



## **Smoking and Sudden Infant Death Syndrome (SIDS): A Selected Annotated Bibliography**

Hogberg L, Cnattingius, S.

### **Influence of maternal smoking habits on the risk of subsequent stillbirth: Is there a causal relation?**

BJOG. 2007 Jun; 114(6):699-704.

**OBJECTIVE:** Maternal smoking has previously been associated with risk of stillbirth. If women who quit smoking reduce their risk of stillbirth, the hypothesis of a causal association would be supported. **DESIGN:** Prospective cohort study. **SETTING:** Nationwide study in Sweden. **POPULATION:** All primiparous women who delivered their first and second consecutive single births between 1983 and 2001, giving a total number of 526,691 women. **METHOD:** A population-based Swedish study with data from the Medical Birth Registry, the Immigration Registry and the Education Registry. Logistic regression analyses were used to estimate odds ratios, using 95% confidence intervals. **MAIN OUTCOME MEASURE:** Stillbirth in the second pregnancy. **RESULTS:** Compared with nonsmokers in both pregnancies, women who smoked during the first pregnancy but not during the second do not have an increased risk of stillbirth (OR 1.02; 95% CI 0.79-1.30), while corresponding risk among women who smoked during both pregnancies was 1.35 (95% CI 1.15-1.58). **CONCLUSION:** The result supports that maternal smoking during pregnancy is causally associated with stillbirth risk. Smoking is a preventable cause of stillbirth, and smoking interventions is an important issue in antenatal care.

Full-text available at: [www.blackwell-synergy.com](http://www.blackwell-synergy.com) (not a U.S. Government site)

Weese-Mayer DE, Ackerman MJ, Marazita ML, Berry-Kravis EM.

### **Sudden Infant Death Syndrome: Review of implicated genetic factors.**

Am J Med Genet A. 2007 Apr 15; 143(8):771-88.

Genetic studies in Sudden Infant Death Syndrome (SIDS) have been motivated by clinical, epidemiological, and/or neuropathological observations in SIDS victims, with subsequent pursuit of candidate genes in five categories: (1) genes for ion channel proteins based on electrocardiographic evidence of prolonged QT intervals in SIDS victims, (2) gene for serotonin transporter based on decreased serotonergic receptor binding in brainstems of SIDS victims, (3) genes pertinent to the early embryology of the autonomic nervous system (ANS) (and with a link to the 5-HT system) based on reports of ANS dysregulation in SIDS victims, (4) genes for nicotine metabolizing enzymes based on evidence of cigarette smoking as a modifiable risk factor for SIDS, and (5) genes regulating inflammation, energy production, hypoglycemia, and thermal regulation based on reports of postnatal infection, low birth weight, and/or overheating in SIDS

victims. Evidence for each of these classes of candidate genes is reviewed in detail. As this review indicates, a number of genetically controlled pathways appear to be involved in at least some cases of SIDS. Given the diversity of results to date, genetic studies support the clinical impression that SIDS is heterogeneous with more than one entity and with more than one possible genetic etiology. Future studies should consider expanded phenotypic features that might help clarify the heterogeneity and improve the predictive value of the identified genetic factors. Such features should be evaluated to the extent possible in both SIDS victims and their family members. With 2,162 infants dying from SIDS in 2003 in the U.S. alone, and improved but still imperfect parent and caretaker compliance with known modifiable risk factors for SIDS, it behooves clinicians, researchers, and parents to combine efforts to reach a common goal. The message of the "Back to Sleep" campaign needs to be re-introduced/re-engineered to reach families and caretakers of all ethnic groups. Clinicians and researchers need to gently inform new SIDS parents about the opportunity to contribute tissue to the NICHD-funded University of Maryland Brain and Tissue Bank. By expanding the network of clinicians, scientists, and families working together, and by combined efforts in a collaborative multi-center study of candidate genes and/or genomics, the discovery of the genetic profile of the infant at risk for SIDS can ultimately be determined

Full-text available at: <http://www3.interscience.wiley.com> (not a U.S. Government site)

Markowitz S.

**Effectiveness of cigarette regulations in reducing cases of Sudden Infant Death Syndrome.**

Journal of Health Economics. Article in Press, Corrected Proof. Available online 8 April 2007.

Sudden Infant Death Syndrome (SIDS) is a leading cause of mortality among infants and is responsible for thousands of infant deaths every year. Prenatal smoking and postnatal environmental smoke have been identified as strong risk factors for SIDS. Given the link between smoking and SIDS, this paper examines the direct effects of cigarette prices, taxes and clean indoor air laws in explaining changes in the incidence of SIDS over time in the United States. State-level counts of SIDS cases are generated from death certificates for 1973-2003. After controlling for some observed and unobserved confounding factors, the results show that higher cigarette prices and taxes are associated with reductions in SIDS cases. Stronger restrictions on smoking in workplaces, restaurants and child care centers are also effective in reducing SIDS deaths.

Full-text available at [www.sciencedirect.com](http://www.sciencedirect.com) (not a U.S. Government site)

Say M, Machaalani R, Waters K.A.

**Changes in serotonergic receptors 1A and 2A in the piglet brainstem after intermittent hypercapnic hypoxia (IHH) and nicotine.**

Brain Res. 2007 Mar 19; [Epub ahead of print].

We studied the effects of intermittent hypercapnic hypoxia (IHH) and/or nicotine on the immunoreactivity of serotonergic (5-HT) receptors 1A and 2A in the piglet brainstem.

These exposures were developed to mimic two common risk factors for Sudden Infant Death Syndrome (SIDS); prone sleeping (IHH) and cigarette smoke exposure (nicotine). Immunoreactivity for 5-HT(1A)R and 5-HT(2A)R were studied in four nuclei of the caudal medulla. Three exposure groups were compared to controls (n=14): IHH (n=10), nicotine (n=14), and nicotine+IHH (n=14). In control piglets, the immunoreactivity of 5-HT(1A)R was highest in the hypoglossal nucleus (XII), followed by inferior olivary nucleus (ION), nucleus of the solitary tract (NTS) and dorsal motor nucleus of the vagus (DMNV), whereas for 5-HT(2A)R, the immunoreactivity was highest in DMNV/NTS and then ION. Compared to controls, IHH reduced 5-HT(1A)R immunoreactivity in all studied nuclei ( $p<0.05$ ) but had no effect on 5-HT(2A)R immunoreactivity. Nicotine reduced 5-HT(1A)R immunoreactivity in the DMNV, ION and NTS ( $p<0.001$ ), and reduced 5-HT(2A)R immunoreactivity in DMNV/NTS ( $p<0.05$ ). Nicotine+IHH reduced 5-HT(1A)R in DMNV, ION and NTS ( $p<0.001$ ) but had no effect on 5-HT(2A)R immunoreactivity. Effects of nicotine on the DMNV were more significant in males compared to the females. These results show for the first time that IHH and/or nicotine can reduce 5-HT receptor immunoreactivity within functionally important nuclei of the piglet medulla. The findings support our hypothesis that 5-HT receptor abnormalities may be caused by postnatal exposures to clinically-relevant stimuli such as cigarette smoke exposure and/or prone sleeping.

Full text available: <http://www.sciencedirect.com> (not a U.S. Government site)

Horsley T, Clifford T, Barrowman N, Bennett S, Yazdi F, Sampson M, Moher D, Dingwall O, Schachter H, Cote A.

**Benefits and harms associated with the practice of bed sharing: A systematic review.** Arch Pediatr Adolesc Med. 2007 Mar; 161(3):237-45.

Objective: To examine evidence of benefits and harms to children associated with bed sharing, factors (eg, smoking) altering bed sharing risk, and effective strategies for reducing harms associated with bed sharing. Data Sources: MEDLINE, CINAHL, Healthstar, PsycINFO, the Cochrane Library, Turning Research Into Practice, and Allied and Alternative Medicine databases between January 1993 and January 2005. Study Selection: Published, English-language records investigating the practice of bed sharing (defined as a child sharing a sleep surface with another individual) and associated benefits and harms in children 0 to 2 years of age. Data Extraction: Any reported benefits or harms (risk factors) associated with the practice of bed sharing. Data Synthesis: Forty observational studies met our inclusion criteria. Evidence consistently suggests that there may be an association between bed sharing and sudden infant death syndrome (SIDS) among smokers (however defined), but the evidence is not as consistent among nonsmokers. This does not mean that no association between bed sharing and SIDS exists among nonsmokers, but that existing data do not convincingly establish such an association. Data also suggest that bed sharing may be more strongly associated with SIDS in younger infants. A positive association between bed sharing and breastfeeding was identified. Current data could not establish causality. It is possible that women who are most likely to practice prolonged breastfeeding also prefer to bed share. Conclusion: Well-designed, hypothesis-driven prospective cohort studies are warranted to improve

our understanding of the mechanisms underlying the relationship between bed sharing, its benefits, and its harms.

Full-text available at: <http://archpedi.ama-assn.org> (not a U.S. Government site)

Bajanowski T, Brinkmann B, Mitchell EA, Vennemann MM, Leukel HW, Larsch KP, Beike J; the GeSID Group.

**Nicotine and cotinine in infants dying from sudden infant death syndrome.**

Int J Legal Med. 2007 Feb 7; [E-pub ahead of print]

The aim of this component of the German Study on Sudden Infant Death was to determine (1) nicotine concentrations in hair (NCH), as a marker of long standing exposure to tobacco, (2) cotinine concentrations in pericardial fluid (CCP) and (3) cotinine concentrations in liquor cerebrospinalis (CCL), the latter measures being markers of recent exposure to tobacco in the last few hours of life. The results obtained were compared with data on parental smoking revealed from interviews. In 100 cases of sudden infant death syndrome, material was taken at autopsy to determine NCH. In 41 cases, NCH and CCP, and in 70 cases, NCH and CCL were determined. Infants of mothers who stated having smoked during pregnancy had higher NCH than infants of non-smoking mothers ( $p = 0.008$ ). Furthermore, there was a weak but statistically significant relationship between NCH's and the daily cigarette consumption of the mother during pregnancy ( $n = 64$ ,  $r = 0.24$ ,  $p = 0.05$ ). In 43% of infants, nicotine could be detected in their hair, although the mothers had said at the interview that they did not smoke during pregnancy. On the other hand, in 33% of infants whose mother stated they had smoked during pregnancy nicotine was not detectable in the infant's hair. CCP's were strongly correlated with CCL's ( $r = 0.62$ ,  $p = 0.0027$ ). For this reason, both parameters were treated as equivalent for the detection of tobacco smoke exposure in the last hours before death. The influence of breast-feeding was evaluated by comparison of the nicotine concentrations in breast fed and non-breast-fed infants from smokers and non-smokers. Fivefold higher nicotine concentrations were determined in non-breast-fed infants of parents who smoked as compared to all other groups. It can be concluded that nicotine intake by passive smoking is much more important than by breast-feeding. We conclude that both interview data and biochemical measures should be sought to understand the true exposure to tobacco smoke.

Full-text available at: <http://www.springerlink.com/content/80q41272721762h3/> (not a U.S. Government site)

Thompson JM, Thach BT, Becroft DM, Mitchell EA; New Zealand Cot Death Study Group.

