# One Surgeon's Army Experience With "Wound Shock" From Pearl Harbor to the Present

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**ABSTRACT** The Army has had extensive experience in the study and treatment of shock, beginning with the American Civil War and continuing to the present. This is the story of one Army surgeon's experience, both in research and treatment of shock, from Pearl Harbor to the present.

## INTRODUCTION

The association of shock with trauma and sepsis has been recognized since the 18th century. Le Dran in 1731, described a case of injury by a missile, which led to a collapse of vital function ending in death even though the patient had relatively little blood loss.[1] He called the phenomenon "secousse" (jar). The U.S. Army called it "wound shock." Shock has since been subdivided into hemorrhagic (hypovolemic), traumatic, and septic shock, all associated with war wounds. Shock can be defined as inadequate capillary perfusion, which would also encompass neurogenic, cardiogenic, and anaphylactic shock as well as other types.[2] During the American Civil War, shock and hemorrhage were considered to be separate conditions. In the Army surgeon general's report written in 1876,[3] it was stated that "the collapse of bleeding resembles syncope as distinguished from shock. Rest in bed, opium and warm fomentation constitute the treatment." Infected wounds were a major cause of death, but many wounded patients, having suffered neither significant blood loss nor infection, also died without apparent cause.

In World War I, in 1918, the surgeon general appointed a Board for the Study of the Severely Wounded, which in turn set up a central laboratory to support the study. One of the board's conclusions was that there was a "toxin" that originated in dead or dying tissue and that caused wound shock.[4] However, a toxin was never found. Blalock[5] in the 1920s "proved" that shock after trauma was the result of blood loss into the tissues. He bluntly traumatized dogs' legs and measured the increase in volume of the legs. He estimated that the increase in weight of the legs, (which consisted of extravasated blood in the tissues), showed enough blood volume loss to account for the shock produced. However, if this is true, why is the mortality of severely traumatized patients so high even if adequate blood volume has been achieved with IV fluids? According to the accepted classification scheme of Trunkey[6] traumatic shock is considered a subset of hypovolemic shock but with features that make it more difficult to treat. It now seems likely that both a toxin and hypovolemia play a part in the development of traumatic shock.

Many trauma patients die with a normal blood volume. In Viet Nam, 153,303 American wounded were admitted to military hospitals.[7] About 3,000 of these died of "shock" despite being adequately treated with IV fluids and appropriate surgical procedures.[8] Severe trauma is a common cause of acute respiratory distress syndrome (ARDS) and multiple organ failure (MOF).

According to the Statistical Abstract of the United States published by the U.S. Department of Commerce, death by septic shock in the United States increased from 35,000 in 1970 to 94,000 in 1980 to 198,000 in 1990. The death rate from septic shock per 100,000 population increased from 1.7 in 1970 to 4.2 in 1980 to 7.9 in 1993. Septic shock is the most common cause of ARDS and MOF.

Something else must be involved besides blood volume loss in septic and traumatic shock. Death after trauma is often the result of MOF, especially ARDS. What is the etiology of ARDS and MOF? Many metabolic changes occur after massive injury, the most important of which have been grouped together as the systemic inflammatory response syndrome (SIRS), usually followed by a compensatory anti-inflammatory response syndrome (CARS).[9] The inflammatory cytokines of SIRS can lead to cellular death and MOF if not adequately balanced by mediators of CARS. However, a number of anti-inflammatory drugs have failed to alter the mortality rate in clinical trials, despite successes in the laboratory and in animal studies.[10] Activated protein C has been shown to reduce the mortality in septic patients, but the effect is minimal in treating ARDS, and there were some problems with bleeding.[11] Activated protein C has two beneficial effects, being both an anti-inflammatory agent and a thrombin inhibitor. Although emphasis has been placed on its anti-inflammatory effect, it is quite possible that the majority of its benefit derives from its ability to prevent clotting.

In early World War II, it appeared that the Army and surgeons in general had forgotten the lessons learned in World War I about debridement and delayed primary closure and blood transfusion. In World War I, shock was thought of as an inadequate blood flow through the capillaries. Giving a

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This manuscript was received for review in May 2008. The revised manuscript was accepted for publication in June 2009.

vasopressor closed off this flow and was usually followed by death. In early World War II, shock was thought of as inadequate blood pressure, and vasopressors were used and were followed by death.

