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Sudden infant deaths: arousal as a survival mechanism

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Abstract

The mechanisms responsible for sudden infant death syndrome (SIDS) are still largely unknown. To explain what factors contribute to the deaths, we suggest a model: the '3 S model for SIDS' that includes 'sicknesses', 'stages of development' and 'surroundings': (1) 'sicknesses' refers to infectious diseases or other medical condition. (2) 'Stages of development' relates to the maturation of vital systems including respiratory, neurovegetative or sleep-wake behavioral controls. (3) 'Surroundings' refers to environmental conditions that enhance the deficiency of cardiorespiratory, vegetative and/or arousal controls. Such conditions were identified by epidemiological studies and include the following main risk factors: the prone body position during sleep, high environmental temperature, maternal smoking or sleep deprivation. An infant could be at higher risk for SIDS because of a deficiency in breathing and cardiac autonomic controls during sleep, inducing repeated episodes of hypoxia and hypoxemia. The risk is increased when the infant has a lower propensity to arouse from sleep and so, to autoresuscitate. The accident has a greater probability to occur when an infection, or an unfavorable environmental factor aggravates the immature cardiorespiratory and sleep/wake behaviors of the infant. The clinical findings could be related to the changes reported in the brainstems of SIDS victims.

Keywords: Sleep; Arousal; Sudden infant death syndrome; Death; Apnea; Hypoxia; Resuscitation; Infection

1. Introduction

It was postulated that an arousal reaction enables a sleeping infant to wake up and survive when exposed to a life-threatening condition. Such condition includes various noxious factors, such as severe obstructive apneas, esophageal refluxes, cardiac rhythm abnormality or external suffocation. If the infant is unable to wake up and resume normal cardiorespiratory control, the abnormal condition is not interrupted and the infant dies (Fig. 1).

Sleep recordings collected in infants who eventually died of sudden infant death syndrome (SIDS) were characterized by more frequent and longer obstructive sleep apnea, less frequent body movements, less arousals by the end of the night, and greater sympathovagal control. In addition, SIDS victims had a high desynchronized peak of sympathetic tonus in the late hours of the night, a finding that was not seen in the control subjects. This particular sympathetic peak appeared at a time of the night when most deaths occur.

This report will focus on the arousal reactions seen in healthy infants studied in conditions known to favor SIDS. All studies on arousals were conducted on healthy infants, born near or at term, studied before or at the age of greatest risk for SIDS. The studies were conducted in pediatric sleep laboratories during whole-night recording sessions. The infants were observed continuously during sleep. In some experiments, the infants' spontaneous arousals were scored. In other studies, the sleeping infants were exposed to an external auditory stressor. The infants were challenged with white noises of various intensities (ranging from 50 to 120 db(A)). The recording of electroencephalographic and behavioral changes associated with the noise challenge was used for the evaluation of auditory arousal thresholds. The determination of the thresholds contributed to the quantification of the infant's sleep-wake control mechanisms and the infant's response to environmental stresses.

2. A prenatal factor: maternal smoking during gestation

According to epidemiological studies, prenatal cigarette smoking was associated with a relative risk ratio for SIDS as high as 4.1. As SIDS has been related to both exposure to prenatal cigarette smoke and impaired arousability from sleep, it was evaluated whether healthy infants born to mothers who smoked during pregnancy had higher auditory

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Abbreviations: SIDS, sudden infant death syndrome; REM sleep, rapid eye movement sleep (active sleep); NREM sleep, non-rapid eye movement sleep (quiet sleep)

