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The San Diego definition of SIDS: practical application and comparison with the GeSID classification

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Abstract The new definition of the term sudden infant death syndrome (SIDS) and the criteria introduced in San Diego for the subclassification of cases have been used to re-classify the first 100 consecutive cases of sudden and unexpected infant deaths that were registered with the German SIDS study (GeSID). Although there are 30 different variables that have to be considered in the general and stratified sections of the San Diego definition, it is practical, in particular, as an international standard to perform scientific studies. The comparison of the San Diego definition and the classification used for GeSID shows similarities in the methods but differences in the criteria used. Nevertheless, the numbers of cases classified as SIDS and borderline SIDS are similar (San Diego $n=69$, GeSID $n=74$). The SIDS IA criteria of the San Diego definition were not fulfilled by any case because metabolic screening and vitreous chemistry were not included in the GeSID investigation scheme. An important advantage of the San Diego definition is the introduction of the category of unclassified sudden infant death, which includes cases for which no autopsy was performed. This demonstrates

that such cases cannot be classified as SIDS. In conclusion, we recommend the universal acceptance and use of the San Diego SIDS definition.

Keywords Sudden infant death syndrome · San Diego definition of SIDS · German study on SIDS · Classification of cases

Introduction

In 1969 Bruce Beckwith [1] introduced the term sudden infant death syndrome (SIDS) and supplied its initial definition. Since then, the concept has been a source of controversial discussion [2], and the application of the refined definition has shown a wide variation. In 1989 the Seattle definition [1] was introduced by a panel of experts [National Institute of Child Health and Human Development (NICHD) definition], the term “thorough post-mortem examination” was defined more precisely, and the examination of the death scene, a complete autopsy and the review of the clinical history were introduced [3]. In the 1990s various authors proposed and used different subclassifications of SIDS cases [4–7]. As a result of Beckwith’s call for a re-examination of the definition in 2003 [5], a panel of experts met in San Diego in January 2004 and proposed a new definition [2]. In addition to a more general definition, which can be used for certification purposes and for general epidemiological studies, a subclassification based on specific epidemiological features and the amount of information available from other sources was also agreed upon.

To test the practicality of the new San Diego definition, 100 consecutive cases of sudden and unexpected infant death which were registered and investigated in the German SIDS Study (GeSID) [7] were reclassified, and the factors responsible for different classification were investigated.

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Table 1 GeSID study: pathological categories, criteria for diagnoses [7]

Pathological category	Results of autopsy and histology
P-cat 1 = SIDS	Without pathological findings from autopsy and additional investigations
P-cat 2 = SIDS+	With minor pathological findings in autopsy and investigations: Minor infections of the respiratory tract Rhinitis, otitis media, pharyngitis, tracheitis Bronchitis, mild/intermediate forms of peribronchitis Mild/intermediate bronchiolitis and interstitial pneumonia Tonsillitis Mild abnormalities and congenital deformations Mild forms of hepatitis/hepatosis Enteritis without dehydration Mild forms of nephritis/nephrosis Local infection with cytomegalovirus Metabolic disorders without symptoms of disease which do not usually cause sudden death (e.g. treated phenylketonuria)
P-cat 3 = SIDS+	Severe findings: Metabolic disorders which can cause sudden death (e.g. fatty acid oxidation disorders, primary metabolic myopathy) [14] Interstitial pneumonia showing BI Severe bronchiolitis Enteritis with dehydration Peri-/myocarditis, especially of the borderline type Mild forms of meningoencephalitis
P-cat 4 = explained death	Clear cause of death: Bronchopneumonia Interstitial pneumonia with BI and carditis Bronchiolitis if obstructive Severe meningoencephalitis Major congenital disorders Generalised infection Myocarditis with necrosis of myocytes
<i>P-cat</i> Pathological category, <i>BI</i> bacterial superinfection	

Materials and methods

German SIDS Study

Between 1998 and 2001 455 infants who had apparently died suddenly and unexpectedly had been reported to the GeSID centre.