**Sudden infant death syndrome: Risk factors for infants found face down differ from other SIDS cases.**

J Pediatr. 2006 Nov; 149(5):630-633.

Objective: To test the hypothesis that infants with sudden infant death syndrome (SIDS) found face down (FD) would have SIDS risk factors different from those found in other

positions (non-face-down position, NFD). Study Design: We used the New Zealand Cot Death Study data, a 3-year, nationwide (1987 to 1990), case-control study. Odds ratios (univariate and multivariate) for FD (n = 154) and NFD SIDS (n = 239) were estimated separately, and statistical differences between the two groups were assessed. Results: Of 12 risk factors for SIDS, there were 8 with a statistically significant difference between FD and NFD infants. After adjustment for the potential confounders, younger infant age, Maori ethnicity, low birth weight, prone sleep position, use of a sheepskin, and pillow use were all associated with a greater risk of SIDS in the FD than the NFD group. Sleeping during the nighttime, maternal smoking, and bed-sharing were associated with a risk of SIDS only in the NFD group. Pacifier use was associated with a decreased risk for SIDS only in the NFD group, whereas being found with the head covered was associated with a decreased risk for SIDS for the FD group. Conclusions: Infants with SIDS in the FD position appear to be a distinct subgroup of SIDS. These differences in risk factors provide clues to mechanisms of death in both SIDS subtypes.

Full-text available at: <http://www.sciencedirect.com> (not a U.S. Government site)

Matturri L, Ottaviani G, Lavezzi AM.

**Maternal smoking and sudden infant death syndrome: Epidemiological study related to pathology.**

Virchows Arch. 2006 Nov 8; [E-pub ahead of print]

Various risk factors have been postulated to be related to sudden infant death syndrome (SIDS). Despite its reduction, thanks to the "Back to Sleep" campaign, SIDS is still a major cause of infant mortality in the first year of life. The purpose of this study was to correlate the different risk factors with the autopsy results and thus to determine if one or more of these variables is really specific for SIDS. We collected 128 sudden infant death victims with clinical diagnosis of SIDS and performed a complete autopsy with in-depth histology on serial sections, particularly of the brainstem, in accordance with our necropsy protocol. Histopathologic and immunohistochemical examination of the central autonomic nervous system revealed, in 78 cases of the SIDS group, the following anomalies: hypodevelopment of the arcuate nucleus, somatostatin positive hypoglossus nucleus, tyrosine hydroxylase negativity in the locus coeruleus, gliosis, and hypoplasia of the hypoglossus nucleus. A significant relation was found between maternal smoke and brainstem alterations.

Full-text available at: <http://www.springerlink.com> (not a U.S. Government site)

Shah T, Sullivan K, Carter J.

**Sudden infant death syndrome and reported maternal smoking during pregnancy.**

Am J Public Health. 2006 Oct; 96(10):1757-9.

We investigated the effect of maternal smoking during pregnancy on the relative risk of sudden infant death syndrome (SIDS) by linking data from Georgia birth and death certificates from 1997 to 2000. We estimated the effect of misclassifying smokers as non-

smokers and the effect of being misclassified on SIDS rates, and we calculated the fraction of cases caused by exposure. Of all SIDS cases, 21% were attributable to maternal smoking; among smokers, 61% of SIDS cases were attributable to maternal smoking. Maternal smoking during pregnancy is associated with a significantly increased risk of SIDS.

Full-text available at: <http://www.ajph.org/> (not a U.S. Government site)

Polanska K, Hanke W, Ronchetti R, Van Den Hazel P, Zuurbier M, Koppe JG, Bartonova A.

**Environmental tobacco smoke exposure and children's health.**

Acta Paediatr Suppl. 2006 Oct; 95(453):86-92.

Almost half of the child population is involuntarily exposed to environmental tobacco smoke (ETS). The ETS exposure gives rise to an excessive risk of several diseases in infancy and childhood, including sudden infant death syndrome, upper and lower respiratory infections, asthma and middle ear diseases. It is also linked to cancer, and behavioural problems and neurocognitive deficits in children. Conclusions: Protecting children from ETS exposure is a complex and important issue. The best improvement in children's health is to be gained when parents stop smoking or, when that is not possible, they stop smoking in their children's environment. Paediatricians, because of their authority, and their frequent and regular contact with parents, play a leading role in protecting children from ETS exposure. An ideal approach to help parents to stop smoking seems to be initial minimal-contact advice provided by their paediatrician with feedback and supplemental printed materials, leading to greater intensity and duration of follow-up home visits.

Full-text available at: <http://www.tandf.co.uk/journals/titles/08035253.asp> (not a U.S. Government site)

Stick S

**The effects of in-utero tobacco-toxin exposure on the respiratory system in children.**

Curr Opin Allergy Clin Immunol. 2006 Oct; 6(5):312-6

Purpose of review: Promotion of cigarettes to children and women has resulted in unacceptably high rates of smoking during pregnancy in most developed countries and the potential to greatly increase smoking by mothers in developing countries. The risks of smoking during pregnancy to mothers and unborn children are well known and include growth retardation, respiratory diseases and sudden infant death syndrome. Determining the effects of exposure on the fetus depends upon accurate assessment of maternal smoking, both active and involuntary, and this can be done using self-reports and a variety of biomarkers in the mother and/or newborn. Recent Findings: The evidence is clear that most of the excess respiratory morbidity in children born to smoking mothers is due to in-utero exposure and that deficits in lung function measured soon after birth persist in children and adults. Recent studies have also indicated that some children are

genetically predisposed to adverse outcomes in response to in-utero exposure. summary: Although many women attempt to quit during pregnancy and effective interventions are available, ultimately the respiratory health of future generations will depend upon effective public health and tobacco control measures designed to prevent smoking uptake by youth and in particular girls and young women.

Full-text available at: <http://www.co-allergy.com> (not a U.S. Government site)

Cnattingius S, Akre O, Lambe M, Ockene J, Granath F.

**Will an adverse pregnancy outcome influence the risk of continued smoking in the next pregnancy?**

Am J Obstet Gynecol. 2006 Sep 29; [E-pub ahead of print]

Objective: The purpose of this study was to study the effect of pregnancy outcomes on risks of continued smoking in subsequent pregnancy. Study Design: Cohort study of first and second single births among 98,778 Swedish women who were daily smokers in first pregnancy. Results: In all, 70.2% of women continued to smoke in second pregnancy. Compared with women with a previous normal pregnancy outcome, risk of smoking in second pregnancy was increased among women with a previous small-for-gestational-age birth (adjusted odds ratio [OR], 95% CI 1.28 [95% CI 1.19-1.37]), and reduced among women who had experienced a stillbirth (OR 0.76 [95% CI 0.63-0.93]) or an infant death because of congenital malformations (OR 0.67 [95% CI 0.49-0.92]). A previous preterm birth, Sudden Infant Death Syndrome, and other causes of infant death did not influence risk. Conclusion: A previous adverse pregnancy outcome has only a modest influence on smoking habits in the successive pregnancy.

Full-text available at: <http://www.sciencedirect.com> (not a U.S. Government site)

Markowitz S.

**The Effectiveness of Cigarette Regulations in Reducing Cases of Sudden Infant Death Syndrome**

NBER Working Paper No. 12527, September 2006

Sudden Infant Death Syndrome is a leading cause of mortality among infants and is responsible for thousands of infant deaths every year. Prenatal smoking and postnatal environmental smoke have been identified as strong risk factors for SIDS. Given the link between smoking and SIDS, this paper examines the direct effects of cigarette prices, taxes and clean indoor air laws in explaining changes in the incidence of SIDS over time in the United States. State-level counts of SIDS cases are generated from death certificates for 1973 to 2003. After controlling for some observed and unobserved confounding factors, the results show that higher cigarette prices and taxes are associated with reductions in SIDS cases. Stronger restrictions on smoking in restaurants and child care centers are also effective in reducing SIDS deaths.

Full-text downloading available at: <http://papers.nber.org/papers/W12527> (not a U.S. Government site)

Lavezzi AM, Ottaviani G, Mauri M, Maturri L.

**Alterations of biological features of the cerebellum in sudden perinatal and infant death.**

Curr Mol Med. 2006 Jun; 6(4):429-35.

This article intends to show how the cerebellum, a structure ordinarily not considered in mediating breathing or cardiovascular control, may play a critical role in compensatory responses particularly to hypoxic insults occurring pre and/or postnatally and thus may be involved in the sudden unexplained perinatal and infant death. Besides the ontogenesis of the cerebellar cortex in man, we reported alterations of biopathological features (neuronal immaturity, altered apoptotic programs, negative expression of somatostatin and EN2 gene, intense c-fos expression positivity, astrogliosis) in the cortex and in the dentate nucleus of the 63% of sudden deaths, and only in 10% of the controls. The correlation of these results with the mother's smoking habit was highly significant. Therefore, we support the hypothesis, already expressed in previous studies on brainstem, of a close relation between maternal cigarette smoking and a wide range of morpho-physiological defects of the brain, leading to unexplained sudden death in stillbirths, newborns, and Sudden Infant Death Syndrome (SIDS) victims.

Mitchell EA, Milerad J.

**Smoking and the sudden infant death syndrome.**

Rev Environ Health. 2006 Apr-Jun; 21(2):81-103

The aims of this review are (a) to critically examine the epidemiologic evidence for a possible association between smoking and the sudden infant death syndrome (SIDS), (b) to review the pathology and postulated physiological mechanism(s) by which smoking might be causally related to SIDS, and (c) to provide recommendations for SIDS prevention in relation to tobacco smoking. Over 60 studies have examined the relation between maternal smoking during pregnancy and risk of SIDS. With regard to prone-sleep-position intervention programs, the pooled relative risk associated with maternal smoking was RR = 2.86 (95% CI = 2.77, 2.95) before and RR = 3.93 (95% CI = 3.78, 4.08) after. Epidemiologically, to distinguish the effect of active maternal smoking during pregnancy from involuntary tobacco smoking by the infants of smoking mothers is difficult. Clear evidence for environmental tobacco smoke exposure can be obtained by examining the risk of SIDS from paternal smoking when the mother is a non-smoker. Seven such studies have been carried out. The pooled unadjusted RR was 1.49 (95% CI = 1.25, 1.77). Consideration of the pathological and physiological effects of tobacco suggests that the predominant effect from maternal smoking comes from the in utero exposure of the fetus to tobacco smoke. Assuming a causal association between smoking and SIDS, about one-third of SIDS deaths might have been prevented if all fetuses had not been exposed to maternal smoking in utero.

Full-text available at:

[http://www.freundpublishing.com/JOURNALS/medicine\\_and\\_medical\\_sciences.htm](http://www.freundpublishing.com/JOURNALS/medicine_and_medical_sciences.htm)

Parker M, Sharif I.

**Inner-city adults' knowledge about the effects of cigarette smoking on child health.**

Clin Pediatr (Phila). 2006 May; 45(4):335-9.