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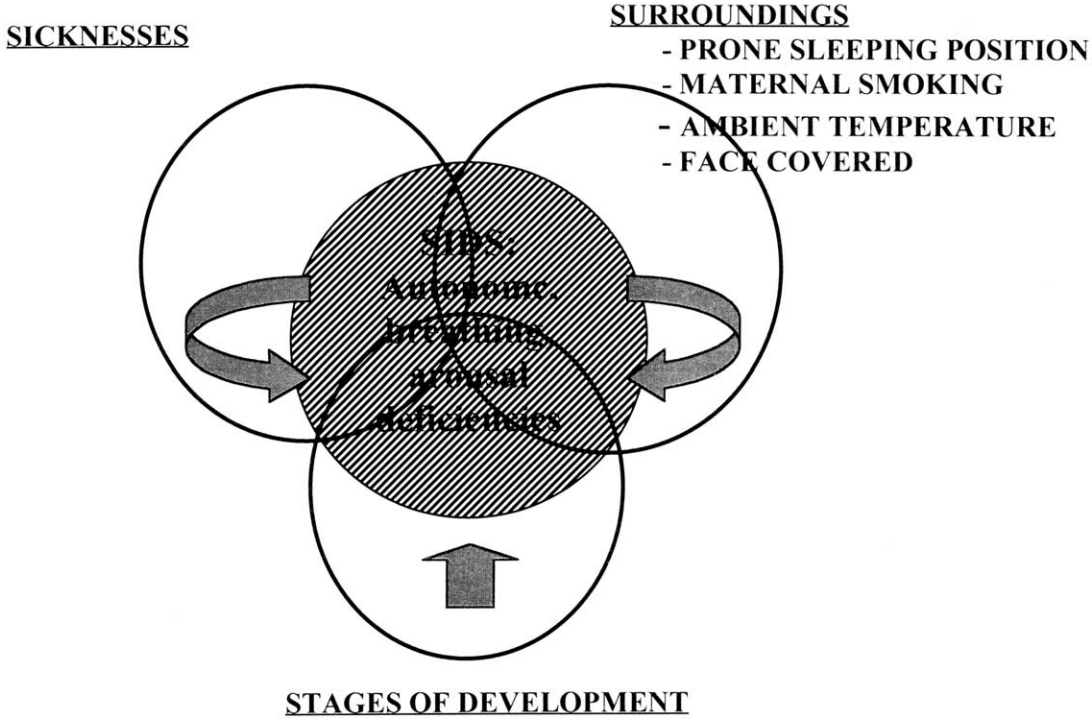

Fig. 1. Model for SIDS.

arousal thresholds than those born to mothers who did not smoke. Twenty-six newborns were studied with polygraphic recordings for one night: 13 were born to mothers who did not smoke, and 13 were born to mothers who smoked (over nine cigarettes per day) [1]. Another group of infants with median a postnatal age of 12 weeks were also studied: 21 born to non-smoking mothers and 21 born to smoking mothers. The auditory arousal thresholds of the infants of both age groups were measured with the use of auditory challenges of increasing intensity, administered during rapid eye movement (REM) sleep. More intense auditory stimuli were needed to induce arousals in newborns ($P = 0.002$) and infants ($P = 0.044$) of smokers than in infants of non-smokers. Behavioral awakening (infants opening the eyes and/or crying) occurred significantly less frequently in the newborns of smokers ($P = 0.002$) than of non-smokers. It was concluded that newborn and infants born to smoking mothers had higher arousal thresholds to auditory challenges than those born to non-smoking mothers. From the present findings, it appeared that the impact of exposure to cigarette smoke occurred before birth.

3. Postnatal factors: risk factors for SIDS

Similar studies on the effects of postnatal environmental risk factors were studied in healthy infants.

3.1. Body position during sleep

When sleeping prone, healthy infants were characterized by higher basal heart rates, significant increases in sleep duration (+16%) and in non-rapid eye movement (NREM) sleep (+25%). The infants had a significant decrease in the number (−40%) and the duration (−43%) of the arousals. To further investigate whether prone sleeping was associated with a higher response threshold to environmental stimuli, 30 3-month-old healthy infants were exposed to an auditory challenge. The infants were sleeping successively prone or supine. Following an auditory challenge, more intense auditory stimuli were needed to arouse the infants in the prone position (median of 70 db(A), range values 50 to more than 100 db(A)) than in the supine position (median of 60 db(A), range values 50–90 db(A)) ($P = 0.011$). Infants with obstructive sleep apneas laid prone or supine to sleep also show different responses to the apneas according to their position. Awakenings were associated to 57.5% of obstructive events recorded supine and in 3 1.3% of those seen prone ($P < 0.001$). Awakenings occurred after 8 s (range 0–21) from the start of the obstructions when supine and 10.5 (range 3.5–23.5) when prone ($P = 0.001$) [2].

