

### Introduction

There has been an increased interest in the development of animal models of trauma largely due to worldwide conflicts involving terrorism. Many governmental agencies have developed funding mechanisms for the treatment of major trauma as well as rehabilitation techniques. Swine have become one of the primary species of interest in this field.<sup>1</sup>

Trauma and hemorrhagic shock are usually combined. Major multiple organ and tissue trauma occurring following an event such as an explosion is referred to as polytrauma. A separate manuscript on hemorrhagic shock as an isolated event is available as well as a manuscript on skin burn injury models in swine.<sup>2</sup> The anatomic and physiologic aspects of these porcine models has been described in depth.

### The Human Condition

The most significant driving force for research in this arena is traumatic blast injury (TBI) in both civilians and military personnel since explosive devices are now being used as a tactical military weapon as well as a weapon of terrorism. TBI typically results in polytrauma involving multi-system injury most commonly neurotrauma, pulmonary injury, extremity injury, hemorrhage and burns.<sup>1, 4-11</sup> There is not a consensus on the most effective form of treatment for fluid resuscitation, blood substitutes or treatment of shock in this condition.<sup>5-11</sup> In addition to TBI, models are also needed for gunshot wound and other types of non-TBI situations such as falls and car accidents. There is also not a consensus on the most effective therapeutic approaches for some of these situations especially when considering pediatric patients.<sup>12</sup>

Many studies have been performed in rodents because of the obvious ease of using such a model as well as the expense. However there is a feeling that many of the physiologic responses may be different in small animals versus a large animal model. Also there is a need for chronic models instead of acute nonsurvival studies performed under anesthesia. Swine are emerging as a large animal model of choice because of anatomic and physiologic characteristics. Primates are reserved for studies in which cognitive dysfunction following survival is being studied. Swine have largely replaced dogs in these types of studies.<sup>3</sup>

### Porcine Models

Swine have increasingly becoming the preferred large animal trauma model except in cases where only primates may be indicated for a particular protocol involving cognitive function. Swine have been chosen because they largely match human anatomy and physiology for some important functions. They have

a large gyrencephalic brain; similar cardiothoracic anatomy and physiology; similar skin and subcutaneous tissues; and many similar abdominal organs. Abdominal organs such as the liver, kidney, and pancreas have a very similar anatomy and physiology. The gross anatomy of the gastrointestinal system has some differences but has very similar physiology of digestion.<sup>2, 3</sup> In addition swine can be procured with an adult human size and sexual maturity at 5-6 months of age if a breed such as the Hanford miniature pig is selected.

### Traumatic Blast Injury Models (TBI)

A model of exposing anesthetized swine to explosive blasts in a tube, a HMMVEE vehicle surrogate and a building mock up for studying combat casualties has been described.<sup>1</sup> Details of the construction of the devices are included in the manuscript. In these models swine under general anesthesia with implanted or area instrumentation we suspended in slings or attached in fixed supports and exposed to various levels of explosive charges placed at varying distances from the animals. Animals were usually fitted with body armor. These models simulate exposure in the open field, in buildings, in alleys and within a vehicle. In all cases the trauma was primarily due to exposure to the pressure wave following the explosion. The three different exposure techniques provided different waveforms due to the geometry of the chamber.

In this particular set of experiments the authors concentrated on neurotrauma and there were variations in pathology dependent upon which of the three settings was utilized.<sup>1</sup> Neurotrauma consisted of rapid onset edema sometimes with the presence of intracranial hemorrhage. There was vasoconstriction of the carotid and cranial cerebral arteries. Neuropathology was most prominent in the white mater with fiber degeneration and astrocytosis. Some animals were recovered and motion analysis technology with swine within an enclosed arena was evaluated and compared to baseline. Animals experienced both short and long term disrupted uncoordinated movement.

This particular model would be difficult to duplicate within academic medical centers, however, use of tubes with compressed air discharge rather than explosive blasts are possible alternatives.<sup>13</sup> This would at least allow the study of overpressure in the absence of thermal and toxic aerosol involvement.

### Isolated Traumatic Techniques and Polytrauma

The military TBI models described above could be used to create polytrauma with multiple organ injury they would not create the model with a particular controlled fashion. Polytrauma models may include injuries of any of the following systems, structures or tissues in any combination: neurologic, thoracic, abdominal, musculoskeletal or cardiovascular. Frequently in humans polytrauma is accompanied by hemorrhagic shock. These models have all been described in anesthetized animals.

