Reports of Scientific Meetings

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Second Annual Conference on Shock

The Second Annual Conference on Shock was held in Colonial Williamsburg, Virginia, June 7–9, 1979. The three-day meeting consisted of four symposia with invited speakers, 90 free papers or poster presentations, and two special lectures by distinguished scientists. The symposia dealt with research in the area of "Pulmonary Pathophysiological Mechanisms in Shock," common and uncommon features of certain "Animal Models in Shock Research," "New Concepts in Shock Therapy" emerging from laboratory and clinical research, and various aspects of "Immune Mechanisms in Shock."

The pulmonary symposium was opened by S. Powers (Albany, New York), who emphasized the need to improve pulmonary microcirculation in the adult respiratory distress syndrome (ARDS). He hypothesized that infusion of hypertonic mannitol was beneficial in critically ill trauma patients with ARDS, and attributed this to alleviation of capillary endothelial swelling. Fibronectin infusion was believed to improve ventilation/perfusion ratios by encouraging restoration of the patency of the pulmonary microcirculation as a result of reticuloendothelial system (RES) clearance of thromboembolic products.

R. Demling (Madison, Wisconsin) presented findings on the effect of hemorrhagic shock on pulmonary capillary permeability. Using a sheep model, he demonstrated that changes of pulmonary lymph protein and flow were accounted for by increased fluid filtration attributable to elevated pulmonary hydrostatic pressure. However, sheep lungs did accumulate fluid after resuscitation with crystalloids. H. Sugarman (Richmond, Virginia) presented a method for detection of altered alveolar–capillary permeability using a radioisotopic technique coupled with computer analysis of lung-emission scans.

H. Hechtman (Boston, Massachusetts) referred to the lung as the source of "evil humors" when its metabolic function is compromised. He noted that such metabolic derangements may occur without histologic changes. Positive end-expiratory pressure (PEEP) was found to decrease the ability of the lung to metabolize plasminogen activator, causing an increase in fibrinolytic activity. Positive end-expiratory pressure also caused a decrease in cardiac output, which Dr. Hechtman attributed to the release of a myocardial depressant substance from the lung. Since this effect can be blocked by indomethacin, it may implicate a role of prostaglandin and/or prostaglandin-related substances such as thromboxanes or prostacyclines in shock-related alterations of pulmonary metabolism.

The symposium on animal shock models turned out to be a particularly lively session. In addition to presentations by an invited panel of researchers, many members of the audience expressed their views on experimental models of shock. The first presentation, by T. E. Emerson (East Lansing, Michigan), gave an overview of the various animal species used in shock research. J. J. Spitzer (New Orleans, Louisiana), who chaired this symposium, reviewed differences in carbohydrate, lipid, and protein metabolism in different types of shock. He emphasized the importance of studying the turnover rates rather than measuring the blood levels of substrates to elucidate metabolic responses in shock. L. Hinshaw (Oklahoma City, Oklahoma) discussed his extensive experience with endotoxic and septic shock models. He stressed the importance of models that simulate clinical sepsis and the need for quantitative rather than qualitative assessments of both hemodynamic and metabolic responses in shock. Members of the audience pointed out the need for the following: more data on man in shock (A. Cowley, Baltimore, Maryland); research on the effects of shock mediators (B. Urbaschek, West Germany); and studies of direct effects of shock on cells by using isolated cell models (B. Trump, Baltimore, Maryland). L. Del Guercio (Valhalla, New York) and R. Wolfe (Boston, Massachusetts) presented comprehensive reviews of metabolic responses in shock. An overview of comparative shock models did not result from this session, but it is clearly a fruitful area for further exploration.

B. Altura (Brooklyn, New York) opened the discussion of shock therapy, stressing agents that stimulate reticuloendothelial system function or affect vascular smooth muscle. Antihistamines (H_1 = receptor blockers) and vasopressin and its analog were considered at some length. I. Chaudry (New Haven, Connecticut), in an exceptionally thorough presentation, reviewed the use of high-energy compounds in the treatment of shock. He emphasized the role of the ATP–$MgCl_2$ complex as a potential therapeutic agent. While high-energy phosphates, in general, were ineffective in restoring liver, muscle, and kidney cellular function when administered after shock, the infusion of ATP-$MgCl_2$ significantly restored these functions. The ATP-$MgCl_2$ complex increased survival after shock, as opposed to ATP or $MgCl_2$ alone, ADP, AMP and adenosine all of which were ineffective. W. Monafo (St. Louis, Missouri) reviewed the history of fluid administration in shock. He presented the pros and cons of crystalloid and colloid infusions, as well as possible advantages of hypertonic sodium solutions. J. Fletcher (Bethesda, Maryland) asked whether prostaglandins should be used as therapeutic agents in shock or whether their endogenous formation should be inhibited by blocking agents. Based on findings of increased survival after inhibition of prostaglandin synthesis, he advocated "blocking" rather than "giving." Summing up the session on shock therapy, A. Baue (New Haven, Connecticut) outlined his concept of specific "limiting organ-systems" in shock based on clinical observations made in casualties during the Korean and Vietnam conflicts. Our current understanding of vital functions affected in shock supports a "progressive, sequential multiple organ