Summary: We sought to determine what adults in an inner-city setting know about the specific effects of adult cigarette smoking on child health. A cross-sectional survey was conducted at an inner-city community health center in the Bronx, New York; 684 subjects participated. Overall, 21% were current smokers, 19% had quit, and 60% had never smoked. While the majority of subjects knew about the effects of smoking on adult health, they were unaware of the extent to which smoking was harmful to child health. Notably, 72% did not know that cigarette smoking increased the risk for ear infections in children, 68% did not know that smoking increased the risk of colds in children, and 61% did not know that smoking increased the risk of sudden infant death syndrome. The findings suggest a need for public health education about the effects of adult smoking on child health.

Full-text available at: <http://cpj.sagepub.com/> (not a U.S. Government site)

Alm B, Lagercrantz H, Wennergren G. **Stop SIDS--sleeping solitary supine, sucking soother, stopping smoking substitutes.**

Acta Paediatr. 2006 Mar; 95(3):260-2.

The recognition of prone sleeping and maternal smoking as modifiable risk factors for sudden infant death syndrome (SIDS), has drastically decreased SIDS incidence. However, during the last years other factors have become necessary to consider to further reduce the risk of SIDS. Side sleeping implies a greater risk than supine sleeping but is still common. Bed sharing may increase the risk of SIDS, while use of a pacifier seems to be protective. Replacement of maternal smoking with nicotine substitutes is not harmless. Conclusion: To further reduce the risk of SIDS, exclusive supine sleeping should be encouraged and side sleeping discouraged. When the breast-feeding is established, a pacifier can very well be used at bedtime. Bed sharing can increase the risk of SIDS if the infant is below 2-3 months of age, especially if the mother is a smoker. Any nicotine use should be avoided during pregnancy and breast-feeding.

Full-text available at: <http://www.tandf.co.uk/journals/titles/08035253.asp> (not a U.S. Government site)

Adgent MA.

**Environmental tobacco smoke and sudden infant death syndrome: A review.**

Birth Defects Res B Dev Reprod Toxicol. 2006 Feb; 77(1):69-85.

Environmental tobacco smoke (ETS), containing the developmental neurotoxicant, nicotine, is a prevalent component of indoor air pollution. Despite a strong association with active maternal smoking and sudden infant death syndrome (SIDS), information on the risk of SIDS due to prenatal and postnatal ETS exposure is relatively inconsistent.

This literature review begins with a discussion and critique of existing epidemiologic data pertaining to ETS and SIDS. It then explores the biologic plausibility of this association, with comparison of the known association between active maternal smoking and SIDS, by examining metabolic and placental transfer issues associated with nicotine, and the biologic responses and mechanisms that may follow exposure to nicotine. Evidence indicates that prenatal and postnatal exposures to nicotine do occur from ETS exposure, but that the level of exposure is often substantially less than levels induced by active maternal smoking. Nicotine also has the capacity to concentrate in the fetus, regardless of exposure source. Experimental animal studies show that various doses of nicotine are capable of affecting a neonate's response to hypoxic conditions, a process thought to be related to SIDS outcomes. Mechanisms contributing to deficient hypoxia response include the ability of nicotine to act as a cholinergic stimulant through nicotinic acetylcholine receptor (nAChR) binding. The need for future research to investigate nicotine exposure and effects from non-maternal tobacco smoke sources in mid to late gestation is emphasized, along with a need to discourage smoking around both pregnant women and infants.

Huang ZG, Griffioen KJ, Wang X, Dergacheva O, Kamendi H, Gorini C, Bouairi E, Mendelowitz D.

**Differential control of central cardiorespiratory interactions by hypercapnia and the effect of prenatal nicotine.**

J Neurosci. 2006 Jan 4; 26(1):21-9.

Hypercapnia evokes a strong cardiorespiratory response including gasping and a pronounced bradycardia; however, the mechanism responsible for these survival responses initiated in the brainstem is unknown. To examine the effects of hypercapnia on the central cardiorespiratory network, we used an in vitro medullary slice that allows simultaneous examination of rhythmic respiratory-related activity and inhibitory synaptic neurotransmission to cardioinhibitory vagal neurons (CVNs). Hypercapnia differentially modulated inhibitory neurotransmission to CVNs; whereas hypercapnia selectively depressed spontaneous glycinergic IPSCs in CVNs without altering respiratory-related increases in glycinergic neurotransmission, it decreased both spontaneous and inspiratory-associated GABAergic IPSCs. Because maternal smoking is the highest risk factor for sudden infant death syndrome (SIDS) and prenatal nicotine exposure is proposed to be the link between maternal smoking and SIDS, we examined the cardiorespiratory responses to hypercapnia in animals exposed to nicotine in the prenatal and perinatal period. In animals exposed to prenatal nicotine, hypercapnia evoked an exaggerated depression of GABAergic IPSCs in CVNs with no significant change in glycinergic neurotransmission. Hypercapnia altered inhibitory neurotransmission to CVNs at both presynaptic and postsynaptic sites. Although the results obtained in this study in vitro cannot be extrapolated with certainty to in vivo responses, the results of this study provide a likely neurochemical mechanism for hypercapnia-evoked bradycardia and the dysregulation of this response with exposure to prenatal nicotine, creating a higher risk for SIDS.

For Full-text: [www.jneurosci.org/](http://www.jneurosci.org/) (not a U.S. Government site)

Lahr MB, Rosenberg KD, Lapidus JA.

**Bedsharing and maternal smoking in a population-based survey of new mothers.**

Pediatrics. 2005 Oct; 116(4):e530-42.

Objective: Sudden infant death syndrome (SIDS) remains the number 1 cause of postneonatal infant death. Prone infant sleep position and maternal smoking have been established as risk factors for SIDS mortality. Some studies have found that bedsharing is associated with SIDS, but, to date, there is only strong evidence for a risk among infants of smoking mothers and some evidence of a risk among young infants of nonsmoking mothers. Despite the lack of convincing scientific evidence, bedsharing with nonsmoking mothers remains controversial. In some states, nonsmoking mothers are currently being told that they should not bedshare with their infants, and mothers of infants who died of SIDS are told that they caused the death of their infant because they bedshared. The objective of this study was to explore the relationship between maternal smoking and bedsharing among Oregon mothers to explore whether smoking mothers, in contrast to nonsmoking mothers, are getting the message that they should not bedshare. Methods: Oregon Pregnancy Risk Assessment Monitoring System surveys a stratified random sample, drawn from birth certificates, of women after a live birth. Hispanic and non-Hispanic black, non-Hispanic Asian/Pacific Islander and non-Hispanic American Indian/Alaskan Native women, and non-Hispanic white women with low birth weight infants are oversampled to ensure sufficient numbers for stratified analysis. The sample then was weighted to reflect Oregon's population. In 1998-1999, 1867 women completed the survey (73.5% weighted response). The median time from birth to completion of the survey was 4 months. Women were asked whether they shared a bed with their infant "always," "almost always," "sometimes," or "never." Frequent bedsharing was defined as "always" or "almost always"; infrequent was defined as "sometimes" or "never." RESULTS: Of all new mothers, 35.2% reported bedsharing frequently (always: 20.5%; almost always: 14.7%) and 64.8% infrequently (sometimes: 41.4%; never: 23.4%). Bedsharing among postpartum smoking mothers was 18.8% always, 12.6% almost always, 45.1% sometimes, and 23.6% never; this was not statistically different from among nonsmoking mothers. Results for prenatal smokers were similar. When stratified by race/ethnicity, there was no association between smoking and bedsharing in any racial or ethnic group. In univariable and multivariable logistic regression, there were no statistical differences in frequent or any bedsharing among either prenatal or postpartum smoking mothers compared with nonsmokers; the adjusted odds ratio for postpartum smokers who frequently bedshared was 0.73 (95% confidence interval [CI]: 0.42-1.25) and for any bedsharing was 1.05 (95% CI: 0.57-1.94). Results for prenatal smoking were similar. This is the first US population-based study to look at the prevalence of bedsharing among smoking and nonsmoking mothers. Bedsharing is common in Oregon, with 35.2% of mothers in Oregon reporting frequently bedsharing and an additional 41.4% sometimes bedsharing. There was no significant association between smoking and bedsharing for either prenatal or postpartum smokers among any racial or ethnic group. Smoking mothers were as likely to bedshare as nonsmoking mothers. The frequency of bedsharing in Oregon was similar to estimates from other sources. Our study has the advantage of being a population-based sample drawn from birth certificates, weighted for

nonresponse. Conclusions: Although a number of case series have raised concerns about the safety of mother-infant bedsharing, even among nonsmoking mothers, this has not yet been confirmed by careful, controlled studies. There have been 9 large-scale case-control studies of the relationship between bedsharing and SIDS. Three case-control studies did not stratify by maternal smoking status, but found no increased risk for SIDS. Six case control studies reported results stratified by maternal smoking status: 1 study, while asserting an association, provided an unexplained range of univariable odds ratios without CIs; 3 found no increased risk for older infants of nonsmoking mothers; and 2 found a risk only for infants <8-11 weeks of age. Despite the preponderance of evidence that bedsharing by nonsmoking mothers does not increase the risk for SIDS among older infants, the recent specter of bedsharing as a cause of SIDS, based on uncontrolled case series and medical examiners' anecdotal experience, has led some medical examiners to label a death "suffocation" or "overlay asphyxiation" simply because the infant was bedsharing at the time of death. This "diagnostic drift" may greatly complicate future studies of the relationship between bedsharing and SIDS. Epidemiologic evidence shows that there is little or no increased risk for SIDS among infants of nonsmoking mothers but increased risk among infants of smoking mothers and younger infants of nonsmoking mothers. It seems prudent to discourage bedsharing among all infants <3 months old. Young infants brought to bed to be breastfed should be returned to a crib when finished. It would be worthwhile for other researchers to reanalyze their previous data to evaluate the consistency of the interaction of young infant age and bedsharing. Large controlled studies that include infants who are identified as dying from SIDS, asphyxia, suffocation, and sudden unexplained infant death, analyzed separately and in combination, are needed to resolve this and other issues involving bedsharing, including the problem of diagnostic drift. Recommendations must be based on solid scientific evidence, which, to date, does not support the rejection of all bedsharing between nonsmoking mothers and their infants. Cribs should be available for those who want to use them. Nonsmoking mothers should not be pressured to abstain from bedsharing with their older infants; they should be provided with accurate, up-to-date scientific information. Infants also should not co-sleep with nonparents. In Oregon, if not elsewhere, the message that smoking mothers should not bed share is not being disseminated effectively. Because it is not known whether the risk caused by smoking is associated with prenatal smoking, postpartum smoking, or both, bedsharing among either prenatal or postpartum smokers should be strongly discouraged. Much more public and private effort must be made to inform smoking mothers, in culturally competent ways, of the very significant risks of mixing bedsharing and smoking. Public health practitioners need to find new ways to inform mothers and providers that smoking mothers should not bedshare and that putting an infant of a nonsmoking mother to sleep in an adult bed should be delayed until 3 months of age.

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Huang ZG, Wang X, Dergacheva O, Mendelowitz D.

**Prenatal nicotine exposure recruits an excitatory pathway to brainstem parasympathetic cardioinhibitory neurons during hypoxia/hypercapnia in the rat:**

### **Implications for sudden infant death syndrome.**

Pediatr Res. 2005 Sep; 58(3):562-7.