The exclusion criteria for the study were:

- Death during the first week of life or later than 12 months after birth,
- Cases where death was attributed to known diseases,

- Unnatural deaths, and
- Parents had insufficient language knowledge, with the result that informed consent could not be obtained.

To define the SIDS cases for the GeSID, the NICHD definition was used [3]:

“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”.

The cases were investigated using a standardized autopsy protocol (SAP). This SAP is in accordance with the European guidelines for medico-legal autopsies [8] and closely reflects the International Standardised Autopsy Protocol [9]. The autopsy included a thorough external examination, a complete internal examination, extensive histology, a full analytical toxicology scheme, radiology, microbiology, virology, and neuropathology [7].

Based on the results of these investigations, all cases were classified into one of four pathological categories (P-cat) using defined criteria (Table 1):

- No pathological findings (SIDS),
- Minor pathological changes (SIDS+),
- More severe findings, which are not yet an equivalent of the cause of death (SIDS+), and
- Findings which explain the death (non-SIDS).

The results of the death scene investigation and the analysis of the clinical history were included in the extended category (E-cat, Table 2).

Table 2 GeSID study: extended categories

Extended category	Previous history and circumstances of the death
1	P-cat 1 and no unusual previous history
2	P-cat 1 or 2 in addition to minor findings in circumstances and previous history: Infection 48 h prior to death Fever <40°C (rectal) Malnutrition
3	P-cats 1–3 and severe findings: Fever >40°C (rectal) Vomiting and/or diarrhoea >24 h Possible suffocation in soft bedding No feeding >12 h until 12th week of life, >14 h after the 12th week of life
4	P-cats 1–4 and findings explaining the death Case reports: Emergency doctor measured rectal temperature of 42°C Significant loss of body weight over several weeks, with clear signs of dehydration

Additional information on pathological categories, criteria deduced from information on the circumstances of the death and the previous history are included

Out of all cases, the first 100 which were registered in 1998 and 1999 in the study centre were re-classified using the criteria of the San Diego definition.

San Diego definition

- In the general section, an addition has been made (to the NICHD definition) to the effect that, in line with the definition, the onset of the fatal episode apparently should have occurred during sleep. The term “death

scene investigation” has been broadened and substituted by “review of the circumstances of death”.

- In the stratified section (Table 3) [2], a subclassification has been proposed, and a criteria was defined for categorizing the circumstances of death, the autopsy findings and the clinical history. The infant’s age was introduced as an additional criterion for differentiating SIDS cases.

Table 3 Criteria used in the San Diego definition

	Clinical history	Circumstances of death	Autopsy
SIDS general definition	Sudden and unexpected death Under 1 year of age Lethal episode during sleep Death unexplained by CH	Unexplained after review of the circumstances	Unexplained after complete autopsy
Specific definition			
Category IA SIDS	1. Older than 21 days, under 9 months 2. Normal CH 3. Full-term pregnancy (>37 weeks) 4. Normal growth and development 5. No similar deaths in siblings/relatives	Scene investigation performed and gave no explanation Safe sleep environment No evidence of an accident	1. No lethal pathological findings 2. No unexplained trauma, abuse, neglect or unintentional injury 3. No substantial thymic stress 4. Toxicology, microbiology, radiology, vitreous chemistry and metabolic screening were negative
Category IB SIDS	1–5 (criteria for category IA SIDS)	Scene investigation was not undertaken	1–4 and 5. One or more of the following analyses were not performed: toxicology, microbiology, radiology, vitreous chemistry and metabolic screening
Category II SIDS	differences to category I criteria: 6. Age range (0–21 and 270–365 days) 7. Neonatal/perinatal conditions that have resolved by the time of death 8. Similar deaths in siblings, near relatives	Mechanical asphyxia or suffocation by overlaying not determined with certainty	1–5 and 6. Abnormal growth and development not thought to have contributed to death 7. More marked inflammatory changes or abnormalities not sufficient to cause death
USID	Criteria for category I or II SIDS are not fulfilled	Alternative diagnoses of natural or unnatural death are equivocal	Autopsy has not been performed

