

donation and recovery process, including the time frame/limit for death to occur. A written informed consent is obtained for organ and tissue donation, according to established TRC policies. The consent must be witnessed and signed by a hospital staff member. The TRC coordinator writes a detailed note in the patient's hospital record regarding the consent process.

9. All necessary laboratory and diagnostic testing is performed according to established TRC policies.
10. The operating room staff is notified of the pending NHBD recovery. Space and OR nursing staff availability will be determined. Anesthesia services will not be required for the customary withdrawal of care. Arrangements for continuous palliative care should be made should donation be precluded.
11. Once all necessary evaluation, organ placement arrangements, and recovery arrangements have been completed, and all members of the organ recovery team are in place, withdrawal of care will take place in accordance with individual hospital policies. The physician may order, as part of his/her usual and customary practice, ongoing pain relief, if in the physician's belief it is medically and ethically necessary. No member of the TRC or the transplant team/center is present for or involved with this portion of the process.
12. The patient's vital signs are closely monitored and recorded every 5 minutes from the time the ventilator/pressor support is discontinued. The patient will be pronounced dead by the physician of record or intensivist designee after 5 minutes of asystole as measured by 1) the absence of electrical activity, and 2) the absence of an arterial pulse waveform, and 3) the absence of ventilatory efforts. Should death not occur within 60 minutes after discontinuing life support, the patient is returned

to the intensive care unit or a private room for ongoing palliative care. After declaration of death, surgical recovery of organs occurs according to standard procedures as directed by the transplant recovery surgeons.

Thank you to Charlie Alexander, RN, BSN, CPTC, Director, Development and Donor Services Center, TRC of Maryland, for the use of the above prepared information

#### Living Donors

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### — Session C —

#### Trauma Airway Management: Hands-On Skills Station

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## Saturday, May 17, 2003

### Simultaneous Morning Sessions

#### — Session A —

##### Pediatrics

Co-Chair: Gail E. Rasmussen, MD, Meridian, Mississippi, USA  
Co-Chair: Jeffrey M. Berman, MD, Chapel Hill, North Carolina, USA

#### Emergency Airway Management in the Pediatric Trauma Patient

Gail E. Rasmussen, MD  
Adjunct Clinical Faculty, Department of Anesthesiology, University of Mississippi Medical Center, Jackson, Mississippi, USA

**Learning Objectives:** To review emergency airway management in the pediatric trauma patient. The lecture will include discussion of the difficult airway algorithm and alternative airway devices and cervical spine immobilization.

The most immediate concern in the management of the pediatric trauma patient begins with the ABCs of resuscitation with airway assessment and assurance of adequate oxygenation. Without adequate oxygenation and effective ventilation, all other resuscitative efforts will be ineffective. Pediatric patients also force our hands more quickly than adults because the apnea-to-hypoxia interval is so much shorter and we are forced to intervene more quickly. Airway management in the trauma setting differs from other scenarios because of the need for cervical spine stabilization and immobilization, which may restrict options for intubation. The differences between adult and pediatric cervical spine injury will be delineated. One must recognize the need for airway intervention in the setting of respiratory distress and impending respiratory failure. This is often overlooked in the initial resuscitation, where there may be more concern for establishment of IV access than airway control.

After initial assessment and relief of anatomic obstruction, patients who do not resume spontaneous ventilation and those with altered levels of consciousness (Glasgow Coma Scale score of 8 or less) will need more definitive airway protection and probably intubation. One must have the proper airway equipment available and checked before this is undertaken. Also, alternative airway adjuncts should be available should intubation prove difficult (including LMAs, jet ventilation equipment, and equipment for cricothyroidotomy).

The trauma patient also poses an increased risk for aspiration of stomach contents because they are considered to be full stomachs. GI prophylaxis is optimal if time allows before undertaking a rapid sequence induction with cricoid pressure. The use of succinylcholine and its relative contraindications in the pediatric patient will be discussed. In the trauma setting, regardless of the age of the patient an anticholinergic agent is recommended (i.e., atropine, 5-10 mcg/kg, up to a maximum of 0.4 mg, or glycopyrrolate, 0.1 mg/kg) prior to induction. There has also been the recommendation, particularly in head trauma, to pretreat with 2 mg/kg of intravenous lidocaine prior to intubation. The sedative-hypnotic selected depends on the hemodynamic stability of the patient and the presence or absence of raised intracranial pressure (ICP). The top three choices include propofol, thiopentothal, and etomidate, depending on the particular circumstance of the patient.

Once endotracheal intubation has been accomplished, confirmation of correct placement is essential, via auscultation. Tracheal rings can be visualized via bronchoscopy and the presence of carbon dioxide determined on capnogram or with an attachable CO2 detector.

The pediatric trauma patient has several unique aspects in clinical practice that must be taken into consideration in the successful management of the emergency airway and ultimately the resuscitation.