Maternal cigarette smoking and prenatal nicotine exposure increase the risk for sudden infant death syndrome (SIDS) by 2- to 4-fold, yet despite adverse publicity, nearly one of four pregnant women smoke tobacco. Infants who succumb to SIDS typically experience a severe bradycardia that precedes or is accompanied by centrally mediated life-threatening apneas and gasping. Although the causes of the apnea and bradycardia prevalent in SIDS victims are unknown, it has been hypothesized that these fatal events are exaggerated cardiorespiratory responses to hypoxia or hypercapnia. Changes in heart rate are primarily determined by the activity of cardiac vagal neurons (CVNs) in the brainstem. In this study, we tested whether hypoxia/hypercapnia evokes synaptic pathways to CVNs and whether these cardiorespiratory interactions are altered by prenatal exposure to nicotine. Spontaneous rhythmic inspiratory-related activity was recorded from the hypoglossal rootlet of 700- to 800-microm medullary sections. CVNs were identified in this preparation by retrograde fluorescent labeling, and excitatory synaptic inputs to CVNs were isolated and studied using patch-clamp electrophysiologic techniques. Hypoxia/hypercapnia did not elicit an increase in excitatory neurotransmission to CVNs in unexposed animals, but in animals that were exposed to nicotine in the prenatal period, hypoxia/hypercapnia recruited an excitatory neurotransmission to CVNs. This study establishes a likely neurochemical mechanism for the exaggerated decrease in heart rate in response to hypoxia/hypercapnia that occurs in SIDS victims.

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Hafstrom O, Milerad J, Sandberg KL, Sundell HW.

### **Cardiorespiratory effects of nicotine exposure during development.**

Respir Physiol Neurobiol. 2005 Jun 18; [Epub ahead of print]

Exposure to tobacco smoke is a major risk factor for the sudden infant death syndrome. Nicotine is thought to be the ingredient in tobacco smoke that is responsible for a multitude of cardiorespiratory effects during development, and pre- rather than postnatal exposure is considered to be most detrimental. Nicotine interacts with endogenous acetylcholine receptors in the brain and lung, and developmental exposure produces structural changes as well as alterations in neuroregulation. Abnormalities have been described in sympathicovagal balance, arousal threshold and latency, breathing pattern at rest and apnea frequency, ventilatory response to hyperoxia or hypoxia, heart rate regulation and ability to autoresuscitate during severe hypoxia. This review discusses studies performed on infants of smoking mothers and nicotine-exposed animals yielding varying and sometimes inconsistent results that may be due to differences in experimental design, species and the dose of exposure. Taken together however, developmental nicotine exposure appears to induce vulnerability during hypoxia and a potential inability to survive severe asphyxia.

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Machaalani R, Waters KA, Tinworth KD.

**Effects of postnatal nicotine exposure on apoptotic markers in the developing piglet brain.**

Neuroscience. 2005; 132(2):325-33.

Exposure to cigarette smoke is a risk factor for the sudden infant death syndrome (SIDS), but the ability to distinguish between the neuropathological effects of pre- versus postnatal exposure is limited in the clinical setting. To test whether postnatal nicotine exposure could contribute to the increased neuronal expression of apoptotic markers that we have previously observed in SIDS infants, as well as including study of gender influences, we developed a piglet model to mimic passive smoking in the early postnatal period. Piglets were exposed to nicotine (2 mg/kg/day infused via an implanted osmotic minipump) within 48 h of birth until the age of 13-14 days, when the brain was collected for study. Four piglet groups included: control females (n=7), control males (n=7), nicotine females (n=7), and nicotine males (n=7). Apoptotic markers included immunohistochemistry for activated caspase-3, and for DNA fragmentation or terminal deoxynucleotidyltransferase-mediated dUTP nick-end labeling (TUNEL) in seven nuclei of the brainstem caudal medulla and two subregions of the hippocampus (CA4 and dentate gyrus). Among control females compared with males, there was less active caspase-3 and less TUNEL in the dorsal motor nucleus of vagus (DMNV), and there was less TUNEL in the nucleus of the spinal trigeminal tract (NSTT). Compared with controls, nicotine-exposed male piglets had increased TUNEL staining in the cuneate nucleus ( $P=0.05$ ), and increased active caspase-3 in the hypoglossal, gracile and dentate gyrus ( $P<0.05$  for each). Nicotine-exposed females showed no change in TUNEL staining in any of the nuclei studied, but increased active caspase-3 in the hypoglossal, DMNV and NSTT ( $P<0.05$  for each). These results show for the first time that postnatal nicotine exposure can lead to an increase in apoptotic markers in the brain. In piglets, these effects showed regional and gender-specific differences, suggesting that passive, postnatal nicotine exposure may be responsible for some neuropathological changes observed in infants dying from SIDS.

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Amarin ZO.

**Obstetricians, gynecologists and the anti-smoking campaign: a national survey.**

Eur J Obstet Gynecol Reprod Biol. 2005 Apr 1; 119(2):156-60.

Objective: To assess the role Jordanian obstetricians and gynecologists play as tobacco cessation counselors through examining their smoking status, opinions on health risks, factors that influence tobacco use and their perceived barriers to providing effective counseling. Study Design: The setting is a tertiary referral university hospital. A pre-tested postal questionnaire survey was mailed to all 462 licensed obstetricians and gynecologists in Jordan. Descriptive statistics were generated and statistical significance was determined by the chi<sup>2</sup>-test. Results: Of 392 respondents, 37.9% were smokers. Most associated smoking with low birth weight and sudden infant death syndrome. Fewer

associated smoking with infertility, ectopic pregnancy, placenta praevia, abruptio placentae and cancer of the uterine cervix. Friends, stress, parents' attitude, genetic predisposition, income and education were implicated factors for smoking. Current smokers were more likely to permit smoking in their practices. Non-smokers were most inclined to record their patients' tobacco habits. Only 54.3% provided cessation counseling. Lack of time and inadequate training were perceived barriers. Conclusions: A high proportion of obstetricians and gynecologists are smokers. A training program is needed to equip health workers with the skills necessary for the implementation of a successful anti-smoking campaign.

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Tong EK, England L, Glantz SA.

**Changing conclusions on secondhand smoke in a sudden infant death syndrome review funded by the tobacco industry.**

*Pediatrics*. 2005 Mar; 115(3):e356-66.

Background: Prenatal and postnatal exposure to tobacco smoke adversely affects maternal and child health. Secondhand smoke (SHS) has been linked causally with sudden infant death syndrome (SIDS) in major health reports. In 1992, the US Environmental Protection Agency (EPA) first noted an association between SHS and SIDS, and both prenatal exposure and postnatal SHS exposure were listed as independent risk factors for SIDS in a 1997 California EPA report (republished in 1999 by the National Cancer Institute) and a 2004 US Surgeon General report. The tobacco industry has used scientific consultants to attack the evidence that SHS causes disease, most often lung cancer. Little is known about the industry's strategies to contest the evidence on maternal and child health. In 2001, a review was published on SIDS that acknowledged funding from the Philip Morris (PM) tobacco company. Tobacco industry documents related to this review were examined to identify the company's influence on the content and conclusions of this review. Methods: Tobacco industry documents include 40 million pages of internal memos and reports made available to the public as a result of litigation settlements against the tobacco industry in the United States. Between November 2003 and January 2004, we searched tobacco industry document Internet sites from the University of California Legacy Tobacco Documents Library and the Tobacco Documents Online website. Key terms included "SIDS" and names of key persons. Two authors conducted independent searches with similar key terms, reviewed the documents, and agreed on relevancy through consensus. Thirty documents were identified as relevant. Two drafts (an early version and a final version) of an industry-funded review article on SIDS were identified, and 2 authors independently compared these drafts with the final publication. Formal comments by PM executives made in response to the first draft were also reviewed. We used Science Citation Index in July 2004 to determine citation patterns for the referenced SIDS reviews. Results: PM executives feared that SHS and maternal and child health issues would create a powerful and emotional impetus for smoke-free areas in the home, public areas, and the workplace. In response to the 1992 US EPA report on SHS, the Science and Technology Department of PM's Switzerland subsidiary, Fabriques de Tabac Reunies, searched for "independent"

consultants to publish articles addressing SHS. The first industry-funded article was a literature review focusing on smoking and SIDS, conducted by consultant Peter Lee and co-author Allison Thornton, which stated that the association between parental smoking and SIDS could have been attributable to the failure to control fully for confounders. That first review has only been cited once, in the subsequent industry-funded review. In 1997, PM commissioned a consultant, Frank Sullivan, to write a review, with coauthor Susan Barlow, of all possible risk factors for SIDS. The first draft concluded that prenatal and postnatal smoking exposures are both independent risk factors for SIDS. After receiving comments and meeting with PM scientific executives, Sullivan changed his original conclusions on smoking and SIDS. The final draft was changed to emphasize the effects of prenatal maternal smoking and to conclude that postnatal SHS effects were "less well established." Changes in the draft to support this new conclusion included descriptions of Peter Lee's industry-funded review, a 1999 negative but underpowered study of SIDS risk and urinary cotinine levels, and criticisms of the conclusions of the National Cancer Institute report that SHS was causally associated with SIDS. In April 2001, the Sullivan review was published in the United Kingdom journal *Paediatric and Perinatal Epidemiology*, with a disclosure statement that acknowledged financial support from PM but did not acknowledge contributions from PM executives in the preparation of the review. By 2004, the Sullivan SIDS review had been cited at least 19 times in the medical literature. Conclusions: PM executives responded to corporate concerns about the possible adverse effects of SHS on maternal and child health by commissioning consultants to write review articles for publication in the medical literature. PM executives successfully encouraged one author to change his original conclusion that SHS is an independent risk factor for SIDS to state that the role of SHS is "less well established." These statements are consistent with PM's corporate position that active smoking causes disease but only public health officials conclude the same for SHS. The author's disclosure of industry funding did not reveal the full extent of PM's involvement in shaping the content of the article. This analysis suggests that accepting tobacco industry funds can disrupt the integrity of the scientific process. The background of this SIDS review is relevant for institutions engaged in the debate about accepting or eschewing funding from the tobacco industry. Those who support acceptance of tobacco industry funds argue that academic authors retain the right to publish their work and maintain final approval of the written product, but this argument fails to recognize that the tobacco industry funds work to ensure that messages favorable to the industry are published and disseminated. Clinicians, parents, and public health officials are most vulnerable to the changed conclusions of the SIDS review. The national SIDS "Back to Sleep" campaign has been very successful in reducing SIDS rates. However, estimates of SIDS risk from SHS (odds ratios range from 1.4 to 5.1) have considerable overlap with estimates of risk from prone sleep positioning (odds ratios range from 1.7 to 12.9). With the Back to Sleep campaign well underway, efforts to address parental smoking behavior in both the prenatal and postnatal periods should be intensified. The tobacco industry's disinformation campaign on SHS and maternal and child health can be counteracted within clinicians' offices.

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Kiechl-Kohlendorfer U, Hof D, Peglow UP, Traweger-Ravanelli B, Kiechl S.  
**Epidemiology of apparent life threatening events.**  
Arch Dis Child. 2005 Mar; 90(3):297-300.