3.2. The influence of ambient temperature

A study was conducted to evaluate the influence of ambient temperature on infant's sleep and cardiorespiratory parameters during sleep. Twenty healthy infants with a median age of 11.5 weeks (range 7–18 weeks) were recorded polygraphically for one night. They were exposed to three different ambient temperatures: 20, 25 and 30°C. Ambient and core temperature was measured. It was found that increases

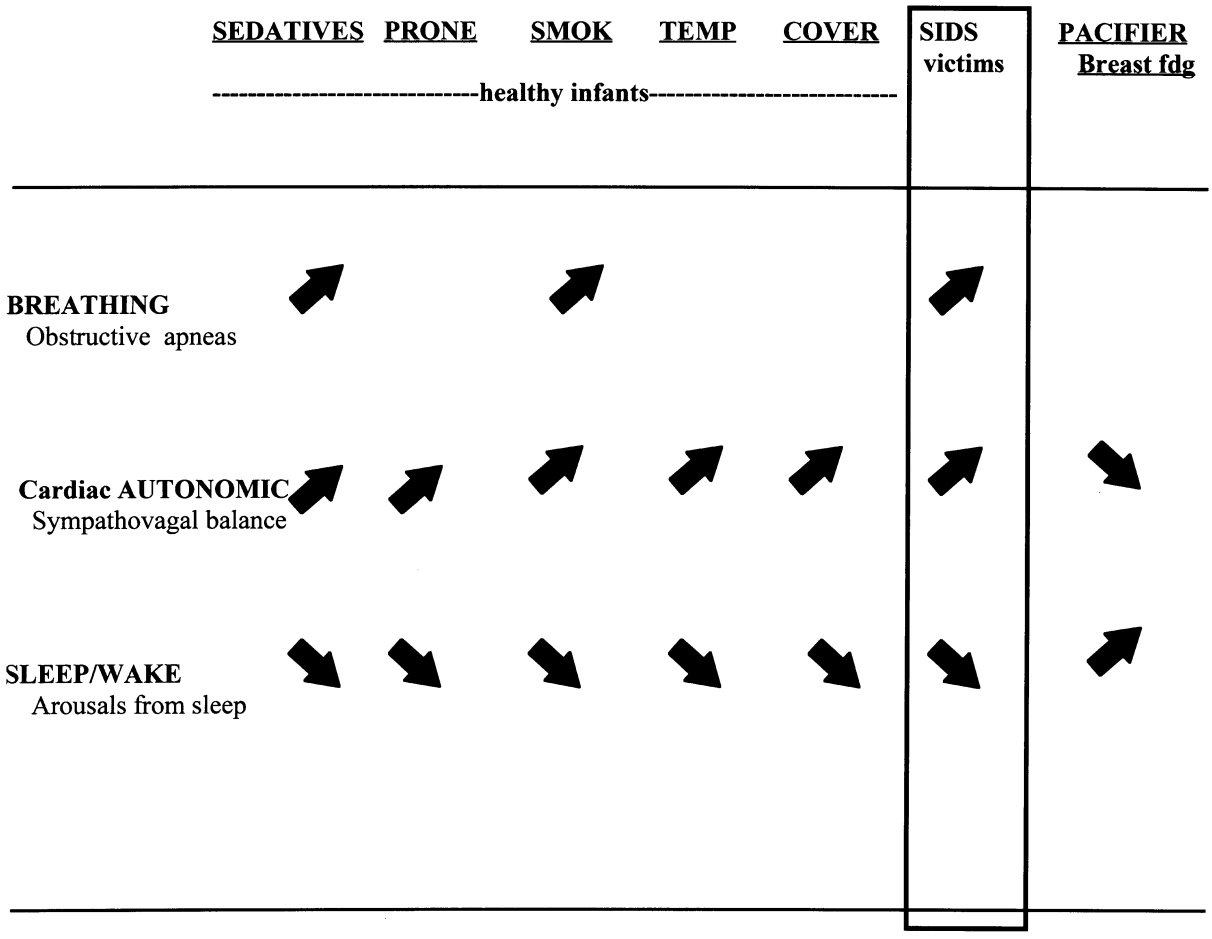

Fig. 2. Environmental factors – SIDS.

in ambient temperature were related to slight inreases in core temperature, but significant increases in central apneas and basal heart rate, together with a reduction in parasympathetic control of the heart rate and in oxygen saturation. The findings were mainly seen during REM sleep.