At the time of Pearl Harbor, I was chief of that part of the surgical service that took care of all trauma, burns, and infections at the North Sector General Hospital at Schofield Barracks.[14] Schofield Barracks was the largest post in the Army, and North Sector General Hospital was the largest hospital in the Army. Schofield had two divisions and the Army Air Corps. The Japanese attacked Schofield first because all the fighter planes were there. The hospital was hit many times the morning of December 7, 1941. Within hours we had several hundred wounded. At that time it was thought that wound shock was the result of leakage of plasma from the blood into the tissue, and that plasma was the best treatment. I treated several hundred wounded at the North Sector General Hospital on December 7, 1941 and after. Our mortality was very high; about 20% of hospitalized wounded died compared with 2% in Korea where adequate blood was available. Concepts of shock in early World War II were far behind those of World War I.

Dr. Churchill, the chief of surgery at Harvard, volunteered to act as surgical consultant for the Army, but according to his memoirs, the Army turned him down, saying it had no need for advice from civilians. However, when our troops became mired down in North Africa in 1942, the Army finally availed itself of his expertise and sent him to North Africa as surgical consultant. He found that many wounded needed blood, plasma by itself being insufficient. He recommended that blood banks be set up to supply blood in the combat zone. The surgeon general refused, saying: (1) it was impossible to transfuse blood in a combat zone, (2) plasma by itself was adequate and even better than blood, and (3) shipping space was too scarce. It was only in 1944 that blood was given to soldiers wounded in the Normandy landings. Later still, it was found that even more blood was required than was lost, probably because of marked hemolysis following severe trauma.

The Korean War saw the emergence of disseminated intravascular coagulation (DIC) as a concept. It is rarely diagnosed in its early stages, because it is widely believed that bleeding and prolongation of prothrombin time and a fall in fibrinogen and platelets are signs of developing DIC. This is not true. Rather these are late developments in DIC and appear only late in the disease, if at all. The only accurate tests for the presence of early DIC are elevation of D dimer and fibrin split products.

A detachment from the Walter Reed Army Institute of Research (WRAIR) was tasked with studying the severely wounded. They paid special attention to renal failure, which was common in the severely wounded. At that time, I was chief of surgery at the Fort Belvoir Army Hospital. Because I was one of the few board-certified general surgeons in the Army at that time, Fort Belvoir was designated a center for receiving patients with surgical and orthopedic wounds. At first the wounded would arrive by hospital train, often 100 or more at a time. These patients had survived 1 or 2 weeks with wounding.

Later patients would arrive by air. One of these cases was a soldier with a severe wound of the left lower abdomen and total destruction of the left hip. Surgery done at a mobile army surgical hospital (MASH) in Korea entailed small and large bowel resection, and the patient was then placed in a body cast for transport to Fort Belvoir. When I removed the cast, the wound was still open and started to bleed. The blood seeped right through the pressure bandages and collected in a pool in the bed. The pooled blood eventually clotted but after about 30 minutes reliquefied. I transfused him with approximately 50 pints of whole blood, and the bleeding finally stopped. However, he developed renal failure shortly thereafter and died a month later. After studying this case, I concluded that the blood was clotting in the microcirculation so fast that all coagulation factors were used up, and the blood became incoagulable. The body's own plasminogen was activated and eventually lysed the clot. I termed this sequence of events disseminated intravascular coagulation (DIC).[12]

I started a research project using animals to study the subject. The chief of laboratory (Cpt. McKay) worked with me in a small abandoned wooden shack behind the laboratory. It was a Saturday afternoon project. We had no budget and used materials from the operating room and laboratory. We made a blood pressure measuring device by bending a piece of glass tubing.