**Aims:** To investigate the epidemiology and risk factors of apparent life threatening events (ALTE). **Methods:** A prospective study enrolled all live-born infants in the Tyrol (1993-2001). Information on pregnancy, sociodemographic characteristics, child care practices, and infant's behaviour in the first four to six weeks of life was collected with a standardised questionnaire, and was available for 44,184 infants. ALTE was identified from hospital admission records. **Results:** During the study period 164 ALTE cases were identified, corresponding to an incidence of 2.46/1000 live births. In 73 of these infants no cause for the event and no comorbidity could be found (idiopathic ALTE). On average ALTE manifested ten weeks earlier than SIDS. Of various SIDS risk factors in the survey area, the prone sleeping position, smoking during pregnancy, low gestational age, profuse night sweating, and family history of infant death showed a moderate relation to the risk of overall ALTE, but only smoking maintained significance in the multivariate risk model. None of these variables was associated with idiopathic ALTE. In contrast to SIDS the frequency of ALTE did not change during the study period. None of the ALTE infants experienced SIDS later in life. Behavioural abnormalities such as feeding difficulties, episodes of pallor, cyanotic episodes, and repeated apnoea episodes were strongly associated with an increased risk of overall and idiopathic ALTE. **Conclusions:** Although there are some similarities in the clinical presentation and epidemiology of SIDS and ALTE, differences clearly predominate. Accordingly, ALTE and SIDS should not be considered different manifestations of the same disease process.

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Anderson ME, Johnson DC, Batal HA.  
**Sudden Infant Death Syndrome and prenatal maternal smoking: rising attributed risk in the Back to Sleep era.**  
BMC Med. 2005 Jan 11; 3(1):4.

**Background:** Parental smoking and prone sleep positioning are recognized causal features of Sudden Infant Death. This study quantifies the relationship between prenatal smoking and infant death over the time period of the Back to Sleep campaign in the United States, which encouraged parents to use a supine sleeping position for infants. **Methods:** This retrospective cohort study utilized the Colorado Birth Registry. All singleton, normal birth weight infants born from 1989 to 1998 were identified and linked to the Colorado Infant Death registry. Multivariable logistic regression was used to analyze the relationship between outcomes of interest and prenatal maternal cigarette use. Potential confounders analyzed included infant gender, gestational age, and birth year as well as maternal marital status, ethnicity, pregnancy interval, age, education, and alcohol use. **Results:** We analyzed 488,918 birth records after excluding 5835 records with missing smoking status. Smokers were more likely to be single, non-Hispanic, less educated, and to report alcohol use while pregnant ( $p < 0.001$ ). The study included 598 SIDS cases of which 172 occurred in smoke-exposed infants. Smoke exposed infants were 1.9 times

(95% CI 1.6 to 2.3) more likely to die of SIDS. The attributed risk associating smoking and SIDS increased during the study period from approximately 50% to 80%. During the entire study period 59% (101/172) of SIDS deaths in smoke-exposed infants were attributed to maternal smoking. Conclusions: Due to a decreased overall rate of SIDS likely due to changing infant sleep position, the attributed risk associating maternal smoking and SIDS has increased following the Back to Sleep campaign. Mothers should be informed of the 2-fold increased rate of SIDS associated with maternal cigarette consumption.

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Stark CJ, Stepan MB.

**A comparison of blood pressure in term, low birth-weight infants of smoking and nonsmoking mothers.**

J Perinat Educ. 2004 Fall; 13(4):17-26.

Infants exposed to the components of cigarette smoke in utero are at an increased risk for perinatal death, low birth weight, sudden infant death syndrome, and premature delivery. The purpose of this pilot study was to compare blood pressure values in term low-birth weight infants ( $\leq 2500$  grams) born to smoking mothers to the blood pressure values of term, low-birth weight infants born to nonsmoking mothers. Data were collected through a retrospective chart review of 30 low-birth weight, term infants at a hospital in the Rocky Mountain region of the United States. Systolic, diastolic, and mean arterial pressure values were obtained from each chart. Fifteen of the infants were born to women who smoked cigarettes during pregnancy, while another 15 infants were born to mothers who did not smoke during pregnancy. While hospitalized at birth, the infants of smoking mothers shared a trend toward higher blood pressure readings for all measures, with the t-test differences reaching statistical significance for systolic arm ( $p = .024$ ), diastolic leg ( $p = .03$ ), and mean arterial pressure of the arm ( $p = .038$ ).

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**Smoking during pregnancy- United States, 1990-2002.**

Morbidity and Mortality Weekly Report 2004 Oct 8; 53(39):911-5.

Cigarette smoking during pregnancy adversely affects the health of both mother and child. The risk for adverse maternal conditions (e.g., premature rupture of membranes, abruptio placentae, and placenta previa) and poor pregnancy outcomes (e.g., neonatal mortality and stillbirth, preterm delivery, and sudden infant death syndrome) is increased by maternal smoking. Infants born to mothers who smoke weigh less than other infants, and low birthweight ( $< 2,500$  grams) is a key predictor for infant mortality. Infertility and conception delay also might be elevated by smoking. National health objectives for 2010 target an increase in cessation to 30% among pregnant smokers during the first trimester

and abstinence from cigarettes by 99% of women giving birth. To assess progress toward these goals, CDC analyzed state-specific trends in maternal smoking during 1990-2002 by using data collected on birth certificates. This report summarizes the results of those analyses, which indicated that whereas participating areas observed a significant decline in maternal smoking during the surveillance period, 10 states reported recent increases in smoking by pregnant teens. Although the widespread public health message to abstain from smoking during pregnancy has helped decrease maternal smoking, to reduce prevalence further, implementation of additional interventions are required.

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McLemore GL, Cooper RZ, et al.

**Cannabinoid receptor expression in peripheral arterial chemoreceptors during postnatal development.**

J Appl Physiol 2004 Oct; 97(4): 1486-95.

Prenatal exposure to tobacco smoke increases risk of sudden infant death syndrome (SIDS). Marijuana is frequently smoked in conjunction with tobacco, and perinatal exposure to marijuana is associated with increased incidence of SIDS. Abnormalities in peripheral arterial chemoreceptor responses during sleep may be operative in infants at risk for SIDS, and nicotine exposure adversely affects peripheral arterial chemoreceptor responses. To determine whether marijuana could potentially affect the activity of peripheral arterial chemoreceptors during early postnatal development, we used in situ hybridization histochemistry to characterize the pattern and level of mRNA expression for cannabinoid type 1 receptor (CB1R) in the carotid body, superior cervical ganglia (SCG), and nodose-petrosal-jugular ganglia (NG-PG-JG) complex in newborn rats. We used immunohistochemistry and light, confocal, and electron microscopy to characterize the pattern of CB1R and tyrosine hydroxylase protein expression. CB1R mRNA expression was intense in the NG-PG-JG complex, low to moderate in the SCG, and sparse in the carotid body. With maturation, CB1R gene expression significantly increased ( $P < 0.01$ ) in the NG-PG-JG complex. CB1R immunoreactivity was localized to nuclei of ganglion cells in the SCG and NG-PG-JG complex, whereas tyrosine hydroxylase immunoreactivity was localized to the cytoplasm. Exposure to marijuana during early development could potentially modify cardiorespiratory responses via peripheral arterial chemoreceptors. The novel finding of nuclear localization of CB1Rs in peripheral ganglion cells suggests that these receptors may have an, as yet, undetermined role in nuclear signaling in sensory and autonomic neurons.

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Moscovis SM, Gordon AE, et al.

**Interleukin-10 and sudden infant death syndrome.**

FEMS Immunol Med Microbiol 2004 Sep; 42(1):130-8.

Uncontrolled pro-inflammatory responses to infections or bacterial toxins have been suggested to play a role in triggering the physiological events leading to sudden infant

death syndrome (SIDS). We tested the hypothesis that these uncontrolled responses might be due to interactions between the gene polymorphisms inducing low levels of IL-10 and exposure to cigarette smoke. In vitro, the IL-10 (G-1082A) polymorphism was associated with low IL-10 levels and the -1082G allele was associated with high levels. The first objective was to assess the distribution of this polymorphism among SIDS infants, parents of SIDS infants and controls, and two ethnic groups: Aboriginal Australians who have a high incidence of SIDS; and Bangladeshis who in Britain have a low incidence of SIDS compared with Europeans. The second objective was to assess effects of human recombinant IL-10 on interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-alpha) responses of human leukocytes to staphylococcal toxins implicated in SIDS. The third objective was to assess IL-10 responses to endotoxin and toxic shock syndrome toxin (TSST) from leukocytes of smokers and non-smokers in relation to the IL-10 (G-1082A) polymorphism. There were major differences in the distributions of these polymorphisms between Europeans and Bangladeshis ( $p=0.00$ ) and between Europeans and Aboriginal Australians ( $p=0.00$ ); however, they were similar for the Bangladeshi and Aboriginal Australian subjects. There were no significant differences in the distribution of these polymorphisms among SIDS infants or parents of SIDS infants compared to control groups. IL-10 significantly reduced IL-6 and TNF-alpha responses to TSST and staphylococcal enterotoxins A and C. At 50 ng/ml(-1), IL-10 significantly increased TNF-alpha but not IL-6 responses to TSST and enterotoxin A. Although IL-10 responses to endotoxin were lower from leukocytes of smokers who were homozygous for the G allele, the differences were not significant; however, significantly lower IL-10 responses were found for smokers who were homozygous for the A allele ( $p=0.01$ ) and heterozygotes ( $p=0.04$ ). The pooled data found smokers had significantly lower levels of IL-10 responses to TSST, but there were no significant differences for smokers compared with non-smokers for the three genotypes. The high incidence of SIDS and serious respiratory infections among Aboriginal Australian infants and the low incidence of these conditions among Bangladeshi infants might be explained in part by our findings of differences in IL-10 responses between smokers and non-smokers. The lowest levels of IL-10 responses were observed among smokers who were homozygous for the A allele which is most prevalent among the Aboriginal Australians (83%) and Bangladeshis (84%). The major difference between the risk factors for SIDS in these two groups is the level of exposure of infants to cigarette smoke associated with maternal smoking.

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Cnattingius S.

**The Epidemiology of Smoking during Pregnancy: Smoking Prevalence, Maternal Characteristics, and Pregnancy Outcomes.**

Nicotine Tob Res 2004; 6(Supp 2):S125-S140.

The prevalence of smoking during pregnancy varies markedly across countries. In many industrialized countries, prevalence rates appear to have peaked and begun to decline, whereas in other countries smoking is becoming increasingly common among young women. Randomized controlled trials have shown that smoking interventions during pregnancy have had limited success. Smoking during pregnancy is in many countries

recognized as the most important preventable risk factor for an unsuccessful pregnancy outcome. Smoking is causally associated with fetal growth restriction, and increasing evidence also suggests that smoking may cause stillbirth, preterm birth, placental abruption, and possibly also sudden infant death syndrome. Smoking during pregnancy also is generally associated with increased risks of spontaneous abortions, ectopic pregnancies, and placenta previa and may increase risks of behavioral disorders in childhood. Smoking during pregnancy will continue to be an important risk factor for maternal and fetal outcomes during pregnancy.

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Klerman LV.