failure" rather than the involvement of one single critical organ. Tracing some of the "fads, fallacies and facts" of past therapeutic approaches, he indicated that many of these measures (vasopressors, colloid *vs.* crystalloid, vasodilators, buffering compounds, etc.) were signally inadequate. Recognizing the sequence of multiple organ failure, current resuscitative and therapeutic efforts can provide a measure of protection to the cardiovascular system, the kidney, the lung, and the myocardium. Less readily monitored organs, such as the liver, remain at risk.

The session on immune mechanisms in shock opened with a talk by D. McKay (Boston, Massachusetts), who discussed the role of disseminated intravascular coagulation in shock. He was followed by K. Brigham (Nashville, Tennessee), who reported on the effect of endotoxin on lung capillary permeability in sheep. Endotoxin caused an increase in protein clearance with a rise in lymph flow and lymph protein. There was clearance up to a molecular radius of 69 Å, but sieving of proteins persisted. The H_1 antihistamine diphenhydramine, but not the H_2 antihistamine, could prevent the endotoxin-induced increase of vascular permeability. Prostaglandin E_1 infusion in high doses reversed the increase in pulmonary capillary permeability after endotoxin without affecting the pulmonary hypertensive response. Leukocytic depletion of animals *via* chemical means blunted the endotoxic effects of lung vascular permeability. The final talk of the session was given by T. Saba (Albany, New York), who reviewed evidence from his laboratory supporting a plasma opsonic depletion in trauma patients and the restoration of opsonic function with cryoprecipitated fibronectin. The data advanced from animal and *in vitro* studies were convincing, while those obtained thus far from man were less so.

A number of the free papers and poster presentations were of particular interest to the anesthesiologist. Two papers by J. W. Holaday and collaborators (Washington, D. C., and Iowa City, Iowa) presented findings on the reversal of endotoxic and hypovolemic shock after injection of naloxone. Dogs subjected to hemorrhagic hypotension received a bolus injection of naloxone (2 mg/kg), followed by a continued infusion of the same drug. After retransfusion of the shed blood, all treated animals survived, while the controls died within 90 min after hemorrhage. Similar results were obtained in rats injected with endotoxin. The authors suggest blockade of beta-endorphin action on opiate receptors as a possible mechanism for the protective effect of naloxone. The (+) isomer of naloxone, which does not bind to the opiate receptor, had no effect.

C. Post (Linkoping, Sweden) presented evidence that the ability of the lung to take up lidocaine is impaired in severely injured traffic accident victims. Due to a reduction of the lung buffer function, administration of therapeutic doses of local anesthetic agents may cause acute toxic reactions in these patients.

D. L. Traber and co-workers (Galveston, Texas) studied the cardiopulmonary effect of fluid resuscitation in burn wound sepsis of sheep. It was found that intravenous fluids did not prevent hypovolemia in this model, which was related to loss of fluid from the vascular compartment rather than to dehydration.

A number of investigators studied the effects of glucocorticoids on hemodynamic parameters during traumatic, septic and cardiogenic shock. Beneficial effects of steroid treatment were seen, in particular, when combined with administration of antibiotics (L. B. Hinshaw, Oklahoma City, Oklahoma) and were attributed to stimulation of the reticuloendothelial system (R. C. Lillehei, Minneapolis, Minnesota) or preservation and enhancement of the activity of circulating proteins (J. E. Kaplan, Albany, New York). A. M. Lefer and K. Crossley (Philadelphia, Pennsylvania) reported myocardial protection from infarction in cats pretreated with the nonsteroidal antiinflammatory agent, ibuprofen.

Speeches by Drs. Harold Green (Winston-Salem, North Carolina) and Lloyd McLean (Montreal, Canada) highlighted the evening program of the shock conference. Dr. Green gave a most stimulating account of his experiences in the laboratory of the late Dr. Carl J. Wiggers, whose contributions in the area of cardiovascular physiology still remain the cornerstone of modern shock research. Dr. McLean stressed the importance of patient evaluation prior to surgery in order to ascertain predisposition to bacterial organisms. An immune-response analysis can often permit separation of patients at risk from those patients with less susceptibility to bacterial invasion and sepsis.

The Annual Conferences on Shock are organized by the Shock Society and provide a lively forum for new information and interchange of ideas between workers from many fields. The full text of the proceedings will be published under the title, "Advances in Shock Research," by Alan R. Liss, Inc., and should be of value to anesthesiologists, surgeons, physiologists, and others concerned with shock and related states.

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