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#### Sedation/Analgesia/Anesthesia for Diagnostic Studies and Treatment Outside the Operating Room

James E. Fletcher, MD  
Department of Anesthesia, University of North Carolina, Chapel Hill, North Carolina

**Learning Objectives:** 1) To review pain management strategies for children with trauma-induced pain and 2) to consider various sedatives, analgesics, and anesthetic agents and the implications of their use on assessment procedures.

In addition to experiencing the pain directly caused by trauma, children who have suffered injury may have to undergo procedures that provoke anxiety and pain as part of their diagnostic workup or treatment. The nature of the injury, ranging from an isolated fractured long bone to a semiconscious head injury with chest contusion, will affect the strategy chosen to manage the patient's comfort and cooperation. Similarly, the proposed intervention will determine the use of anxiolytics, analgesics, sedatives, and anesthetics.

Diagnostic studies may involve painful procedures such as tapping of the peritoneal cavity or invasive radiology such as angiography. Immobility is important for noninvasive radiology such as CT or MRI, particularly in the latter instance. Alternatively, a therapeutic intervention such as placement of a chest drain or fixation of a broken limb will require analgesia to facilitate cooperation.

Central to any such intervention is an assessment of the patient's cardiorespiratory system, including keen attention to either pre-existing or trauma-induced compromise of the airway or circulating blood volume.

Pain should be assessed frequently in the pediatric population, as children are reluctant to report pain. The pain experience includes sensory qualities—where, when, how much—and motivational-affective qualities—emotional, aversive ("hurt"), and pain-reducing behavior. Parental guidance is useful in understanding the child's pain and distress behaviors. Children who have difficulty communicating, such as those with cognitive deficits or who do not speak English, are particularly difficult to assess. Age-specific methods of assessment are available. The pain language used by the child should be determined (e.g. 'hurt', 'booboo'). Self-reporting is preferred in most children over 4 years of age; for those above age 7 years, a numerical pain scale may be used. Observation of body posture, activity, and facial expression may also help, although some apparently "normal" behavior may represent a coping mechanism for pain.

Sedation, anesthesia, and systemic analgesia represent a spectrum of CNS depression, which has the potential to compromise the airway and cardiovascular system, while also providing humanitarian relief of suffering and facilitating successful diagnostic studies and treatment. "Conscious sedation" involves the use of CNS depressants to produce inattention, anxiety, and analgesia. The essential feature of this technique is that the patient remains conscious and able to respond to a mild stimulus—ideally, a voice. Once consciousness is lost, the child has lapsed into a state of light anesthesia, with its accompanying risks. As it is not possible to predict the effect of medication and the interaction of the medication with the patient's medical state, full resuscitative equipment and expertise must be available at all times when sedation is administered.

Often, sedative/analgesic drugs can be combined usefully with local anesthetic techniques. Options include IV (PCA) opioids, oral analgesics/sedatives, inhalation of nitrous oxide, ketamine, behavioral techniques, epidural local anesthetics and opioids, NSAIDs. Each drug has a specific profile of anxiolysis, analgesia, and sedation, as well as specific pharmacological features such as speed of onset and duration of action, which affect selection. Because of this, the non-analgesic, slow onset/offset sedative chloral hydrate is relatively unhelpful in comparison to morphine or fentanyl, combined with midazolam. Often, behavioral techniques can be combined with pharmacological methods. However, opioid analgesics and local anesthetics remain the cornerstone of procedural pain management. Sedative/anxiolytics should be reserved for non-painful procedures, as they will not relieve pain, while making assessment more difficult. All drugs should be given incrementally to effect.

#### Pediatric Prehospital Care

Dr. Charles D. Deakin  
Consultant Anaesthetist, Southampton University Hospital, Southampton, UK

#### Learning Objectives:

- To understand injury patterns in children.
- To understand how differences in paediatric anatomy and physiology relate to injury patterns.
- To understand the principles of prehospital trauma care in children.

- *To understand splinting, packaging, and transport of injured children.*

**Injury Patterns in Children.** The commonest cause of death and injury in infants and children is trauma. In urban settings, 35% of accidents are due to pedestrian injury from motor vehicles, and a similar percent from falls from heights. Drowning and choking also contribute significantly to pediatric mortality, although the incidence of both is gradually decreasing. In Europe, blunt trauma accounts for 98% of injuries, whereas the pattern is very different in the USA, with penetrating trauma approaching 50% of all serious injuries. Child abuse is an under-reported cause of pediatric injury.

**Paediatric Anatomy and Pathophysiology.** Anatomical and physiological differences in children result in increased risk for specific injuries. The head is disproportionately large, which, combined with weak neck muscles and underdeveloped protective arm reflexes, predisposes children to head injury. Raised intracranial pressure is more common than in adults and occurs more rapidly following head injury. Respiratory muscles are also underdeveloped, making respiratory failure more common and worsening secondary brain injury from ischemia and hypercapnia. Bone requires more energy than adults to cause fractures, and in chest trauma, lung contusion without overlying rib fracture is common. Abdominal organs are disproportionately large, and the liver and spleen are particularly susceptible to rupture following abdominal trauma. The large surface area:volume ratio predisposes to hypothermia.