**Protecting children: Reducing their environmental tobacco smoke exposure.**

Nicotine Tob Res 2004 Apr; 6(Supp 2): S239-S253.

The present review examines the current status of efforts to reduce environmental tobacco smoke exposure (ETS) among infants and young children. Estimates of the number of children exposed vary, but it is probably over 20 million or about 35% of all U.S. children. Healthy People 2010 sets as an objective the reduction, to 10%, of the proportion of children regularly exposed to tobacco smoke at home. Children with ETS exposure are at higher risk for upper respiratory illnesses, asthma, otitis media, and sudden infant death syndrome. Eight experimental or quasi-experimental studies of attempts to reduce children' ETS exposure with sample sizes of greater than 100 were conducted in the United States and published between 1990 and 2003. Most of these studies showed a significant impact on maternal smoking and on the number of cigarettes smoked in the home, although intervention-control differences were relatively small. Despite support from professional organizations and federal government groups, many pediatricians and family physicians do not routinely engage in intensive efforts to reduce children's ETS exposure. Training in techniques for reducing tobacco dependence should be included in professional education programs. Public and private insurance should reimburse providers for efforts in this area. An overall strategy for reducing children's ETS exposure should combine individual counseling and education in offices, clinics, and homes with community education and regulatory and economic policies (i.e., smoking bans and excise taxes). Additional funding is needed for studies of provider knowledge, attitudes, and practices; of the effectiveness of various communication strategies; and of office- and community-based strategies to reduce ETS exposure.

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Chong, DS, Yip PS, Karlberg J.

**Maternal smoking: An increasing unique risk factor for Sudden Infant Death Syndrome in Sweden.**

Acta Paediatrica 2004 Apr; 93(4):471-8.

Aim: To assess the change of risk factors that are specific to sudden infant death syndrome (SIDS) after the initialization of a campaign to reduce the risk (RTR) of SIDS

compared to non-SIDS postneonatal deaths. Methods: Data were extracted from the Swedish Medical Birth Registry, 1982-1991 and 1993-1998. 1105 infants died from SIDS during the postneonatal period. 2115 postneonatal deaths were from other causes and 11,050 live birth controls were selected. Risk factors previously identified to be related to SIDS were defined as high parity, prematurity, young maternal age, low Apgar score, birth during the night, single motherhood, multiple births, maternal smoking, male gender, short length standard deviation score (SDS) and small weight-to-length SDS. Results: Non-SIDS deaths were more significantly related to a low 5-min Apgar score, smaller weight-to-length SDS, and/or short length SDS values; while SIDS deaths were more closely related to mothers with higher parity or multiple births, mothers who smoked during pregnancy and single-parent (mother) families. Maternal smoking was even more prominent among SIDS deaths in the post-campaign period. The adjusted odds ratios, compared with non-SIDS deaths, increased from 1.84 (95% CI: 1.48, 2.28) in the pre-campaign period to 4.11 (95% CI: 2.72, 6.21) in the post-campaign period. Conclusions: Maternal smoking during pregnancy remains the most important modifiable risk factor for SIDS in the post-campaign period in comparison with non-SIDS postneonatal deaths. Other than putting babies in a supine sleeping position, maternal smoking should be the next most important issue to be considered, if there is to be a second campaign.

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Sundell HW.

**SIDS prevention--Good progress, but now we need to focus on avoiding nicotine.**

Acta Paediatrica 2004; 93(4): 450-2.

Chong et al. examined risk factors for sudden infant death syndrome (SIDS) before and after the start of the Swedish campaign to reduce the risk of SIDS. They found that maternal smoking was the strongest risk factor for SIDS in the post-campaign compared to the pre-campaign period. Conclusion: After successful results of the SIDS campaigns to prevent prone sleeping, strong efforts need to be undertaken to eliminate maternal smoking during pregnancy altogether without replacing cigarette smoking with other nicotine delivery devices such as snuff, gum or patches.

Full-text available at: [www.ingentaconnect.com](http://www.ingentaconnect.com) (not a U.S. Government site)

Albrecht SA, Maloni JA, et al.

**Smoking cessation counseling for pregnant women who smoke: Scientific basis for practice for AWHONN's SUCCESS project.**

J Obstet Gynecol Neonatal Nurs 2004 May-Jun; 33(3): 298-305.

Objectives: To review the literature addressing smoking cessation in pregnant women. To develop the project protocol for the Association of Women's Health, Obstetric and Neonatal Nurse's (AWHONN) 6th research-based practice project titled "Setting Universal Cessation Counseling, Education and Screening Standards (SUCCESS): Nursing Care of Pregnant Women Who Smoke." To evaluate the potential of systematic

integration of this protocol in primary care settings in which women seek care at the preconception, pregnant, or postpartum stages. Literature Scores: Computerized searches in MEDLINE and CINAHL, as well as references cited in articles reviewed. Key concepts in the searches included low-birth-weight infants and effects of prenatal smoking on the infant and the effects of preconception and prenatal smoking cessation intervention on premature labor and birth weight. Literature Selection: Comprehensive articles, reports, and guidelines relevant to key concepts and published after 1964 with an emphasis on new findings from 1996 through 2002. Ninety-eight citations were identified as useful to this review. Literature Synthesis: Tobacco use among pregnant women and children's exposure to tobacco use (secondhand smoke) are associated with pregnancy complications such as placental dysfunction (including previa or abruption), preterm labor, premature rupture of membranes, spontaneous abortions, and decreased birth weight and infant stature. Neonates and children who are exposed to secondhand smoke are at increased risk for developing otitis media, asthma, other respiratory disorders later in childhood; dying from sudden infant death syndrome; and learning disorders. The "5 A's" intervention and use of descriptive statements for smoking status assessment were synthesized into the SUCCESS project protocol for AWHONN's 6th research-based practice project. Conclusions: The literature review generated evidence that brief, office-based assessment, client-specific tobacco counseling, skill development, and support programs serve as an effective practice guideline for clinicians. Implementation and evaluation of the guideline is under way at a total of 13 sites in the United States and Canada.

Full-text available at: [jognn.awhonn.org](http://jognn.awhonn.org) (not a U.S. Government site)

Spencer N, Logan S.

**Sudden Unexpected Death in Infancy and socioeconomic status: A systematic review.**

J Epidemiol Community Health 2004 May; 58(5):366-73.

This paper aimed to systematically review observational studies documenting the relation between sudden unexpected death in infancy and socioeconomic status. A search of two electronic databases (Medline 1966 to November 2002; Embase 1981 to November 2002) yielded 52 case-control or cohort studies meeting the inclusion criteria. An increased risk of sudden unexpected death in infancy was reported in 51 studies and 32 of 33 studies reporting graded measures of socioeconomic status showed a dose-response relation of sudden death with socioeconomic status. Of the 10 studies in which adjustment was made for maternal smoking, socioeconomic status retained an independent effect on infant death in nine. The effect of socioeconomic status was also independent of birth weight in 10 of 11 studies and independent of sleeping position in two. The included studies reported a significant association of socioeconomic status with sudden unexpected death in infancy with risk of infant death increasing with greater exposure to adverse social circumstances. The findings support a significant role for adverse social circumstances in the pathways to sudden unexpected death in infancy.

Full-text available at: [jech.bmjournals.com/](http://jech.bmjournals.com/) (not a U.S. Government site)

Sartiani L, Cerbai E, et al.

**Prenatal exposure to carbon monoxide affects postnatal cellular electrophysiological maturation of the rat heart: a potential substrate for arrhythmogenesis in infancy.**

Circulation 2004 Jan14; 109: 419-23.

Background: Maternal smoking is an independent risk factor for sudden infant death syndrome (SIDS). Carbon monoxide (CO) is a major component of smoke. No information is available about the effect of CO and/or smoking on postnatal maturation of the heart. The aim of this study was to investigate the effect of prenatal exposure to CO on cellular electrophysiological maturation in male Wistar rats. Methods and Results: The patch-clamp technique was used to measure action potential (AP) and ionic currents (Ito and I<sub>Ca,L</sub>) from rat ventricular myocytes. During growth, AP duration measured at -20 and -50 mV (APD-20 and APD-50) decreased progressively in both groups; the process was significantly delayed in rats exposed prenatally to 150 ppm CO: At 4 weeks, APD-20 and APD-50 were 89.5±18.2 and 147.7±24.5 ms in CO (n=13) and 35.6±4.5 and 77.8±8.3 ms in control rats (Ctr; n=14; P<0.01 and P<0.05, respectively) and normalized at 8 weeks. At 4 weeks, the density of I<sub>Ca,L</sub> was significantly higher (21.3±1.6 pA/pF, n=17, versus 15.9±1.6 pA/pF, n=22; P<0.05) and the density of Ito significantly lower (9.6±1.5, n=22, versus 15.2±2.2 pA/pF, n=19; P<0.01) in CO than in Ctr and normalized thereafter. Conclusions: Prenatal CO exposure affects the physiological shortening of APD in neonatal rats. We speculate that a prolonged myocyte repolarization induced by prenatal exposure to smoke may establish a period of vulnerability for life-threatening arrhythmias in infancy.

Full-text available at: [circ.ahajournals.org/](http://circ.ahajournals.org/) (not a U.S. Government site)

Carpenter RG, Irgens LM, et al.

**Sudden Unexplained Infant Death in 20 regions in Europe: Case control study.**

The Lancet 2004 Jan 17; 363(9404): 185-91.

Background: After striking changes in rates of sudden unexplained infant death (SIDS) around 1990, four large case-control studies were set up to re-examine the epidemiology of this syndrome. The European Concerted Action on SIDS (ECAS) investigation was planned to bring together data from these and new studies to give an overview of risk factors for the syndrome in Europe. Methods: We undertook case-control studies in 20 regions. Data for more than 60 variables were extracted from anonymised records of 745 SIDS cases and 2411 live controls. Logistic regression was used to calculate odds ratios (ORs) for every factor in isolation, and to construct multivariate models. Findings: Principal risk factors were largely independent. Multivariately significant ORs showed little evidence of intercentre heterogeneity apart from four outliers, which were eliminated. Highly significant risks were associated with prone sleeping (OR 13•1 [95% CI 8•51-20•2]) and with turning from the side to the prone position (45•4 [23•4-87•9]). About 48% of cases were attributable to sleeping in the side or prone position. If the mother smoked, significant risks were associated with bed sharing, especially during the first weeks of life (at 2 weeks 27•0 [13•3-54•9]). This OR was partly attributable to

mother's consumption of alcohol. Mother's alcohol consumption was significant only when baby bed-shared all night (OR increased by 1.66 [1.16-2.38] per drink). For mothers who did not smoke during pregnancy, OR for bed sharing was very small (at 2 weeks 2.4 [1.2-4.6]) and only significant during the first 8 weeks of life. About 16% of cases were attributable to bed sharing and roughly 36% to the baby sleeping in a separate room. Interpretation: Avoidable risk factors such as those associated with inappropriate infants' sleeping position, type of bedding used, and sleeping arrangements strongly suggest a basis for further substantial reductions in SIDS incidence rates.

Full-text available at: [www.thelancet.com](http://www.thelancet.com) (not a U.S. Government site)

Sawnani H, Jackson T, et al.