After several years of study there and later at Walter Reed Army Institute of Research, I wrote a book, Syndromes of Disseminated Intravascular Coagulation, published in 1966.[13] In it I said that DIC could cause multiple organ failure, including lung failure, kidney failure, liver failure, and other organ failures as a result of occlusion of the microcirculation by capillary thrombi. DIC followed hemolysis, sepsis, or both. Dr. Leonard Heaton, the surgeon general, wrote a forward for the book. In it he said: "Col. Hardaway's clear and comprehensive study presents solid evidence that well over forty different diseases, syndromes and traumatic and septic states may now be linked together through a common factor of intravascular coagulation, and equally important, that wide spread capillary clotting is responsible for certain of the serious clinical manifestations so frequently associated with these entities. Thus a more rational basis for therapy is possible now. Relationship of intravascular coagulation and clinical shock in its various forms is an important aspect of Col. Hardaway's study. Renewed interest in shock justifiably has come about in recent years because of this study. The management of traumatic shock and related injuries continues to be of vital importance to the Army Medical Service in its efforts to improve survival of the injured soldier. The information provided in a study of clinical shock alone is well worth the attention not only of military surgeons but also the student, practitioners, and research workers concerned with any of the clinical conditions associated with intravascular coagulation. Col. Hardaway

should be proud of his accomplishment achieved through patience, dedication and persistence over the years. The Army Medical Service is proud of his achievements and its own role in providing support for this important work through its clinical and research facilities."

In 1960, I was assigned to the Walter Reed Army Institute of Research as director of the Division of Surgery. I was surprised to learn that there was to be an international meeting on shock and that I was the host. It was a good meeting, but not much of moment came from it. Its conclusion was that shock research should be carried out in humans as well as animals. I immediately started the world's first shock-trauma unit at Walter Reed Army Medical Center. Results of the center were reported in JAMA in 1967.[15] This was the first report of "shock lung," later called ARDS.

Considerable animal and clinical research over the past 40 years supports the theory that DIC is a cause of traumatic and septic shock. The shock trauma unit established at Walter Reed Army Medical Center in 1960 was duplicated 5 years later and sent to Viet Nam, where it was active for 6 years. It was part of the division of surgical research established about 1950, which studied shock in animals as well as humans. A surgical research unit was established at Brooke Army Medical Center at Fort Sam Houston, Texas. Wound shock was the subject of much research at both institutions, although the Brooke Center specialized in burn research and became the world's foremost burn center.

Research carried out at Walter Reed and later in Viet Nam and other military medical facilities included clinical trials as well as animal experiments. In one clinical trial conducted at Walter Reed and other military hospitals, a thrombolytic was tested in the treatment of septic and traumatic shock.[16] Twenty patients suffering from ARDS secondary to trauma or sepsis were selected for treatment with thrombolytics after respiratory support, including positive end expiratory pressure (PEEP), had failed to bring PaO2 up to 60 mmHg, a situation normally associated with a fatal outcome. These patients were treated with urokinase plasminogen activator. Every case responded favorably, the average PaO2 rising from 47.7 mmHg to 231.5 mmHg, ($p = 0.0001$). The treatment was not given until all other treatment modalities had failed and the patients were in extremis. Although mortality was still high, none died of ARDS but rather of renal and liver failure. This was probably because of unique characteristics of the lungs. If the lung microcirculation is blocked for 6 hours and circulation is then restored, the lung will probably resume function, because oxygen is present, and lung tissue has a low metabolic rate. If liver and kidney (or brain) are deprived of circulation for 6 hours, there is tissue necrosis, and organ function will not return. The patients in this study experienced no bleeding or changes in clotting parameters, which were normal both before and after treatment. Patients were not included in the protocol until 48 hours after injury or surgery, and were excluded if they had a head injury or a history of clotting defect or stroke.

