I am an anesthesiologist from California. I have no conflict of interest and am sponsoring my own participation at this meeting. I believe that emerging theories can serve as guides to evaluate potential anesthetic toxicity during early life.

A “Stress Mechanism” that explains Capillary Gate Theory and Unified Stress Theory has been formulated on the basis of current peer-reviewed literature.(1) It describes how the Coagulation Cascade, the Central Nervous System and the Autonomic Nervous System function together to govern thrombin production to control the cell-based process of repair and development.(2,3) All cells respond to thrombin via receptor combinations that are unique to each type of cell. Thrombin utilizes ATP to energize the cellular and enzymatic actions involved in tissue repair and maintenance. The mechanism explains how thrombin production is affected by stressful stimuli and forces, including drug effects.

98% of the human genome has no known function in the mature animal, but recent studies indicate that this “excess” DNA functions as the blueprint for embryological development.(4,5) It is believed that the embryological development process governs DNA expression and is closely-related to a Stress Mechanism that completes the embryological development of organs and tissues. I hypothesize that embryological development occurs via the generation of thrombin at precise time intervals, locations and quantities to govern three-dimensional embryological tissue proliferation of various cell types, and that additional quantities of thrombin are subsequently generated by the Stress Mechanism to complete the development process.

Human development involves both cell proliferation and apoptosis and remains active for at least a year after birth. During this time there is increased risk that medications such as coumadin, salicylates and thalidomide(6,7) that interfere with thrombin production or thrombin effects may disrupt the development process.(8-11) Thrombin generally promotes cell activity, vitality and proliferation and inhibits apoptosis, so that sudden declines in thrombin can cause apoptosis. In contrast, for reasons that are not clear, thrombin elevations may cause apoptosis and other toxic effects in neurons.(12,13) Considering both evidence and theory, I believe that the most logical means to assess the potential effects of anesthetics and other drugs on the newborn is to focus on drug-induced perturbations of thrombin production.

The Stress Mechanism also explains Crile’s Hypothesis(14) and suggests a simple, safe and practical approach for minimizing toxicity and optimizing stress control to reduce morbidity and mortality in all anesthetized patients.(15) Synergistic interactions of hypnotic and analgesic agents can be manipulated to minimize toxic hypnotic agent exposure via greater reliance on benign analgesics plus deliberate mild hypercarbia.

Many details of the Stress Mechanism remain unclear, but it can be tested in its present form. If proven, it would offer wide improvements in medical practice. I have prepared papers describing the Stress Mechanism, together with proposals for testing it, and have submitted these for review and consideration by the committee. I welcome suggestions or help that might facilitate the empirical testing of the mechanism and would be happy
to answer questions. I thank the FDA for allowing me the opportunity to present these materials.

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