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PROTECTING LITTLE LIVES, PROVIDING A GUIDING LIGHT FOR FAMILIES
3. Results: We found 11 mutations and 8 rare variants in 24/201 SIDS cases (11.9%), with 79% in 45 infants or 137 adult controls. Based on their functional effect, we considered the genetic variants found in 17/201 SIDS cases (8.4%) as likely contributors to SIDS. Thirteen (76%) of the mutations were found in SONSIA.

Discussion: Our study, based on the largest data set of DNA samples from SIDS victims so far, provides evidence that a relatively high proportion of SIDS cases involved variations in SLC5A7 genes. Taking into account that 34-50% of deaths affected by LQT5, the responsible variation is still not found, the present findings suggest that the number of SIDS cases accounted for by LQT5 may be even higher.

146 (S)

SEROTONIN TRANSPORTER GENE VARIATION IN SIDS

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1. The 5-HTT gene polymorphisms in the promoter and intron 2 have been investigated in 218 SIDS cases, 33 cases of infectious death, and 89 controls. The promoter genotypes and the 5-HTT alleles (p = 0.05 and p = 0.08 respectively) are significantly different between the groups. The 5-HTT gene polymorphisms are associated with SIDS cases, with 13.1% of the SIDS cases including the allele p < 0.05.

147 (S)

STILLBIRTH VERSUS SIDS. PATHOLOGY OF THE AUTONOMIC NERVOUS SYSTEM AND DNA POLYMORPHISMS IN SIUD AND SIDS

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1. Pathogenesis of sudden intrauterine unexpected death (SIUD) and sudden infant death syndrome (SIDS) seems to be different. In most cases, SIUD is due to congenital anomalies, whereas SIDS is due to variations in the functioning of the autonomic nervous system. The main differences between the two conditions are in the genetic factors, the mode of inheritance, and the pathophysiological mechanisms involved.

2. The paper presents the results of a study on the pathophysiological mechanisms involved in SIUD and SIDS. The study was conducted on a large series of patients of SIDS, of unexpected neonatal and late fetal deaths, revealed analogous and frequent features of the autonomic structures that control the respiratory activity, as well as of the cardiovascular, upper digestive and arousal functions. The research revealed a new approach to SIDS by molecular line with late death stillbirth which has a six-fold greater incidence than SIDS. The common denominator of all these deaths was the absence of neurological symptoms, generally associated with the presence of congenital anomalies and in some cases of acquired lesions. Particularly frequent is the hypoxia and/or agenesia of the autonomic nervous system, which involves central components, observed with the incidence of about 50% in both stillbirth and in SIDS victims. In stillbirth this anomaly is frequently associated with hypoplasia of the reticular formation, lung hypoplasia and chronic hypoxia.
Regarding the cardiac conduction system, accessory atrio-ventricular pathways (mainly Mahaim fibers) were seen in 30% of SIDS cases. Under particular conditions and autonomic neuronal stimulation, these accessory pathways can trigger potentially lethal arrhythmias, generally due to junctional reentry. The chronic prenatal exposure to cigarette smoke was significantly associated with bradycardia and cardiac conduction abnormalities, as well as early coronary lesions.

The research was extended to the detection of DNA mutations and polymorphisms potentially involved in SIDS etiopathogenesis. Analysis of SCNA and MCAO genes allowed exclusion of LOTS and deficiency of fatty acids b-oxidation in our samples, while detection of the promoter long (L) allele of 5-HTT gene resulted more frequent in SIDS infants (75%) than in controls (50%).

148 (S)

LIPOPROTEIN-LIKE PROSTAGLANDIN D SYNTHASE LOCALIZES SPECIFICALLY TO NEURONS IN BRAINSTEM OF SUDDEN INFANT DEATH SYNDROME VICTIMS

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Prostaglandin (PG) D, is the most abundant PG in the brain. It is involved in induction of sleep in the CNS and modulates inflammatory reaction in peripheral tissues. Lipoprotein-like PG synthase (L-PLDG) is responsible for biosynthesis of PGD, in the brain and is a unique function protein which catalyzes biosynthesis of PGD, and also function as lipoprotein. We have previously reported that expression of L-PLDG was progressively increased in perinatal oligodendroglia/CNS in mouse models for genetic neurological disorders and in OLI and astrocytes which were positive for apolipoprotein, a stress protein, in demyelinating plaques of human brains with multiple sclerosis. These lines of evidence suggest that L-PLDG is induced as a stress reaction. In this study, we investigated whether upregulation of L-PLDG was also induced in patients from sudden infant death syndrome (SIDS) victims. Six infants enrolled with SIDS in Osaka prefecture between 1981 to 1996 were eligible for the study. The age of SIDS victims ranges from 2 to 11 months old and 4 non-SIDS age-matched autopsy brains were used as control. Immunostaining of L-PLDG was performed in all samples and examined to ascertain expression in neurons. We observed expression of astroglia and microglia as detected by thioflavin acetylated protein (TAPP) and CD68 respectively as well as TGF-mediated tight-lining (TUNEL) positive adipocytic cells. In the SIDS brains, immunoreactivity for L-PLDG was observed in OLI and neurons. In the brained, however, L-PLDG was confined to neurons and its immunoreactivity was by far intense when compared with those in the cerebral cortex and brainstem of control samples. These L-PLDG-positive neurons comprise inferior olivary nucleus, hypoglossal nucleus, and cuneiform nucleus in the medulla. L-PLDG immunoreactivity was intense in SIDS brainstem irrespective of activation of astroglia and microglia as well as the number of adipocytic cells.

