

# Medical, Forensic and Social Quandaries of Sudden Infant Death Syndrome Today

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**Abstract:** *Sudden Infant Death Syndrome (SIDS) is described as the sudden, unexplained death (with no attributable cause, during sleep) of a seemingly healthy child before reaching the first year of life. Statistically, SIDS is recognized today as a leading cause of death in infants aged 1 to 12 months. In the present article the authors have analyzed known risk factors, classifications and current standards of forensic investigation while highlighting the necessity of detailed clinical history, autopsy, scene of death examination and lab findings (radiology, metabolic anomalies, infectious diseases and toxicology) in SIDS diagnosis. For an infant death to be considered SIDS, all other possible causes of death must be first excluded, the diagnosis requiring detailed collection and analysis of antemortem patient data and a complete autopsy. Although the forensic methods of today are more exact, the distinction between SIDS and other causes of death (e.g. unintentional asphyxiation, infanticide) remains very difficult in some cases.*

**Keywords:** *Sudden Infant Death Syndrome; risk factors; diagnosis; differential diagnosis; autopsy.*

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During the Second International Conference of Sudden Infant Death held in 1969 in Seattle, SIDS was defined as “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” (Krous et al., 2004).

In 1986, the U.S National Institute of Health coined the term ALTE “apparent life-threatening event” for a sudden state of apnea with change in skin color (pallor/cyanosis), muscle tonus and sensation of suffocation or drowning (McGovern & Smith, 2004; Mueller-Nordhorn et al., 2020). Although sometimes viewed as a precursor to SIDS, urgent medical intervention in cases of ALTE can prevent death.

Subsequent studies of the American Academy of Pediatrics have dispelled the notion that ALTE precedes SIDS (Rini et al, 2016):

- Approximately 50% of ALTE cases happen during periods of wakefulness, while SIDS is known to appear during sleep (McGovern& Smith, 2004; Rini et al., 2016);
- ALTE is more common in infants of Asian descent while SIDS has a higher incidence in African American populations (Farrell et al., 2002);
- ALTE, manifesting with apnea and bradycardia is less frequent during the second part of the night as opposed to SIDS;
- SIDS favors infants born to young mothers while ALTE is more common in infants with older mothers;
- ALTE has an equal distribution among sexes while SIDS is more frequent in males (McGovern& Smith, 2004; Rini et al., 2016);

Common risk factors are smoking during pregnancy and a prone sleeping position (Kiechl-Kohlendorfer et al., 2004; Luijckink et al., 2020; McGovern& Smith, 2004; Rini et al., 2016; Sontag et al., 2020).

Statistically, this syndrome is a leading cause of death in infants aged 1 to 12 months (8 days to 1 year), with a peak at 2 to 4 months (Mahat-Shamir, 2020). About 90% of the cases are under 6 months of age, the incidence decreasing after 8 months. Death occurs most frequently in winter, during sleep, and is more common in males (American Academy of Pediatrics, 2005; Lavista Ferres et al., 2020, Lupu et al., 2017; Vennemann et al., 2007).

A number of risk factors are acknowledged for SIDS (De Faria et al., 2020), including the prone sleeping position (and lateral), soft bedding, overheating during sleep, sleeping in the same bed with the parents, exposure to cigarette smoke, toxic/drug abuse during pregnancy, young age

of the mother and short periods between pregnancies (Sanchez et al., 2020; Shipstone et al., 2020). Social risk factors include lack of monitoring of infant during sleep, lack of attention (Goian & Breaz, 2020) and parents that are uninterested/uneducated in childcare (Ruiz-Botia et al., 2020). Children with a history of ALTE/BRUE, complications before/during/after birth, premature births (esp. with bronchopulmonary dysplasia) and a family history of SIDS (prior sibling death due to SIDS increases the risk up to 10 times depending on the study) are correlated with a higher risk of SIDS. Genetics is one of the various possible risk factors. A study has shown that about 10% of the 321 infants admitted to an ICU at Rady Children's Hospital died (Kingsmore et al., 2020). Among them, 10 cases were diagnosed with genetic diseases (Kingsmore et al., 2020; Koeffler et al., 2020).