CH Clinical history, USID Unclassified Sudden Infant Death

Table 4 Comparison of the two classifications used

San Diego	GeSID (extended category)					Sum
	1 (SIDS)	2 (SIDS+)	3 (SIDS+)	4 (explained)	Unclassified	
SIDS I A	–	–	–	–	–	0
SIDS I B	3	18	4	–	–	25
SIDS II	–	19	25	–	–	44
USID	–	–	5	–	10	15
Explained	–	–	–	16	–	16
Sum	3	37	34	16	10	100

Results

German SIDS Study

In 10 out of 100 cases, the parents did not wish to participate in the study. These cases were therefore excluded from the study and defined as “unclassified”. Of the remaining 90 cases, 3 were classified as category 1 SIDS (typical SIDS), 37 infants showed minor changes or symptoms (category 2 SIDS, SIDS+), 34 cases had more severe changes and/or symptoms (category 3 SIDS, SIDS+) and, in 16 cases, a cause of death was found; these cases were thus excluded from the SIDS group (category 4; explained death, non-SIDS).

San Diego: general definition

The 10 excluded cases were classified as unclassified sudden infant death (USID). All of the remaining 90 infants died suddenly and unexpectedly; they were aged between 8 and 365 days.

Out of these 90 cases,

- Only one infant did not die during sleep (this 19-day-old boy died in his mother’s arm), which meant that the case had to be excluded from SIDS (final classification, explained death due to autopsy findings).
- The result of the death scene led to an exclusion of two infants from SIDS (ambient temperature $\geq 27^{\circ}\text{C}$, body temperature $> 42^{\circ}\text{C}$, thick blanket, two/three layers of clothing, intrathoracic petechia, dehydration, brain oedema = explained death [10]).
- Autopsy results (including related investigations) led to an exclusion of 13 infants from SIDS [11 infants died of a natural death (severe dilatative cardiomyopathy, $n=1$; intussusception of the thin bowel, $n=2$; pneumonia, $n=6$; meningitis, $n=1$; and septicemia, $n=1$), whereas two infants died of unnatural causes (suffocation by soft covering, $n=1$ and methadone poisoning, $n=1$ [11]). These 13 cases have to be classified as explained deaths.
- The clinical history (and autopsy findings) gave an explanation for the death in one case, but this had been already excluded from SIDS due to the autopsy findings.

The remaining 74 cases were classified as SIDS. Out of these, there were eight with no information on clinical history. The classification of these was based on the parental statement that the infant did not have preceding health or developmental problems.

San Diego: detailed classification

None of the cases could be classified as SIDS IA because vitreous chemistry and metabolic screening (except for fat staining of the liver and muscle and urine screening for acetone and glucose) were not included in the GeSID protocol. The remaining 74 SIDS cases were further subdivided as the following:

- Six infants who did not meet the defined age range,
- Sixteen infants who displayed an exceptional clinical history,
- Eight infants who were born before the 37th week of gestation,
- Eleven infants who did not display normal growth and development,
- Four infants for whom similar deaths of siblings or near relatives had occurred,
- Six infants who were not found in a safe sleep environment,
- Seven infants who showed signs of physical violence or neglect,
- One infant who showed severe thymic stress,
- One infant with a non-fatal methadone poisoning, and,
- Four infants with significant pathological results of microbiological screening.

A total of 25 out of the 74 cases could be classified as SIDS IB. In these cases, the death scene was not investigated, or the analyses listed (Table 3) were not carried out.

Forty-four out of 74 infants who met the general definition were classified as SIDS II because they were outside the age range of SIDS I ($n=6$), similar deaths had occurred in the family ($n=4$), they showed perinatal or neonatal problems ($n=12$), there was suspicion of overlying ($n=1$) and they displayed abnormal growth and development ($n=11$) and/or more intensive inflammatory changes ($n=10$).

Five out of the 74 cases meeting the criteria of the general definition had to be excluded from SIDS:

- In two cases because an unexplained trauma was found that did not cause the death,
- In two cases in which there was suspicion of neglect and,
- In one case in which methadone was detected in a non-fatal concentration (mother was a known drug user).

