Reviewer’s report

Title: A perspective on SIDS pathogenesis. The hypotheses: plausibility and evidence

Version: 6 Date: 1 March 2011

Reviewer: Bradley T Thach

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The authors present a point of view for the cause of Sudden Infant Death Syndrome. A major problem, as I see it, even if this article is an “opinion” or “point of view”, the article fails to provide a definition of SIDS for the purposes of understanding the author’s views. There are a number of definitions in use and the author cites only the most recent one, one which divides sudden, unexplained infant deaths into several subcategories. The author however appears to regard “SIDS” as a single entity. This may have been appropriate twenty years ago but this no longer seems tenable. For example, does the author dismiss prolonged QT Syndrome as a potential cause of Sudden Infant Death Syndrome even when the genetic and family history is ambiguous in support of these diagnoses?

Of even more relevance is his position on "accidental suffocation" and/or "positional asphyxia". For example, if a medical examiner finds strong support for one of these diagnoses in the death scene report, does the author believe that death due to bacterial toxins is the most probable cause of death?

Death due to asphyxiation when a baby’s head wedged between soft surfaces has long been a standard diagnoses that predates the earliest SIDS definition appearing in the early 1960’s. As far as this reviewer can tell the “wedging/asphyxia” diagnoses remained valid from the 1960’s onward. In spite of this, the author views the evidence for unintentional asphyxia as “less convincing” that the bacterial toxin hypothesis. This in spite of the many studies in infants, mechanical and animal models that support accidental suffocation when the infants airways are covered by bedding due to rebreathing, thermal stress or other mechanisms.

In short, not knowing whether or not the author views the accidental suffocation diagnosis as valid or invalid in any particular infant death case makes it impossible to evaluate the author’s opinion as to the root cause of sudden unexpected infant deaths.

Also, the author’s detailed review of the literature on petechia in such deaths is thorough and commendable. However, since the presence of petechia is still viewed by all or almost all medical examiners as a nonspecific finding in sudden infant death cases it seems very unreasonable to use presence and distribution of petechia as a primary basis for a causal theory.

Finally, the author appears to adhere to bacterial toxins as “the cause of SIDS”
and says little about viral inflammatory release of toxic cytokines (increased in the brain and spinal fluid of SUDI infants) as a potentially important link in the pathway to death.

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.