**Neurotrauma:** Isolated neurotrauma is induced both using open and closed cranial techniques. One method involves use of a modified nail gun with a disc to produce a 46 J shock to produce a subdural hematoma.<sup>14</sup> Other methods involve a circular craniotomy with a fluid percussion of a calculated force or a weight drop or spring loaded device method.<sup>9, 15</sup> In pediatric studies in piglets with postoperative survival for 7 days the severity of the focal injury has been shown to increase progressively with maturation in groups which varied in age (5 d, 1 m, 4 m).<sup>15, 16</sup> An open cranial model of pediatric subdural hematoma was produced in the same age groups by injection of autologous blood into the subdural space. A burr hole was made off midline in a standardized location using suture lines as markers. A 24 ga angiocatheter was placed and blood was injected at a rate of 2 ml/m at a predetermined volume of 4.5 ml in 5 d and 5.4 ml in 4 m piglets (approximately 10% of the intracranial volume). The amount and rate are important to prevent mortality due to sudden increases in the intracranial pressure.<sup>17</sup> The hole is closed with tissue glue and the scalp sutured. As with the focal trauma there is more resistance to permanent damage in the younger animals. The amount of trauma and location can obviously be varied by location and delivery of traumatic energy.

**Chest/Pulmonary Injury:** Chest injury with or without accompanying pulmonary injury may be accomplished by administration of trauma using a captive bolt gun.<sup>14, 18</sup> The amount of injury will vary depending upon the location, angle and cartridge used. In one study a delivery of 119 J resulted in ecchymosis, rib fractures, pulmonary contusions, pleural rents, pneumothorax and hemothorax.<sup>14</sup> Depending upon the severity of the lesion animals may require resuscitation, treatment for blood loss or cardiac arrhythmias.

**Abdominal Trauma:** Trauma to the abdominal cavity may be limited to increases in intraabdominal pressure, injury to single organs or multiple organ and tissue trauma.<sup>19, 20</sup> Intraabdominal pressure can be increased by placing a catheter into the cavity and either distending it with a gas or a liquid. This procedure

causes an increase in cerebral perfusion pressure secondary to increases in intrathoracic pressures and functional obstruction to the cerebral venous outflow.<sup>19</sup> Liver injury is a common model of intraabdominal trauma of an isolated organ. One method of inducing the injury is to crush and avulse a lobe with a clamp.<sup>21</sup> The left lateral lobe of the pig is amenable to this procedure. Other injuries can include those that penetrate the intestinal tract and lead to chronic sepsis models.<sup>3</sup>

**Musculoskeletal:** Femoral or other bone fractures may be produced using the captive bolt gun technique described above.<sup>14</sup> Crush injury to the muscles results in delayed systemic manifestations due to traumatic rhabdomyolysis and renal failure.<sup>22</sup> Another major complicating factor to this syndrome is the development of compartment syndrome with increased pressure within the affected muscle mass.<sup>3</sup>

### Coagulopathy

Coagulopathy is a complex complication of trauma that may be reproduced in porcine models.<sup>21, 23</sup> Factors involved include: tissue injury, hemorrhage, shock, dilution, acidosis, hypothermia, inflammation.<sup>23</sup> Many of the primary clinically relevant models have been produced in swine.<sup>23</sup> These models included traumatic liver injury, hypothermia, acidosis, hemorrhage and fluid dilution.<sup>14, 21, 23</sup> After the liver injury was induced as described above then hypothermia can be induced by cold fluid lavages or cooling blankets. Swine are particularly susceptible to lactic acid infusions, consequently dilute hydrochloric acid infusions are used to produce acidosis.<sup>23</sup> The dilution and hemorrhagic shock techniques are described elsewhere on this website.<sup>2, 3</sup>

### Training in Trauma

The military has developed an intense training program in dealing with mass casualty situations using multiple porcine models.<sup>20</sup> Five or six animals receive a variety of minor and major injuries and are routed to an emergency room situation for the teams to triage and treat. Injuries include airway compromise, cardiopulmonary penetrating wounds, abdominal penetrating wounds, traumatic amputations, shrapnel wounds, neck/carotid injury, simulated burn wounds and scalp lacerations. These may be combined in various fashions. This is combined with didactic training and post laboratory evaluations of the experience.

### Conclusions

Trauma models are a major part of research in the 21st century due to the ongoing worldwide terrorist activities and resultant combat situations. They are also applicable to the study of injuries related to major natural disasters such as earthquakes, tsunamis, tornados and volcanoes. The pig has emerged as a large animal model of choice for these studies because of the comparative anatomy and physiology as well as a comparable body size. Miniature breeds are becoming increasingly important in these studies because of the need to develop chronic models to study the aftereffects of treatments. This is especially true of models involving the neurological system. Behavioral and locomotion study procedures have been modified to meet these particular needs.

Another challenge is that ethics require that the trauma studies be performed in anesthetized animals and that analgesics are administered. These are complicating factors to the physiologic outcomes of many of these studies. It is important for veterinarians to be informed of the physiologic effects of the agents selected for these studies in order to minimize the complicating effects. For example inhalant anesthetics significantly increase cerebral blood flow and tiletamine/zolazepam has significant cardiodepressant activity for up to three days following administration.<sup>3</sup>

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