**The effect of maternal smoking on respiratory and arousal patterns in preterm infants during sleep.**

Am J Respir Crit Care Med 2004 Mar 15; 169(6): 733-8.

Prenatal exposure to cigarette smoke is associated with an increased risk of sudden infant death syndrome. The effect of maternal smoking on apnea and arousal patterns in preterm infants is currently unknown. Multichannel polysomnographic studies were performed in preterm infants. Thirty infants were enrolled into the study; 16 exposed prenatally to cigarette smoke [S] and 14 controls[C]. There was no difference in the gestational and post-conceptional ages at the time of study. Maternal smoking was associated with a significant increase in apneic index in these infants (28.6 + 6.4/hr [S] vs 13.2 + 3.9 [C]; P <0.05), and the difference was noted for obstructive events and only during active sleep. The arousal index was significantly decreased in maternal smoking group (34.5 + 2.3/hr[S] vs 46.3 + 5.6/hr[C]; P<0.05) with a specific decrease in percentage of arousal following respiratory events (10.7 + 2.1%[S] vs 29.4 + 5.4%[C]; P <0.05). In conclusion, preterm infants exposed prenatally to cigarette smoke have increased respiratory events during active sleep, predominantly due to obstructive apnea, and possibly a higher arousal threshold during apneic events. These alterations in respiratory and arousal patterns in preterm infants born to smoking mothers may lead to significant vulnerability in this population.

Full-text available at: [ajrccm.atsjournals.org/](http://ajrccm.atsjournals.org/) (not a U.S. Government site)

Chang AB, Wilson SJ, et al.

**Altered arousal response in infants exposed to cigarette smoke.**

Arch Dis Child 2003 Jan; 88(1): 30-33.

A failure of the arousal mechanism is a key feature in the apnoea theory for sudden infant death syndrome (SIDS). In infants studied at an age when the incidence of SIDS is highest, we evaluated whether in utero smoke exposed infants have altered arousal response to standardized auditory stimuli, and/or sleep pattern, as recorded on overnight complex sleep polysomnography. Methods: A standardized sequence of audiology stimuli was applied binaurally to 20 in utero smoke and non-smoke exposed infants aged 8–12 weeks during a rapid eye movement (REM) and NREM epoch, in a controlled

(temperature, position, pacifier use, noise) sleep environment. Infants were monitored for 10–12 hours using complex sleep polysomnography. Results: Five infants exposed to in utero tobacco smoke did not have Behavioral arousal response, whereas all non-smoke exposed infants aroused during NREM ( $p = 0.016$ ). There was, however, no difference in REM sleep, and the groups did not differ in routine overnight complex sleep polysomnography parameters. Conclusion: At the age when the incidence of SIDS is at its peak, infants of smoking mothers are less rousable than those of non-smoking mothers in NREM sleep; this may partly explain why such infants are more at risk of SIDS.

Full-text available at: [www.archdischild.com](http://www.archdischild.com) (not a U.S. Government site)

Kahn A, Sawaguchi T, Sawaguchi A, et al.

**Sudden infant deaths: From epidemiology to physiology.**

Forensic Sci Int 2002 September 14; 130(Suppl 1): S 8-20.

The incidence of sudden infant death syndrome (SIDS) has dropped significantly in most countries following the development of education campaigns on the avoidance of risk factors for SIDS. However, questions have been raised about the physiological mechanism responsible for the effects of these environmental risk factors. Since 1985, a series of prospective, multi centric studies have been developed to address these questions; over 20,000 infants were recorded during one night in a sleep laboratory and among these, 40 infants eventually died of SIDS. In this review, the following methods were employed: sleep recordings and analysis, monitoring procedure, data analysis of sleep stages, cardiorespiratory and oxygen saturation, scoring of arousals, spectral analysis of the heart rate and the determination of arousal thresholds, and statistical analysis and the results including sleep apneas, arousals and heart rate and autonomic controls in both future SIDS victims and normal infants were introduced separately. In addition, the physiological effect of prenatal risk factors (maternal smoking during gestation) and postnatal risk factors (administration of sedative drugs, prone sleeping position, ambient temperature, sleeping with the face covered by a bed sheet, pacifiers and breastfeeding) in normal infants were analyzed. In conclusion, the physiological studies undertaken on the basis of epidemiological findings provide some clues about the physiological mechanisms linked with SIDS. Although the description of the mechanisms responsible for SIDS is still far from complete, it appears to involve both arousal responses and cardiac autonomic controls during sleep–wake processes.

Full-text available at: [www.sciencedirect.com](http://www.sciencedirect.com) (not a U.S. Government site)

Hafstrom O, Milerad J, Sundell HW.

**Prenatal nicotine exposure blunts the cardiorespiratory response to hypoxia in lambs.**

Am J Respir Crit Care Med 2002 Dec; 166(12): 1544-49.

Because smoking during pregnancy is a major risk factor for late fetal death and the sudden infant death syndrome, we investigated cardiorespiratory defense mechanisms to hypoxia in 7 prenatally nicotine-exposed (N) lambs (approximate maternal dose: 0.5

mg/kg/day) and 11 control (C) lambs all at an average age of 5 days. The ventilatory response to 10% oxygen (hyperpnea) was significantly attenuated during quiet sleep in N lambs compared with C lambs and in N lambs aroused from sleep later compared with C lambs ( $161 \pm 90$  versus  $75 \pm 66$  seconds,  $p < 0.05$ ). The ventilatory response to hypoxia was similar in the two groups during wakefulness (W), whereas the heart rate response (tachycardia) was significantly lower in N lambs compared with C lambs during both activity states. The ventilatory response to hyperoxia was significantly lower in N lambs compared with C lambs during both activity states. Transition from W to quiet sleep was associated with a significant decrease in ventilation in C lambs but not in N lambs. In conclusion, prenatal nicotine exposure, at a dose comparable with moderate smoking, blunts major elements of the cardiorespiratory defense to hypoxia, i.e., the heart rate and ventilatory and arousal responses, and abolishes the normal decrease in ventilation during sleep compared with W.

Full-text available at: [ajrccm.atsjournals.org/](http://ajrccm.atsjournals.org/) (not a U.S. Government site)

Mathews TJ, Menacker F, MacDorman MF.

**Infant Mortality Statistics from the 2000 period linked birth/infant death data set.**

National Vital Statistics Reports 2002 August 28; 50(12): 1-28.

**Objectives:** This report presents the 2000 period infant mortality statistics from the linked birth/infant death data set (linked file) by a variety of maternal and infant characteristics. **Methods:** Descriptive tabulations of data are presented and interpreted. **Results:** Infant mortality rates ranged from 3.5 per 1,000 live births for Chinese mothers to 13.5 for black mothers. Among Hispanics, rates ranged from 4.5 for Cuban mothers to 8.2 for Puerto Rican mothers. Infant mortality rates were higher for those infants whose mothers had no prenatal care, were teenagers, had 9-11 years of education, were unmarried or smoked during pregnancy. Infant mortality was also higher for male infants, multiple births, and infants born preterm or at low birth weight. The three leading causes of infant death--Congenital malformations, low birth weight, and Sudden infant death syndrome (SIDS)--taken together accounted for 45 percent of all infant deaths in the United States in 2000. Cause specific mortality rates varied considerably by race and Hispanic origin. For infants of black mothers, the infant mortality rate for low birth weight was nearly four times that for white mothers. For infants of black and American Indian mothers, the SIDS rates were 2.4 and 2.3 times that for non-Hispanic white mothers.

Full-text downloading available at: [www.cdc.gov/nchs/about/major/dvs/mortdata.htm](http://www.cdc.gov/nchs/about/major/dvs/mortdata.htm)

Williams SM, Mitchell EA, Taylor BJ.

**Are risk factors for sudden infant death syndrome different at night?**

Arch Dis Child 2002 Oct; 87(4): 274-278.

**Aims:** To determine whether the risk factors for SIDS occurring at night were different from those occurring during the day. **Methods:** Large, nationwide case-control study, with data for 369 cases and 1558 controls in New Zealand. **Results:** Two thirds of SIDS deaths occurred at night (between 10 pm and 7 30 am). The odds ratio (95% CI) for prone

sleep position was 3.86 (2.67 to 5.59) for deaths occurring at night and 7.25 (4.52 to 11.63) for deaths occurring during the day; the difference was significant. The odds ratio for maternal smoking for deaths occurring at night was 2.28 (1.52 to 3.42) and that for the day 1.27 (0.79 to 2.03); that for the mother being single was 2.69 (1.29 to 3.99) for a night time death and 1.25 (0.76 to 2.04) for a daytime death. Both interactions were significant. The interactions between time of death and bed sharing, not sleeping in a cot or bassinet, Maori ethnicity, late timing of antenatal care, binge drinking, cannabis use, and illness in the baby were also significant, or almost so. All were more strongly associated with SIDS occurring at night. Conclusions: Prone sleep position was more strongly associated with SIDS occurring during the day, whereas night time deaths were more strongly associated with maternal smoking and measures of social deprivation.

Full-text available at: [www.archdischild.com](http://www.archdischild.com) (not a U.S. Government site)

Kelmanson IA, Erman LV, Litvina SV.

**Maternal smoking during pregnancy and behavioural characteristics in 2 - 4-month-old infants.**

Klinische Padiatrie 2002 Nov-Dec; 214(6): 359-364.

The study aimed to assess potential relationship between maternal smoking during pregnancy and behavioral characteristics in 2-4-month-old infants. It covered period from 1999 to 2000 and comprised 250 randomly selected, apparently healthy singleton born infants from community setting (129 boys, 121 girls). The mothers were asked to complete the questionnaires addressing infant, maternal, demographic major characteristics with particular emphasis on maternal smoking during pregnancy. To objectively assess Behavioral peculiarities of the infants, the mothers were requested to complete the Early Infancy Temperament Questionnaire. Of 250 mothers, 64 women (25.6 %) smoked during pregnancy. The infants of smoking mothers were more often born low birth weight and were also lighter at study; more frequently they were born at earlier gestational age, had lower Apgar score at 5th minute, were less frequently breast fed at birth and at the time of study. Mothers who smoked during pregnancy were younger, had lower educational level, and less frequently were married. The infants born to smoking mothers had more frequent fussy periods occurring at about the same time of the day, protesting behavior at face washing and washing in bath, indifferent attitude to the mother when held by new person, extreme reactions (either indifference or much feeling) during diapering and bowel movement, less attention to the parents during parent-infant play activity, and more sensitivity to the wet diaper. They were also characterized by more intensive reactions (displayed more amount of energy regardless of positive or negative behavior) compared with the babies from the non-smoking group. This association remained after adjustment has been made for major potential confounders, and had a significant "dose-response" effect. Maternal smoking during pregnancy may serve as a risk factor for infant's Behavioral deviations.

Full-text available at: [www.thieme-connect.com/ejournals/toc/klinpaed](http://www.thieme-connect.com/ejournals/toc/klinpaed) (not a U.S. Government site)

Gordon AE, El Ahmer OR, Chan R, et al.

**Why is smoking a risk factor for sudden infant death syndrome?**

Child Care Health Dev 2002 Sep; 28 (Suppl 1): 23-25.

