Investigation of Sudden Infant Death Syndrome

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Foreword

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The sudden and unexpected death of an infant is a tragic event that has occurred throughout human history. Until relatively recently, death at any age was so common an event that the sudden demise of a seemingly healthy infant was accepted as one of the risks of human existence. Only in the present era has the sudden unexpected death of an infant become recognised as a distinctive tragic event worthy of serious investigation.

An introduction to this problem occurred early in my career. I was attracted to the field of pathology in the first year of medical school. The birth of my first two daughters occurred during those student years, and watching their development proved so fascinating that it was a major factor determining my decision to become a paediatric pathologist. Graduating in 1958, a classmate planning a career in paediatric radiology and I were given the unique opportunity of being the first interns in clinical paediatrics at Children's Hospital in Seattle. We were ideal test pilots for a programme then being developed for future graduates aiming for a career in clinical paediatrics. That remarkable exposure to the field of disease in infants and children was followed by an opportunity to serve a first year of residency in Pathology at Children's Hospital of Los Angeles, prior to three years as resident in general pathology at Cedars of Lebanon Hospital in the same city. I returned to Children's Hospital for a final year of training in paediatric pathology.

The needs of a growing family necessitated supplementation of income during my resident training years. The Office of the Chief Medical Examiner of Los Angeles County served a huge metropolitan area including some ninety cities and towns. The central office was responsible for all coroners' cases in the downtown area and for suspected homicides from the entire county. Other cases for which the office was responsible were examined by deputy forensic pathologists in funeral homes in the area where death occurred. Most deputies were advanced residents in pathology. I served in this capacity three evenings a week and most Saturdays for three years.

A senior staff member in the central office was responsible for assigning cases to deputies. During my tenure this duty was in the hands of Phillip Schwartzberg. Because of my interest and training in paediatric pathology, Mr Schwartzberg made a point of assigning me to cases of infant and child death whenever possible, rather than the usual assignment of deputies to a particular area of the county. Though this required driving to disparate locations, it presented an unprecedented opportunity for me to investigate a substantial proportion of sudden and unexpected infant deaths occurring in a vast metropolitan region totalling some ten million inhabitants, exceeding the population of most states.

The tragedy now termed SIDS has undoubtedly existed throughout history, but escaped general recognition due to its low prevalence compared to the prevalence of infant mortality in past ages. Its subtle manifestations had also contributed to varying interpretations as to cause of death. The person responsible for deputy assignments made it possible for me to examine an average of one or two cases of sudden unexpected infant death each week. This unique experience made obvious the fact that a substantial majority of these tragedies manifested striking similarity in history and anatomic features.

A notable feature of those sudden and unexpected deaths for which no cause was apparent was an almost complete sparing of infants in the first month of life. Most deaths occurred during the 2nd through the 4th month, the victims having been unexpectedly found dead in their cribs without prior symptoms, and sounds of distress were never reported. Post-mortem examination revealed a stereotyped pattern of findings. Though none of these explained the cause, their consistent presence suggested a common mechanism for a majority of 'crib deaths'. The infants in question

were consistently found dead, never being witnessed in the process of dying. An important finding in most cases was the presence of numerous petechial haemorrhages confined to serosal surfaces of the thorax. For example, while the entire intrathoracic surfaces of the thymus typically displayed numerous petechiae, the posterior aspect of the cervical lobes above the left innominate vein typically contained no petechiae, consistent with 'damping' of negative pressure by that vessel. The localised distribution of haemorrhages strongly suggested the presence of increased intrathoracic negative pressure during the dying process, with sudden end-expiratory airway occlusion as the presumptive mechanism of most of these deaths.

Among the proposed causes of these deaths was accidental suffocation in bedding. Vigorous struggle was implied by the consistent finding of tightly clenched fists, often clutching fibres of bedding materials, and disarrayed covers. However parents consistently reported hearing no sounds of struggle, and the face was often uncovered when found.

Prone sleep position was a frequently suggested contributory or causative factor. During the 1960s, prone sleep position for infants was virtually universal, as the result of numerous well-publicised studies that demonstrated significantly enhanced quality of sleep for infants placed in that position. Though some infants were found with the face straight down, head position alone seemed unlikely as the cause, as simply turning the head a few degrees would have created access to air passages, and many were found with face to the side. Though sleep position seemed a potential factor in the mechanism of death, this explanation was not consistent with the paucity of 'crib deaths' during the first month, the age when accidental suffocation would seem most likely to occur. Causation seemed to be linked to postnatal rather than developmental age, as prematurely born, and term infants presented similar postnatal age distribution curves.