The anatomic and forensic pathology classification of SIDS consist of:

- *Classic SIDS*: unexpected infant death, no pathological findings after complete examination after death (exception being pleural and thymus petechiae, cerebral edema or glial cell hyperplasia);
- *Borderline SIDS*: unexpected infant death with some findings (ear infection, bronchitis, inflammatory bowel disease, etc.) during autopsy, but no conclusive cause of death;
- *No autopsy*;

The SIDS definition in use was established in 2004 in San Diego, California, and describes a sudden and unexpected death of an infant younger than 1 year, that takes place during sleep and remains without known cause after complete autopsy and analysis of patient history and circumstances of death. Other names for this diagnosis are sudden death, crib death and unexpected infant death. During the 2004 meeting, experts including forensic pathologists, pediatricians and pediatric pathologists agreed on a classification that is still in use worldwide (Shipstone et al, 2020; Luijerink et al., 2020).

*Category IA SIDS* includes cases that subscribe to the 2004 definition and all the following:

- *Clinical*: age 21 days-9 months, normal patient history, normal growth and development, no family history of SIDS;
- *Circumstance of death*: no explanation found after scene investigation, death occurred in safe environment, no evidence of accidents;
- *Autopsy*: no fatal findings, no unexplained abuse, trauma, neglect, no thymic stress effect, moderate bronchial and/or lung tissue

lymphoid infiltrates, less than 10 neutrophils per alveola in less than 10 alveoli, negative toxicology, chemistry, metabolic, radiology, microbiology reports;

*Category IB SIDS* includes cases that subscribe to the 2004 definition and all criteria for IA but without death scene investigation and/or one or more of the following was not performed: radiology, toxicology, microbiology, metabolic screening, biochemistry.

*Category II SIDS* includes cases that subscribe to I but lack one or more of:

- *Clinical*: other age than category I, positive family history, pathological conditions resolved by time of death;
- *Circumstances of death*: possible mechanical asphyxia or suffocation during sleep;
- *Autopsy*: growth and development variations and marked inflammation (lymphoid infiltrate in more than one lung section, more than 10 inflammatory cells per alveoli in more than 10 alveoli) not considered cause of death;

*Unclassified SIDS*: Cases that do not subscribe to category I or II but for which other causes of death cannot be diagnosed or cases with no autopsy.

*Post-resuscitation cases* “temporarily interrupted SIDS”

The American Academy of Pediatrics changed in 2016 the term ALTE with ESIR/BRUE “brief resolved unexplained event”, underlying the transient nature of the episode and its unknown cause (Arane et al., 2017; Tieder et al., 2016). The event involves an infant younger than 1 year, is sudden, short and must contain at least one of the following: cyanosis and/or pallor, irregular breathing, muscle hyper/hypotonicity, decreased alertness and reaction to stimuli. The ESR/BRUE diagnosis is chosen when the patient history and physical exam reveal no pathological causes for the event.

Investigating a case of SIDS requires close collaboration between health professionals with experience in the syndrome such as pediatricians, the forensic pathologists, and pathologists and the family/caregiver (Jorch et al., 2007; Krous et al., 2004; Shipstone et al., 2020).

A large number of factors must be taken into account when dealing with a case of SIDS from the health of the mother during pregnancy, details on before/during/after birth, the environment, position in which the infant

was found (prone, supine, lateral, Fowler), ambient temperature, clothing of infant and bedding.

The autopsy protocol was standardized by the Global Strategy Task Force of SIDS International (Bajanowski et al., 2007). The macroscopic examination consists of an external overview of the body, weight and size measurements, cranial and thoracic circumferences, organ weights as well as procuring samples for further tests.

The following criteria can help support the SIDS diagnosis:

- Watery, serous, hematic fluid or mucous secretions or foam from mouth and/or nose;
- Marble-like skin, change in color of skin to red/blue;
- Marks on pressure points;
- No traumatic lesions, appearance oh healthy infant;
- Environment with no apparent relation to death;

If intoxication, suffocation, hypo/hyperthermia, neglect or abuse can be inferred from the autopsy and subsequent tests, the SIDS diagnosis is excluded (Kon et al., 2020).

