UNIVERSITY OF WASHINGTON

UW Medicine
SCHOOL OF MEDICINE

Understanding Sudden Infant Death Syndrome

David Jardine, M.D.
Associate Professor, Anesthesiology and Pediatrics, University of Washington

The human cost of SIDS

Sudden infant death syndrome (SIDS) remains the leading cause of post neonatal deaths, claiming the lives of 2,295 infants in 2002, the last year for which statistics are available. Each year, there are more infants will die of SIDS than there infants born with either sickle cell disease or cystic fibrosis. This illness devastates families by suddenly and unexpectedly robbing them of a healthy infant.

Research and management of risk factors

The cause of SIDS has managed to elude investigators for over 40 years. During this time, a number of ideas about the possible causes of SIDS have been carefully studied and found to be wanting. Even though we have not found the cause of SIDS, epidemiologic research has led to the identification of risk factors that increase an infant's chance of dying from SIDS. The best known risk factor is prone sleeping (stomach sleeping). SIDS deaths have fallen by 40% after the initiation of the "Back to Sleep" public health campaign that warns parents about the risks of sleeping prone. This intervention is responsible for a large portion of the decline in infant mortality in the United States in recent years.

Research – new opportunities

There are exciting new developments in the area of SIDS research. Recently developed DNA microarray technology permits scientists to look at the actions of thousands of genes in a single experiment. This powerful new technology has the potential to help us understand diseases that previously have been baffling. One of the greatest strengths of this new technology is that the information it provides can guide scientists into new and unexpected areas of research. This aspect of DNA microarray technology is especially promising for a difficult area like SIDS research which has proved to be frustrating for such a long time.

As we have gained a better understanding of the risk factors for SIDS, it has become apparent that many of the SIDS risk factors seem to increase an infant's risk of overheating. In our laboratory, we have developed a mathematical model that shows it is possible for a sleeping infant to be too well insulated, even when his blankets are not too thick. If an overheated infant is not uncovered, the model shows that the infant's temperature may reach lethal levels within several hours. Animal experiments in our laboratory and in other laboratories have shown that the predictions of the mathematical models are accurate. These three pieces of evidence (the risk factors, the mathematical model and the animal model), strongly suggest that overheating may cause some cases of SIDS.

DNA microarray technology offers an exciting way to investigate the possibility that overheating may cause some cases of SIDS. Heat stress (and other stresses), cause cells to turn on certain genes and to turn off other genes. It is probable that there is a unique pattern of gene expression that can serve as a "fingerprint" for heat injury. DNA microarray technology can be used to reveal these patterns. In our laboratory, we will be investigating this possibility in the next 24 months. If we can show that overheating causes some SIDS deaths, we can give parents specific information on how to avoid this risk. By designing interventions to eliminate the cause of the problem (overheating), we should be able to save more lives than we can by simply identifying the risks without understanding the cause.

Hyperthermia as a Cause of Some Cases of SIDS

An NIH Funded Investigation

Goals of the Investigation

We believe that some infants who expire from SIDS may have been overheated (hyperthermic) before death. The goal of our investigation is to find evidence that this has happened. We know from animal studies and from a limited amount of human information that certain genes are turned on by overheating. To determine if these genes have been turned on in SIDS victims, we are using a new and exciting technology called microarray analysis. Using this technology, we can look at all of the genes in the body (more than 30,000 genes) to determine which genes are turned on and which genes are turned off. We hope to find a pattern of gene expression which is uniquely associated with overheating and can serve as a "biological fingerprint" to show that overheating has occurred. In addition to looking at genes, we are also looking to see if one of the proteins known to be made during heat stress is present.

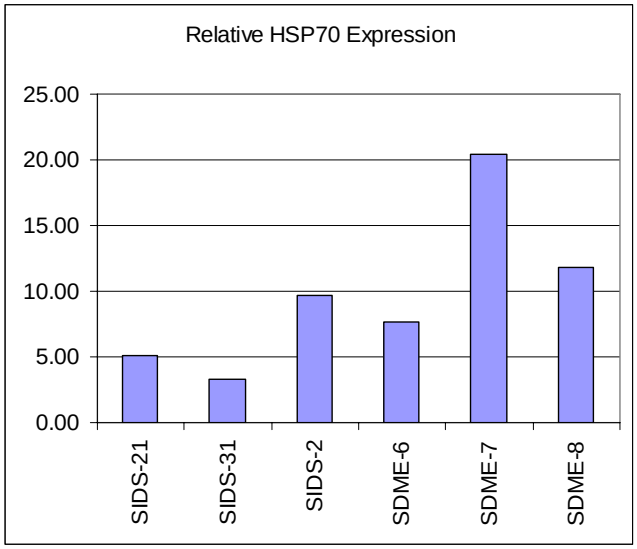
Sample collection and analysis

Two issues are crucial to the success of this investigation: (1) We must obtain a large enough number of samples for our testing to be valid. (2) The samples must be well preserved.

Because a number of changes occur in cells after death, it was possible that the two substances which we need to test (RNA and proteins) might have degraded to the point that the tests would not be informative. Fortunately, we have been able to isolate good quality RNA from more than 70% of these samples. We have been able to perform microarray analyses on limited number of these samples. Although it is too early to know with certainty, the results of these analyses suggest that many of the genes known to be turned on by heat were turned on in infants who expired from SIDS. In addition, when we tested these samples for HSP70 (a protein which is rapidly made after overheating), we found evidence that all of the samples had increased amounts of HSP70. One sample showed remarkably high levels of HSP70.

More samples urgently needed

We have enlisted three centers to contribute samples to this investigation. Both the racial makeup of the populations and the geographic location have a bearing on the risk of SIDS, so ***it is important to obtain samples from diverse populations***. Most importantly, we need tissue samples from control infants (infants who have expired suddenly from known cause such as trauma or drowning).



Relative levels of HSP70 in liver samples from SIDS victims. We would expect that HSP70 levels would be nearly zero under normal circumstances. All samples appear to show increased amounts of HSP70, especially sample SDME-7.

Timeline

The initial results of this investigation appear promising. Within the next year, we will be performing an increasing number of microarray analyses and Western blot analyses. Because this is an ongoing investigation, sample collection will continue for the foreseeable future.

How You Can Help

We need tissue samples from SIDS victims and from control patients (healthy infants that have suddenly died from a known cause such as trauma). At the time of postmortem examination, a small piece of liver tissue (about the size of a pencil eraser) is placed in a tube of nontoxic preservative solution. This sample is then sent by courier (FedEx) to the University of Washington. We provide all the supplies and pay for transport of the specimens. We currently have approval for this study from our Institutional Review Board (IRB) and have experience working with IRBs at other institutions. Because this investigation is considered minimal risk, it usually not necessary to obtain informed consent (this varies by site). We will be happy to help you obtain IRB approval at your institution. If you are interested in participating in this investigation, please contact David Jardine, M.D. (dsj@u.washington.edu) or call 206-616-4858.