Together with our previous works, these findings suggest that induction of L-PLDG occurs as a result of recurrent hypothalamic ischemia and its timing is much earlier than activation of astrocytes or cell death. Moreover, up-regulated L-PLDG may produce extra amount of PGG2, which exerts inflammatory reactions in brainstem or otherwise, reduces arrhythmia in SIDS victims. This study implies that PGG2, produced by L-PLDG, may play a crucial role in the pathogenesis of SIDS.

149 (S)

PULMONARY HEMORRHAGE IN SUDDEN AND UNEXPECTED DEATH IN CHILDREN: NATURAL DEATH OR HOMICIDE?

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Introduction: The presence of saponishes within lung alveoli means that a bleeding occurred at least 3 days prior to death. We reviewed a series of pediatric autopsies to know in which amount and frequency saponishes are formed.

Methods: A Pare staining was performed on at least one (right inferior lobe of the 8 systematically made lungs) slice in 176 consecutive autopsies. 147 sudden unexpected death cases (13 months < 28 days; 17 children < 12 months; 117 infants, < 28 days) and 23 non natural deaths (13 neonates < 28 days; 5 children < 12 months; 21 infants). The number of saponishes was counted on 40 fields (40) for each case. The classification was made in 4 grades according to their number: QD = no saponishes; G1 = 1 to 20; G2 = 21 to 40; G3 = 41 to 60; G4 > 60. Results: The majority of cases had no QD (0) or only a few (G1) saponishes. There were 36 children in grades G2 and G3 and 12 of 28 non natural deaths (27%) and 28 of the 147 natural deaths (19%) (not significant). The death causes found in each group were compatible with repeated pulmonary bleedings: the non natural deaths were 5 child abuses and 3 Shaken Baby Syndromes, 2 upper airway obstructions and 1 repeated thoracic traumas and 2 accidents (1 overlying co-sleeping and 1 beddding accident related to a re-ognathic). The natural deaths with saponishes were of cardiac (18) and pulmonary causes (2 pulmonary hypertension), 15 infections with a pulmonary localization, 1 D. Georges syndrome with hypocaesmia (may-goyspant) and 1 neurological disease with numerous loss of consciousness and apnea. Conclusion: If the presence of numerous pulmonary saponishes cannot be explained by a medical cause, child abuse or negligence such as repeated upper airway obstructions, Shaken Baby Syndrome or thoracic traumas must be considered.

150 (S)

UNDERSTANDING ONE OF THE THREE RISK FACTORS OF SIDS: A CRITICAL PERIOD OF DEVELOPMENT IN BRAINSTEM NUCLEI INVOLVED IN THE CONTROL OF RESPIRATION

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In 1984, Filiano and Kenney proposed the Triple Risk Model for Sudden Infant Death Syndrome, which states that SIDS occurs, and only occurs, when both a vulnerable infant encounters a blow, an external stimulus or attack during a critical period of postnatal development. All three factors have to be present simultaneously for death to occur. The first factor can result from diverse causes, such as pre-natal exposure to nicotine and other drugs, organic damage, and non-lethal genetic defects. The second factor precipitated the Back to Sleep Campaign and has significantly reduced, though not eliminated, the incidence of SIDS. The third factor, though suspected, has not been well studied and characterized. Using 

151 (ST)

PLACENTAL ETIOLOGIES OF FETAL GROWTH RESTRICTION AND STILLBIRTH

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Learning Objectives
1. Review of current knowledge in placental growth
2. Review placental conditions that are associated with growth restriction and stillbirth

Abstract/Summary
The placenta is a unique organ which forms during gestation and loses its utility after parturition. Although hosted by the mother and supports the fetus, it originates from the embryo thus of fetal origin. The interface of maternal tissues and the developing placenta is complex. Recent developments describing some of the basic molecular pathways have contributed significantly to our understanding of normal placental growth.

Between 1994-2005, we examined 737 stillbirth and their placentas at Women and Infants Hospital, Brown Medical School. There were 411 cases that showed findings consistent with established cause/strong association with stillbirth such as amniotic fluid infection syndrome, placental abortion, fetal vascular compromise, twin-twin transfusion syndrome, maternal fetal hematocyte, multiple congenital malformations with or without aneuploidy. 286 cases did not show an established cause or association with stillbirth. When growth restriction was analyzed as an independent variable, 28% (131) of the 471 cases with impaired fetal and/or placental growth. In contrast, 5% (15) of the cases in the undetected group were growth restricted.

Placental findings in this group included abnormalities of placental shape, lesions that might compromise fetal circulation such as abnormal umbilical cord insertions, vitous remodeling abnormalities, abnormal vasculatures and impaired trophoblast turnover.