The following criteria support infanticide:

- Appearance of neglected infant, malnourished;
- Traumatic lesions;
- Clues indicating a change in position after death or that death occurred in another position than stated;
- Lesions around mouth/nose;
- Bite marks, contusions;
- Lesions in different stages of healing;
- Scars;
- Fractures (esp. different stages);
- Altered pupils.

During autopsy the organs known to have a role in SIDS (brain, lungs and heart) must be thoroughly examined in order to correctly differentiate between sudden and unexpected infant death and other possible causes. In 2003, at the State-of-the-Art Conference on the Stratification of SUDI, a neuropathological examination protocol was accepted, involving procurement of tissue from the hippocampus, the frontal and parietal lobes, the corpus striatum of the thalamus, mesencephalon, pons, cerebellum and the cervical part of the spinal cord for histopathological investigations. Immuno-histochemistry can be used to evaluate gliosis, neurons, axons and microglial cells as well as traumatic injury. After examination, the pathologist can differentiate between brains

with potentially or conclusively lethal changes and brains with nonspecific lesions. Lung tissue is procured from the central section and the periphery of each lobe and from the tracheal branching in order to differentiate between age dependent features, specific and non-specific changes (minor inflammatory infiltrate, hemorrhagic petechiae, alveolar bleeding).

It has been demonstrated that alveolar bleeding does not correlate with hemorrhage of the nose/mouth or with intrathoracic hemorrhagic petechiae in cases of sudden infant death with adequate sleeping conditions (Krous et al., 2007; Lavezzi et al., 2020; Osawa et al., 2020). Heart tissue samples obtained from the left ventricle show T cell infiltrates that require further immunochemistry and/or biomolecular testing to diagnose acute fatal myocarditis (Bajanowski et al., 2007). If family history is positive then metabolic and genetic investigations are required (Ferrante et al., 2020). Blood, bile and urine samples are also taken for genetic/molecular tests while fibroblast cultures are used to diagnose chromosome anomalies (Hashiyada et al., 2019). Bacteriologic and virus tests are done when histology has revealed an infection (Bajanowski et al., 2007). Toxicology reports are obtained from ventricle or femoral artery blood, brain fluid, vitreous humour, urine, stomach content and liver tissue to determine alcohol/drug levels.

Post-mortem examination can reveal a cause of death in approximately 3% of cases based on clinical findings, 5-25% after re-evaluation of death circumstances, 5-13% after macroscopic examination of the body, 12-15% after histology, 1-5% after microbiology, 1% after metabolic testing and 1% after toxicology (Jorch et al., 2007).

SIDS has a number of differential diagnoses that must be excluded first amongst which are pathologies of the central nervous system (hemorrhage, meningitis, tumor, congenital defects, etc.), respiratory system (pneumonia, laryngitis, aspiration, etc.), digestive tract (dehydration), metabolic anomalies, accidents in bed (asphyxia) or in the car seat (posture asphyxia), infanticide.

Even if medicine evolved tremendously to where almost any diagnosis can be delivered in short time, uncertainty still conduct to cases when the cause of death is difficult to be settled. In case of infants, is even more difficult based on the lack of the subjective response from the patient. Given that, early screening might prevent this sudden infant death syndrome in certain cases (De Visme et al., 2020; Merino et al., 2020) and even decrease the number of such occurrences (Goldwater et al., 2020).

## Conclusions

Whenever the cause of death in an infant is unknown and there is a strong suspicion of sudden death, a complete autopsy alongside thorough patient history and histology testing must be observed. The forensic pathologist in charge must correlate the clinical data of the infant, the social context and the place of death with the oftentimes subtle autopsy findings in order to correctly diagnose SIDS.

Post-mortem lab tests help exclude other pathologies, while the family history can reveal cases of unexplained infant death, sudden cardiac arrest, genetic or metabolic disorders.

A detailed image of the scene of death obtained through interviewing the parents/family members/caregivers (Sandu, 2020) and through careful analysis might support the diagnosis.

Despite careful and complex medical investigations, sometimes differentiating between SIDS and other causes of death (e.g. unintentional suffocation, infanticide) can be particularly difficult, even today.

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