The comparison of the GeSID classification and the San Diego definition shows that there are similarities (Table 4). In particular, the cases of GeSID categories 2 (SIDS+) and 3 (SIDS+) can be assigned to the categories IB and II of the San Diego definition.

Discussion

Compared to the NICHD definition, the San Diego general definition of SIDS includes one new element: the onset of the fatal episode should occur during sleep. Because the GeSID criteria were based on the NICHD definition, this new element was easy to incorporate. Only one out of the 100 GeSID cases had to be excluded from SIDS because the lethal episode happened while the infant was awake in its mother's arm.

The detailed reclassification of the GeSID cases using the San Diego definition required a completely new analysis of each case. The general and stratified sections of the San Diego definition includes 30 different variables in the results of specific investigations—autopsy findings, including additional investigations, death scene investigation and clinical history. This set of information differs from the information that was used for the GeSID and had to be selected retrospectively from all the information available. Although the definition is complex, it is practicable.

The definition of category IA SIDS includes very narrow criteria that can only be fulfilled by a small number of cases. None of the GeSID cases met all these criteria because a metabolic screening (except for fat staining of liver and muscle and for glucose determination in urine that are currently considered inadequate and insufficiently precise) and vitreous chemistry had not been performed. If these two criteria were not considered, 11 out of 90 cases could be classified as SIDS IA (12%). The analyses of some large SIDS studies shows that none of the protocols used in the past required as mandatory all the investigations which need to be carried out in SIDS IA cases [Nordic study, International Standardised Autopsy Protocol, GeSID, Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI) study [9, 12] and Australasian SIDS autopsy protocol [13]]. Therefore, the question arises as to whether it is impractical to have such a small subgroup when the worldwide incidence rate has reduced so markedly. If the

only difference between SIDS IA and IB is the non-conducting of an investigation and it is only of significance in a small number of cases, cases of subgroups IA and IB can be grouped together for the purpose of epidemiological analyses.

An important advantage of the San Diego definition is the introduction of the USID group with respect to cases without autopsy. This new category makes it absolutely clear that a sudden and unexpected infant death cannot be classified as SIDS unless an autopsy has been performed. Another important advantage is the flexibility of the definition. As stated by Krous et al. [2], this definition can and will be modified “in the future to accommodate new understanding of SIDS”.

By defining subsets of sudden infant deaths, it should be possible to monitor both changes in epidemiological patterns and public health recommendation. Finally, if the definition should be generally accepted and applied, a “more valid international comparison” may be possible [2].

It is a problem that there are cases which fulfil the criteria for the general SIDS definition but which have to be excluded from SIDS altogether if there are positive findings in toxicology, microbiology, vitreous chemistry or metabolic screening tests. These investigations are not explicitly included in the general definition, but they are in the stratified one. For example, if no toxicology test had been performed, a case of fatal poisoning could not have been detected, and the case could be classified as SIDS in accordance with the general definition, category IB or II SIDS in accordance with the criteria of the subclassification. This does not constitute an improvement compared to the NICHD definition.

The most obvious differences between the GeSID classification and the San Diego definition are exemplified in cases that were classified as GeSID category 3 SIDS (more severe pathological findings which do not necessarily explain the cause of death, $n=34$). When the San Diego definition was used, five of these cases must be excluded from SIDS: in one case, an unexplained fracture of the humerus was found, two cases raised suspicion of neglect, and in two cases, microbiological tests showed the presence of *Streptococcus pneumoniae*. On the other hand, four cases (GeSID category 3) could be classified as SIDS IB because the time interval between the last feeding and the discovery of death was included as a criterion in GeSID (Table 2, E-cat 3) but not in the San Diego definition.

In conclusion, our study shows that the new San Diego classification has strengths and weaknesses. Overall, in our opinion, the strengths outweigh the weaknesses, and we recommend its acceptance and use. We recommend its endorsement by professional forensic, pathological and paediatric societies and its adoption in the investigation of sudden infant deaths.

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