Following five years of residency training in Los Angeles, three of which were spent at Los Angeles Children's Hospital, I returned in 1965 to Children's Hospital in Seattle as head of anatomical pathology and subsequently as Director of Laboratories. Prior to my return a combination of circumstances had created an ideal setting for serious research into this problem. The unexpected sudden death of an infant born to a member of a prominent and influential Seattle family had led to widespread community awareness of this problem, and of the need for investigation of potential causes. Upon learning of my training, experience, and interest in this problem, the Director of Forensic Pathology was delighted to delegate responsibility to me for post-mortem studies of all infant deaths in King County, which included the city of Seattle and surrounding areas. This opportunity would soon lead to a research grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) to make possible extensive studies on all sudden and unexpected deaths of infants in King County, Washington. With the valuable co-leadership of Drs Abe Bergman and George Ray, and widespread community awareness, and support, our research team was able to carry out extensive studies of every potential case of the tragic phenomenon that would soon become generally designated as SIDS. This term was introduced at the NICHD-sponsored Second International Conference on Causes of Sudden Death in Infancy, held in Seattle in February, 1969, and was the title of a book containing proceedings of that conference, published by the University of Washington Press in 1970.[1] Despite early debates about precise definitions, this term soon became the favoured designation for this tragic event. Investigations by our group and many others, influenced, and supported by prior experience with this problem, led to presentations at national meetings, publications, and to general awareness of and interest in this problem.

Though sudden and unexpected death of infants obviously has many causes, a substantial subset of cases shared many circumstances and pathological findings in common, suggesting that a single cause or mechanism seemed likely for many such deaths. Shortly after beginning our studies in 1965, a preliminary publication alerted paediatricians to the existence and significance of this phenomenon.[2] This was soon followed by a more extensive illustrated report in a widely distributed medical periodical.[3] emphasising the narrow age range that spared the first several weeks of postnatal life, peaking in the second, and third months, with a rapid decline beginning in the fourth month, its consistently silent occurrence during sleep, and pathological findings indicating complete airway obstruction as the mechanism of death for a substantial majority of sudden and unexpected infant deaths.

The term SIDS and the concept it embodied were debated for a few years, but soon achieved widespread

acceptance. A 37-page monograph published in 1973[4] was reprinted in 1975 by the US Government Printing Office by order of the Department of Health, Education and Welfare (DHEW) and sent to all practising physicians in the nation, leading to widespread awareness of the existence, nature, and importance of this entity.

While the concept of SIDS is widely accepted, it remains a topic of controversy. Clinical and pathological evidence indicating its association with sleep during a brief period of postnatal life is generally accepted. Its age distribution indicates a relatively narrow period of vulnerability, peaking in the second, and third postnatal months. Obstruction of the upper airway is widely accepted as the likely mechanism, but the exact nature of that obstruction is not revealed by the usual post-mortem dissection. In addition to intrinsic variability in structure, the laryngeal inlet is a dynamic area subject to alteration by the motility of adjacent structures. The most informative anatomical treatise on laryngeal anatomy in infancy and childhood that I have found is the chapter by Karl Peter in the two-volume treatise on paediatric anatomy edited by Peter, Wetzel, and Heiderich.[5] The larynx is situated high in the neck at birth, with the tip of the epiglottis at the level of the top of the first cervical vertebra. Throughout infancy and childhood the larynx descends in position. At six years of age it lies below that vertebra, later attaining its final position below the third vertebra. The configuration of the epiglottis and shape of the inlet manifests great individual variability, making it impossible to define specific shapes and dimensions for various age periods. Inlet configuration also changes in various positions of head and neck.

Pathologists typically examine the larynx after removal from the body. The larynges of SIDS victims that we and others have illustrated in publications may have provided a misleading impression of laryngeal inlet structure and patency in SIDS victims. Dissection in situ, including the influence of head and neck position in SIDS victims, could provide valuable information. Embalming of the body preserves anatomical relationships during manipulation, and it is possible that the well-justified emphasis of forensic pathologists upon performing dissections prior to embalming might have contributed to a lack of knowledge concerning the anatomy of this critical region in SIDS. In-situ study of this region in both unembalmed and embalmed bodies of apparent SIDS victims, with emphasis upon the effect of various head positions upon laryngeal inlet patency, could provide important information concerning the potential cause of death. Regrettably this consideration did not occur to me when I had ready access to abundant case material.