A new study was conducted to evaluate the influence of ambient temperature on infants' arousals from sleep [3]. Two groups of healthy infants with a median age of 11 weeks were recorded polygraphically during one night: 31 infants were studied at 24°C and 31 infants at 28°C. To determine their arousal thresholds, the infants were exposed to white noises of increasing intensities during REM and NREM sleep. The arousal thresholds decreased across the night in the infants sleeping at 24°C ($P = 0.017$). The finding was not found for the infants sleeping at 28°C. When analyzing the arousal responses according to time of the night, it was found that the auditory thresholds were significantly higher at 28°C than at 24°C between 03:00 and 06:00 h ($P = 0.003$). These findings were only seen in REM sleep.

3.3. Sleeping with the face covered by a bed sheet

To evaluate the influence of covering the face of sleeping infants with a bed sheet, 18 healthy infants with a median of 10.5 weeks (range 8–15 weeks) were recorded polygraphically for one night [4]. They slept in their usual supine position. During sleep, a bed sheet was gently placed on their face during 60 min. With the face free or covered by the sheet, the infants were exposed to white noises of increasing intensities during REM and NERM sleep. Compared to face free, during the face-covered periods, the infants had increases in pericephalic ambient tempera-

ture ($P < 0.001$), increases in REM sleep ($P = 0.035$) and body movements ($P = 0.011$) and a decrease in NREM sleep ($P < 0.001$). With their face covered, the infants had higher auditory arousal thresholds ($P = 0.006$) in REM sleep only. A positive correlation was found between pericephalic temperature and arousal thresholds in REM sleep ($r = 0.487$; $P = 0.003$).

4. Postnatal factors: protective factors

The use of pacifiers during sleep and breastfeeding were associated with a reduced risk of SIDS. Fifty-six healthy infants were studied polygraphically during one night: 36 infants used a pacifier regularly during sleep; 20 never used a pacifier [5]. Thumb users or occasional pacifier users were not included in the study. The infants were recorded at a median age of 10 weeks (range 6–19 weeks). To evaluate their auditory arousal thresholds, the infants were exposed to white noise of increasing intensity during REM sleep.

Polygraphic arousals occurred at significantly lower auditory stimuli in pacifier-users than in non-users (mean of 60 ± 11.6 with pacifiers, for 71 ± 15.3 without pacifier; $P = 0.010$). Compared to non-users, pacifier-users were more frequently bottle-fed than breastfed ($P = 0.036$). Among infants sleeping without a pacifier, breast-fed infants had lower auditory thresholds than bottle-fed infants (mean of 67.7 ± 13.0 breast-fed, for 77.7 ± 17.5 bottle-fed; $P = 0.049$).

5. Conclusions and perspectives

The physiological studies undertaken on the basis of epidemiological findings provide some clues about physiological mechanisms linked with SIDS. SIDS derives from multifactorial conditions, that include three main groups of causes: maturational processes, medical conditions, and environmental factors (Fig. 1). All three could contribute to SIDS, either independently, or in combination. They appear to lead to the same common final pathway: a decreased propensity to arouse from sleep.

Prenatal and postnatal factors associated with an increased risk for SIDS were shown to increase the infant's arousability from sleep. Alternatively, those factors from the infant's microenvironment reported to decrease the risk for SIDS were found to be associated with lower auditory arousal thresholds.

Additional studies showed that the infants' reactions to environmental stresses include changes in breathing and autonomic controls during sleep. These changes were associated with obstruction of the upper airways and increases in sympatho-vagal balance (Fig. 2). In addition to decreasing the auditory arousal thresholds, protective factors such as breastfeeding or the use of a pacifier, favor a decrease in sympatho-vagal control of the heart rate.

Complex control mechanisms thus appear to be involved in the autoresuscitative response. These reactions that occur in response to potentially life-threatening events, may be especially important during the late hours of the night, when most SIDS deaths occur.

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