microbiologic, radiologic, vitreous chemistry, or metabolic screening studies.

Category II SIDS

Category II includes infant deaths that meet category I criteria except for ≥1 of the following.

Clinical

• Age range outside that of category IA or IB (ie, 0–21 days or 270 days [9 months] through first birthday).
• Similar deaths among siblings, close relatives, or other infants in the custody of the same caregiver that are not considered suspect for infanticide or recognized genetic disorders.
• Neonatal or perinatal conditions (for example, those resulting from preterm birth) that have resolved by the time of death.

Circumstances of Death

• Mechanical asphyxia or suffocation caused by overlaying not determined with certainty.

Autopsy

• Abnormal growth and development not thought to have contributed to death.
• Marked inflammatory changes or abnormalities not sufficient to be unequivocal causes of death.

Unclassified Sudden Infant Death

The unclassified category includes deaths that do not meet the criteria for category I or II SIDS but for which alternative diagnoses of natural or unnatural conditions are equivocal, including cases for which autopsies were not performed.

Postresuscitation Cases

Infants found in extremis who are resuscitated and later die (“temporarily interrupted SIDS”) may be included in the aforementioned categories, depending on the fulfillment of relevant criteria.

DISCUSSION

Before the meeting, participants were asked to submit their own definitions of SIDS. From this pool, a common definition that incorporated agreed-upon points was formulated. Although in previous definitions SIDS was a diagnosis of exclusion, it was recognized that there were certain repetitive features common to the majority of cases. It was these features that led early investigators to suggest that most, but not all, sudden, unexplained, postneonatal deaths represent a distinct syndrome, reflecting a common cause or, more likely, a common mechanism of death. The elements of this presumptive syndrome were ignored during formulation of the previous exclusion-based definitions, however. Major features emphasized in early SIDS studies included an association with sleep and a relatively narrow age range and frequency distribution, sparing the first weeks of extrauterine life, peaking during the 2nd to 4th months, and declining rapidly thereafter. Deaths with onset while awake are rare and most probably involve a different mechanism of death, compared with classic SIDS deaths. A general definition that involved these specific criteria was created, to include as many cases as possible in the SIDS classification. This was thought to be useful for certification purposes and also for general epidemiologic studies. The phrase “death scene examination” was changed to “review of the circumstances of death,” with the aim of encouraging more comprehensive assessments of the events surrounding death. For example, although an infant’s death may occur in a hospital after attempted resuscitation and thus the scene is technically an emergency department, the circumstances involve the crib, room, and house where the infant was found. Review of the circumstances of death includes not only examination of the death scene but also assessment of all of the environments an infant might have been in before or after death.

After implementing a broad overall definition, participants decided to subcategorize SIDS cases on the basis of specific epidemiologic features and the amount of information available. This was prompted partly by the knowledge that the number of classic SIDS cases, typical of those occurring in the 1970s and 1980s (before the Back to Sleep and Reduce the Risks campaigns), had decreased and it was likely that the remaining cases represented a relatively more heterogeneous group, with varied underlying mechanisms of death.

Stratification of cases of sudden infant death into subcategories was therefore undertaken to:
• Provide recommended guidelines for general case assessment, classification, and diagnosis.
• Assist pathologists by detailing steps for infant death investigation and diagnostic categorization.
• Identify and include cases that recently have been excluded incorrectly from SIDS groups because of findings of bed-sharing and prone sleeping position.
• Formalize current practices among pathologists of separating cases on the basis of the degree of certainty and the confidence with which a diagnosis of SIDS can be made.
• Reduce diagnostic confusion by introducing uniform terms.
• Provide a framework for researchers and identify the most typical cases for study.
• Assist in the evaluation of published data.
• Provide a readily accessible categorization of SIDS cases on the basis of age groups and investigative information.

Dividing cases of sudden infant death that fit the general definition of SIDS into subgroups should not have an effect on epidemiologic studies of the syndrome as a whole, because most cases would still be classified as SIDS. However, researchers looking for classic SIDS cases to study could take them from category IA. The group considered it important that researchers specify which subgroups were used for studies, because that would enable immediate assessment of the rigor with which cases had been investigated and determination of how closely the study group represented classic SIDS cases. It was also recommended that future research should be undertaken to examine similarities and differences among the subgroups, which might clarify specific causes.