Even if this approach were to reveal insight into the cause and mechanism of SIDS, the rarity of this event indicates that the vast majority of infants have airways capable of remaining patent in any sleep position throughout the brief period of risk.

Though SIDS long remained unrecognised in the era when infant mortality was a common occurrence, the sudden and unexpected death of a seemingly thriving infant now constitutes a major concern for those confronted with this tragic event. The term SIDS will likely either undergo future refinement, with more rigorous limitation to a subset of cases comprising a majority of those currently included under that term, or replacement by terms for recognised causes of sudden unexpected death of an infant. But regardless of designation, there will always be a need for authoritative information on dealing with this tragedy. The present volume provides an impressive fulfilment of that need.

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Preface

On a beautiful early fall day in 2003, our lives turned upside down. Twice. In the early morning, our only son was born. He was greeted by his three sisters, his grandparents, and his parents, all of us who had been anticipating his arrival with so much excitement and love. A brother, a son, a grandson! The miracle of birth is life-changing, no matter how many times it is experienced.

Six hours later, our son stopped breathing. We went to the lowest of all possible lows in a matter of minutes. He was resuscitated, but his brain had been without oxygen for too long. He would never breathe on his own again. Two days later, he was removed from life support. We left the birthing floor of the hospital with an empty baby carrier, and empty hearts.

An autopsy was performed. We needed an answer. The result? SIDS. We buried our son and trudged forward. Most of what came next is a blur.

When parents lose a child, they are robbed of the hopes and dreams that are attached to that child. The wonder of what he would have become, how he would have changed the world. We'll never know.

When you lose an infant, you are also robbed of memories. Our son was with us for only six hours. There wasn't enough time to create memories. All of the memories of his short life can fit into a small hat box. And most of that box is filled with the bereavement cards we received. We have a few photos, a handprint, a snippet of his hair. But we can't remember the sound of his cry. The smell of his baby-ness. Mostly we remember the pain of his loss. Because instead of experiencing his life, we now endure a lifetime without him.

As if that isn't all difficult enough, imagine the result of an autopsy coming back as inconclusive. The experts have no idea why our son died. When cause of death is labelled as 'SIDS/or SUDI/SUID', you are also robbed of answers and of any chance of closure. The death of our infant was sudden. And it was unexplainable. The acronym fits. But there is no resolution in that. It is salt in the wound.

Our bereavement process started on that life-changing day and continues to this day. When we were able to come up for some air, and look a little more into SIDS, what we found was ever so frustrating. Any published work we could find focused on risk factors such as smoking, infant sleeping position, etc. None of that applied in our situation. But that seemed to be the end of the research story. Until about two years ago when we found some new research being conducted out of Seattle Children's Hospital that focused on physiological contributors to SIDS. We felt hope for the first time. From there, we dove in deep. And here is what we found.

For a first-world developed nation, it is inconceivable that so many infants die each year in the United States without warning and without explanation. SIDS is the leading cause of death in infants 1 month to 1 year of age in all developed nations. About 3500 infants die of sudden unexpected causes (SUDI or SUID) in the US each year alone! And that number has not improved since the mid-90s. There are pockets of research all over the world, but progress is slow. There are some data collected at the time of death, but the data are inconsistent, and difficult to access.

The answers to finding the causes of SIDS lie in research. And research needs accurate, consistent, accessible, and usable data. In 2017, in honour of our son, we formed the Aaron Matthew SIDS Research Guild of Seattle Children's Hospital, whose vision is a world where no parent ever experiences the loss of a child again to SIDS. The guild is focused on four key areas: 1) raising awareness of SIDS and SUDI/SUID with the aim of raising much needed research funding; 2) building a worldwide research collaboration to solve this terrible mystery; 3) working with government to enable researchers to access all available autopsy data in a responsible way; and 4)

developing the first global infant genome database for medical professionals and researchers worldwide with a goal of reducing infant mortality.

We have never felt more hopeful about the future of infant health and survival rates. The collection of knowledge and research in this book is so critical to truly understanding the mechanisms and factors surrounding a SIDS diagnosis. We are blessed to have so many experts working on this topic, as we dedicate our lives to making a difference in the name and memory of our son Aaron. Through our collective work, we will be comforted in knowing that his short life changed the world for so many others.

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