The fact that hypoxia and death could be prevented by a plasminogen activator is evidence that the problem was primarily because of intravascular coagulation (DIC) occluding the microcirculation of the organs, especially the lungs, liver, and kidneys. The administration of a thrombolytic lysed these microclots, restoring circulation to the organs and saving the animal's or human life. Mortality in strictly controlled pig studies was reduced from 100% to 0% in both traumatic[17] and septic[18] shock. Traumatic shock was produced by blunt trauma to the thighs under anesthesia. Septic shock was produced by IV injection of heat-killed *Escherichia coli* organisms or pneumococci in extremely small doses. No bleeding or changes in coagulation parameters occurred either before or after treatment with plasminogen activator. They were normal both before and after treatment. In a series of hemorrhagic shock in dogs, the addition of 10 cc of the dogs' own blood, which had been frozen and thawed (producing hemolysis), converted a near 100% survival to 100% mortality rate.[19]

The treatment of hypovolemic (traumatic) shock has been studied in great part by the Army. Most research has focused on what is the best IV fluid for the resuscitation of hemorrhagic shock. Many fluids have been tested including whole blood, red cells, Ringer's lactate, plasma, albumin, various colloids including dextran, and others. The best of the lot was found to be whole blood and Ringer's lactate.[20] This treatment is only effective if hemorrhage can be controlled. Many ways of controlling hemorrhage have been studied including ligation, pressure pants, tourniquet, pressure dressings, clot-producing dressings, and factor VII. All may be helpful under certain circumstances. The Army presently has a research team in Iraq that is studying shock and wounds. It has been studying the causes of bleeding with severe wounds and the possible use of clot-forming dressings and blood fractions, including factor VII. In the prehospital setting, it is recommended that patients be treated with hexastarch rather than crystalloid solutions. It should be administered sparingly, however, and without any attempt to raise blood pressure to normal until the patient reaches the hospital. The use of PolyHeme as a blood substitute is also being studied.[21–23]

The idea that heparin might be used to prevent and treat DIC has been proven false for several reasons: (1) heparin will not dissolve clots; (2) heparin is inactive in a pH below 7.2, and capillary blood pH in shock is usually below 7.2; (3) heparin may cause bleeding; and (4) heparin affects clotting time. Plasminogen activator on the other hand dissolves fibrin and does not affect fibrinogen. It acts only in the circulatory system and has no effect on clots outside the system. Therefore it does not cause bleeding and does not affect clotting parameters. It is thus safe to give for DIC.[24]

Traumatic shock and septic shock are entities separate from hemorrhagic shock with a different etiology and treatment. If they fail to respond to volume therapy, animal studies and a phase I clinical trial show that they may be treated safely and effectively with a thrombolytic. This treatment must be started at the first signs of DIC. If there is any bleeding or changes in the

clotting mechanism, a thrombolytic is contraindicated. DIC at this stage can be diagnosed only by elevation of fibrin split products or D dimer. Administration of a thrombolytic at this stage appears to actually prevent any clotting defect that might be caused by DIC.[25] More extensive trials are needed to further document this approach to treatment of traumatic and septic shock. A prospective randomized phase III study entitled "Treatment of ARDS with Plasminogen Activator" is currently underway at Mercer University School of Medicine in Macon, Georgia.

Army medical personnel have had years of unparalleled opportunity to study war wounds and accompanying shock - hypovolemic, traumatic, and septic. My own research, beginning with my experience in treating and observing the wounded at Pearl Harbor and on through the Korean and Viet Nam wars to the present, has led me to the following proposal for management of shock. "Pure" hypovolemic shock will always respond to appropriate IV fluids if hemorrhage can be controlled. Hypovolemic shock as a result of hemorrhage, as opposed to dehydration, is best treated with whole blood and Ringer's lactate. Hexastarch may be preferable to Ringer's lactate in the prehospital setting. Traumatic shock is the result of severe tissue damage, and IV fluids may not be sufficient. In this case, DIC may be present and can be treated with plasminogen activator. DIC usually does not occur until 2 or more days after wounding and seldom causes bleeding. If IV fluids are inadequate for septic shock, DIC is probably present. The DIC of septic shock, whether because of bacteria or viruses, can also be treated with thrombolytics.[25] Combinations of these three types of shock are quite common, especially in such wartime environments as Iraq and Afghanistan.

Today's military doctors are uniquely placed to observe and test new treatments of severe wounds and resulting wound shock. I am proud to have contributed to a tradition of Army surgeons treating war wounds as first described by Homer in his epic of the Trojan War and extending to the battlefields of today's conflicts. Homer recognized their importance when he noted that "surgeons are worth more than armies to the public weal."

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