The age range of 3 weeks to 9 months was chosen on the basis of an analysis of data from the Avon and Confidential Enquiry Into Stillbirths and Death in Infancy studies in the United Kingdom, New Zealand Health Information Services data, the Chicago and San Diego SIDS studies in the United States, studies at the Rettsmedisinsk Institut in Oslo, Norway, and the Westphalian and German Sudden Infant Death studies in Germany, by Edwin Mitchell. Pooling of data from those studies showed that the 5th to 95th percentile limits for SIDS deaths were ∼3 weeks to 9 months.

Prone position was considered an established risk factor for SIDS deaths but not a cause of suffocation unless specific circumstances (such as a face-down position on an incompletely filled waterbed or in a thin plastic bag) could be demonstrated. For this reason, infants found prone with no evidence of suffocation could be included in any of the categories, depending on other features. Prone sleeping involves an array of potential problems, including diaphragmatic splitting/fatigue, rebreathing of carbon dioxide, reflex lowering of vasomotor tone with tachycardia, blunting of arousal responses (including decreased cardiac responses to auditory stimulation), alteration of sleep patterns, upper airway obstruction resulting from soft bedding, and overheating, and is most likely a problem only among infants with underlying susceptibilities. Similarly, although there is evidence of increased risk of infant death in shared sleeping situations, shared sleeping does not automatically exclude SIDS as a possibility, if it can be shown that the infant was not at risk of accidental asphyxia. It should be recognized that the position in which the infant is found sometimes reflects agonal movement and is not necessarily the position of the infant at the onset of the fatal event.

It was acknowledged that a number of different and variably defined terms were being used to classify unexpected infant deaths. Sudden unexpected death in infancy is a general term that covers SIDS and other types of unexpected infant deaths. When an infant dies suddenly and unexpectedly and intentional or unintentional fatal injury can be excluded, death may be attributable to a specific disease entity, such as myocarditis, or to SIDS. Deaths that cannot be precisely subcategorized or classified have been deemed undetermined, undeterminable, unascertained, or unascertainable, but this has created concerns about the specificity of these terms. The merits of replacing the term SIDS with sudden unexplained infant death were briefly discussed during the meeting, but it was the consensus of the group that SIDS still served a useful purpose. The term unclassified sudden infant death was proposed to account for cases in which the criteria for category I or II SIDS were not met or an autopsy was not performed. These cases may represent SIDS deaths, but there is insufficient information available to make that judgment or there are certain atypical features, such as inflicted but nonlethal injury, that are insufficient by themselves to establish a cause of death but are thought to preclude use of the term SIDS. Atypical features may also include underlying organic diseases, such as an anomalous coronary artery without evidence of myocardial ischemia, which may also preclude a confident statement about a possible cause of death.

The investigation of infant deaths should be conducted according to established protocols and should include careful evaluation of the death scene, external examination of the body with photographic documentation, radiologic examination, internal examination with photographic documentation, and histologic, microbiologic, toxicologic, biochemical, metabolic screening, and genetic studies if indicated. Guidelines for and confirmation of the usefulness of such stepwise examinations are available in the literature.

Finally, it should be reiterated that these proposals represent nothing more than attempts to improve definitions and to facilitate more accurate investigation, diagnosis, and categorization of cases of unexpected infant death. Considerable public, professional, and media attention has been paid recently to certain high-profile court cases in which the standards of investigation and pathologic analyses were far from acceptable. This does not mean that the underlying concepts are flawed; rather, it means that diagnostic terms and protocols should be more rigorously defined and standard investigative approaches should be maintained. The proposed framework is a work in progress, which will need to be continually reformulated and refined as more knowledge becomes available and our understand-
ing of these complex and challenging cases becomes clearer. (At a pathology workshop in Canberra, Australia, in March 2004, forensic and pediatric pathologists representing forensic institutions and hospitals from all Australian states and territories unanimously endorsed the new general San Diego definition and recommended its national implementation.)

REFERENCES


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