Smoking is a major risk factor for both Sudden Infant Death Syndrome (SIDS) and respiratory tract infections. Such infections, both viral and bacterial, also increase the SIDS risk. This study investigated the effect of cigarette smoke at two stages of infection: 1) mucosal surface colonization; 2) induction and control of inflammatory responses. For colonization, RSV or influenza. An infected cells bound several bacterial species in significantly higher numbers due to increased expression of host cell antigens. Buccal epithelial cells from smokers bound significantly more bacteria. For *Staphylococcus aureus*, this was associated with increased tar levels. Some SIDS deaths have been proposed to result from high levels of pro-inflammatory mediators elicited by infection and/or cigarette smoke during a developmental period when infants are less able to control inflammatory responses. Inflammatory responses were compared between blood samples from smokers (n = 42) and non-smokers (n = 60) stimulated with TSST-1 or LPS. Non-smokers had significantly higher IL-6 (P = 0.011), IFN (P = 0.003) and IL-10 (P = 0.000) baseline levels. Non-smokers had higher IFN (P = 0.008) and IL-1 (P = 0.001, 0.007) responses to LPS and higher IL-10 responses to TSST-1 (P < 0.05) and LPS (P < 0.000). This study highlights that smoking increases the SIDS risk by greater susceptibility to viral and bacterial infections and enhanced bacterial binding after passive coating of mucosal surfaces with smoke components. In animal models, IL-10 reduced the lethal effect of staphylococcal toxins. In this study, smokers had lower IL-10 responses to TSST-1 and LPS. Dose response effects of cigarette smoke exposure needs to be established in relation to inflammatory response control and infantile infections.

Full-text available at: [www.blackwell-synergy.com](http://www.blackwell-synergy.com) (not a U.S. Government site)

Tutka P, Wielosz M, Zatonski W.

**Exposure to environmental tobacco smoke and children health.**

Int J Occup Med Environ Health 2002; 15(4): 325-335.

This paper reviews the investigations of the effects of pre- and/or postnatal exposure to environmental tobacco smoke (ETS) on children health reported in the literature. The evidence from epidemiological studies demonstrates that children's exposure to ETS is a risk factor for a variety of diseases, including respiratory disorders and middle ear disease. However, the current research base on the ETS-associated risks is still inadequate to fully support strategies, programs and policy development in this area. For example, it is not definitively determined what methods should be used for assessing ETS exposure and predicting potential health risks of exposed children. Based on the available data, we tried to find out which methods seem to be most desirable for quantifying ETS exposure in children. It is our opinion that among all biomarkers, the measurements of blood, saliva or urinary cotinine and hair nicotine are, as for today, the most specific and sensitive methods for an objective assessment of ETS exposure in children. A combination of the measurement of body fluids cotinine and hair nicotine with the

questionnaire and interview-derived information seems to be the optimal method for assessing ETS exposure in children.

Froen JF, Akre H, Stray-Pedersen B, Saugstad OD.

**Prolonged apneas and hypoxia mediated by nicotine and endotoxin in piglets.**

Biol Neonate 2002; 81(2): 119-125.

Objective: Infections and maternal smoking are risk factors for SIDS, and toxins from common bacteria have been proposed as a causative link between infections and SIDS. Nicotine can be transferred in significant amounts postnatally to the infant through environmental tobacco smoke or maternal smoking before nursing. We investigated the acute effects of nicotine and endotoxin on repeated apnea by laryngeal reflex stimulation and the following autoresuscitation. Design: Thirty-four 1-week-old (+/- 1 day) piglets were sedated and randomized to 1 of 4 pretreatment groups: (1) 1 microg endotoxin i.v./kg; (2) 5 microg nicotine i.v./kg; (3) 1 microg endotoxin i.v./kg and 5 microg nicotine i.v./kg, and (4) placebo. Apnea was induced by insufflation of 0.1 ml of acidified saline (pH 2) in the subglottic space of the trachea three times with intervals of 2 min. Results: Pretreatment with endotoxin caused a significant increase in plasma TNF-alpha in the endotoxin groups (mean value +/- SEM 953 +/- 246 and 980 +/- 226 pg/ml, respectively) but no significant change in plasma IL-1 beta. Blood pressure, respiratory rate or S(a)O(2) was not significantly affected before induced apnea. Both pretreatment with nicotine and endotoxin caused prolonged apneas by 35-45%, a complete loss of normal hyperventilation during autoresuscitation, and prolonged hypoxia after apnea. Conclusions: Nicotine and endotoxin interferes with autoresuscitation after apnea. This experimental model on piglets may shed light over important mechanisms involved in the causation of SIDS.

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Mahabee-Gittens, M.

**Smoking in parents of children with asthma and bronchiolitis in a pediatric emergency department.**

Pediatr Emerg Care 2002 Feb; 8(1): 4-7.

Objectives: To determine smoking habits, levels of nicotine-addiction, readiness to quit, and beliefs about the effects of environmental tobacco smoke (ETS) of parents of children with bronchiolitis and asthma who present to a children's emergency department (ED). Design/Methods: This was a cross-sectional prevalence study of parents or legal guardians of children with asthma or bronchiolitis presenting to a pediatric ED. Results: Two hundred forty-nine parents/legal guardians comprised the study group. The mean age (+/-SD) was 30.0 (+/-8.9) years; 88% were female; 51% were nonwhite; 37% were educated beyond high school. The self-reported smoking prevalence was 41% (95% CI = 32-51). Smoking prevalence among parents of wheezing children varied according to education, income, and race, but not according to gender, age, or employment status. Of

the 102 smokers in the sample, 84 (82.4%, 95% CI = 73-88) reported that they wanted to quit; 78 (76.5%, 95% CI = 68-84) stated that they wanted to quit within the next month. Forty-nine percent (95% CI = 39-59) scored above 4 on the Fagerstrom Test for Nicotine Dependence and were considered nicotine-dependent. The majority of smokers admitted to smoking around their children (66.7%, 95% CI = 57-75). Many parents knew that ETS might contribute to the development of the following illnesses: colds/upper respiratory tract infections - 77.5%, otitis media - 68.6%, pneumonia - 50%, wheezing/asthma attacks - 86.3%, and SIDS - 31.4%. Conclusion: The prevalence of smoking and nicotine addiction among parents of children with asthma or bronchiolitis who bring their children to a pediatric ED is high. Many parents have some knowledge about the effects of ETS, and the majority would like to quit. Future studies to help determine the best way to deliver advice to parents on ETS exposure reduction and smoking cessation are warranted.

Full-text available at: [www.pec-online.com/pt/re/pec/home.htm](http://www.pec-online.com/pt/re/pec/home.htm) (not a U.S. Government site)

Panaretto KS, Smallwood VE, Cole P, et al.

**Sudden infant death syndrome risk factors in North Queensland: A survey of infant-care practices in Indigenous and non-Indigenous women.**

J Paediatr Child Health 2002 Apr; 38(2): 129-134.

Objective: To assess the prevalence of sudden infant death syndrome (SIDS) risks factors in the Indigenous and non-Indigenous community of Townsville, a large remote urban centre in north Queensland, Australia. Methods: Thirty Indigenous and 30 non-Indigenous women with young children were surveyed using sections of the West Australian Infancy and Pregnancy Survey 1997-1998. The prevalence of SIDS risk factors was compared between the two groups and medians and univariate associations were generated where appropriate. Results: The Indigenous women were significantly younger and more likely to be single. The median age of the infants was 8 months (range 0.3-26 months) with no difference between the two groups. Thirty-seven per cent of Indigenous infants slept prone (cf. 17% of non-Indigenous infants;  $P = 0.03$ ), and 77% shared a bed (cf. 13% of non-Indigenous infants;  $P < 0.001$ ). The Indigenous households had significantly more members, with 57% including extended family members (cf. 20% non-Indigenous group;  $P = 0.003$ ). Fifty-three per cent of the Indigenous women smoked during pregnancy (cf. 23% of non-Indigenous women;  $P = 0.017$ ), 60% were smokers at the time of the interview, and smoking occurred inside 40% of Indigenous houses (cf. 20% and 20% for non-Indigenous women, respectively;  $P < 0.001, 0.09$ ). Conclusion: This small survey suggests that the prevalence of SIDS risk factors is higher in the Indigenous population, and a new approach to education is needed urgently to promote SIDS awareness among Indigenous women.

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McDonnell M, Mehanni M, McGarvey C, et al.

**Smoking: The major risk factor for SIDS in Irish infants.**

Ir Med J 2002 Apr; 95(4): 111-113.

The objective of this particular study was to examine the effect of infant cigarette smoke exposure on the risk of Sudden Infant Death Syndrome in a contemporary Irish epidemiological database. For each infant that died of SIDS between January 1994 and December 1998, four controls were matched for age and geographical location, yielding a total sample size of 825 infants. Parents of the infants who died were interviewed, and information was collected on socio demographic details, pregnancy, medical history, parenting practices, and lifestyle habits. Study results showed that 74% of SIDS mothers, and 63% of SIDS fathers smoked during pregnancy compared to 28% of control mothers and 27% of control fathers. For other household members, 29% in the SIDS group smoked, compared to 7% in the control group. There was also a dose response effect, with an increased risk when mothers, fathers, or other household members smoked more than 10 cigarettes a day. The risk increased when both parents smoked, compared to only the mother smoking. These results confirm that cigarette smoke exposure is a serious SIDS risk factor, increasing the risk of SIDS in Ireland almost fourfold.

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[www.imj.ie/DTIndex.aspx?tabindex=&tabid=&subtabindex=9&subtabid=174](http://www.imj.ie/DTIndex.aspx?tabindex=&tabid=&subtabindex=9&subtabid=174) (not a U.S. Government Site)

Horne RS, Ferens D, Watts A, et al.

**Effects of maternal tobacco smoking, sleeping position, and sleep state on arousal in healthy term infants.**

Arch Dis Child Fetal Neonatal Ed 2002 Sep; 7(2): F100-F105.

Objectives: To investigate whether a history of maternal tobacco smoking affected the maturation of arousal responses and whether sleeping position and infant age alters these relations. Design: Healthy term infants (13 born to mothers who did not smoke and 11 to mothers who smoked during pregnancy) were studied using daytime polysomnography on three occasions: (a) two to three weeks after birth, (b) two to three months after birth, and (c) five to six months after birth. Multiple measurements of arousal threshold in response to air jet stimulation were made in both active sleep (AS) and quiet sleep (QS) when infants slept both prone and supine. Results: Maternal smoking significantly elevated arousal threshold in QS when infants slept supine at 2-3 months of age ( $p < 0.05$ ). Infants of smoking mothers also had fewer spontaneous arousals from QS at 2-3 months in both prone ( $p < 0.05$ ) and supine ( $p < 0.001$ ) sleeping positions. In infants of non-smoking mothers, arousal thresholds were elevated in the prone position in AS at 2-3 months ( $p < 0.01$ ) and QS at 2-3 weeks ( $p < 0.05$ ) and 2-3 months ( $p < 0.001$ ). Conclusions: Maternal tobacco smoking significantly impairs both stimulus induced and spontaneous arousal from QS when infants sleep in the supine position, at the age when the incidence of sudden infant death syndrome is highest.

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