**Principles of Prehospital Trauma Care in Children.** Unlike adults, primary cardiac arrest is rare, and cardiac arrest in children is usually due to hypoxia where bradycardia rapidly progresses to asystole. Ventricular fibrillation is rare and often due to hyperkalaemia, tricyclic overdose, solvents, or hypothermia. Treatable causes of pulseless electrical activity must be excluded rapidly (hypovolaemia, tension pneumothorax, cardiac tamponade).

Airway management in the traumatised child is a priority. A short neck, large tongue, large tonsils, large epiglottis, and high anterior larynx make endotracheal intubation more difficult. Attempts at pediatric intubation in obtunded children are likely to fail without the use of appropriate sedative and neuromuscular blocking drugs. The laryngeal mask airway is now being introduced to prehospital care in Europe for the management of difficult paediatric airways. Prehospital surgical airways are particularly challenging. Gastric decompression with an orogastric tube may improve tidal volumes and lower airway pressures. Cardiovascular compensation to acute hypovolaemia is more marked in children than adults and a hypotensive child will be severely hypovolaemic. Bleeding into body cavities must be carefully excluded. Venous access is difficult because of small size, overlying adipose tissue, and venous collapse. Intraosseous access should be gained early. Effective analgesia is particularly important in children, and requires opioids and local or even general anaesthesia.

**Splinting, Packaging, and Transport of Injured Children.** Careful splinting and packaging of children is vital for successful and safe transfer, particularly by air. Parents are generally a better alternative to sedation during transfer of the injured child.

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#### Pediatric Head Injury: Where Have We Been; Where Are We Going?

Jeffrey M. Berman, MD

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**Learning Objectives:** 1) To appreciate changes in morbidity and mortality statistics, 2) to appreciate the evolution of clinical management of pediatric head injury, 3) to appreciate evolving management strategies, and 4) to understand current guidelines.

**Mortality.** The December 6, 2002, MMWR reported an 11.4% decline in mortality related to traumatic brain injury (TBI). These statistics, which cover the decade from January 1989 to December 1998, also document the changes in the etiology of injury among patient groups, including children. The three leading causes of TBI death are motor vehicles, firearms, and falls. Motor vehicle crashes persist as the leading cause of TBI and subsequent deaths amongst children (1–19 years of age).

**Evolution of Clinical Management.** In the past, clinical management of head injury focused on control of ICP. The modalities used to accomplish that goal were hyperventilation (to PaCO<sub>2</sub> into the mid 20s), barbiturates (including barbiturate coma), steroids, fluid restriction, osmolar and diuretic therapy (mannitol, furosemide), and nursing care delivered in the head-up position (~30°). Simultaneous with a shift in focus to prevention of secondary brain injury, more sophisticated means to measure cerebral hemodynamics became available. These technologies made it apparent that in order to avoid secondary injury the therapeutic focus ought to be on brain perfusion, especially in the penumbra of primary injury. To achieve this endpoint, a variety of modalities coupling brain monitoring with pharmacological and/or mechanical interventions are being employed (e.g., measurement of jugular venous saturation, drainage of CSF, osmotic therapy using hypertonic saline, induced mild hypothermia, and maintaining normocapnia).

**Current Guidelines.** Current recommendations are based on the aforementioned principle of maintaining cerebral perfusion. At a minimum, ICP monitoring ought to be employed in every child who has sustained a severe TBI (GCS score <8). Cerebral perfusion pressure ought to be maintained >40 mmHg in younger children and >50 in older children and adolescents. PaCO<sub>2</sub> ought range from 35–38 unless treating impending intracranial herniation. Osmolar therapy using mannitol or hypertonic saline may be of use but lacks definitive evidence, as does the use of barbiturates.

**Conclusion.** Though much progress has been made in the identification of cellular mechanisms and likely triggers of pathophysiology, we have yet to produce unequivocal definitive therapies for TBI. Nevertheless, prevention efforts and aggressive neurointensive care focused on prevention of secondary brain injury have yielded very gratifying reductions in morbidity and mortality. As every year, we are hoping that discovery of the "silver bullet" is just days or months away. We are closer but have not yet achieved that goal.

#### Fluid Management of the Injured Child

Calvin Johnson, MD

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**Learning Objective:** To educate the participant about assessing volume status, recent advances in fluid management, and a rational therapeutic approach for fluid administration in the injured child.

The leading cause of death in children age 1 to 14 years in the developed world is trauma. The major cause of disability in children is trauma. It has been reported that inade-

quate evaluation and inappropriate treatment contributes to 30% of early deaths in children with severe trauma.<sup>1</sup>

Prompt and accurate assessment and treatment are critical in the prevention of unnecessary pediatric morbidity and mortality from trauma. The most crucial first step in providing for the injured child is the establishment of adequate oxygenation and ventilation. Once oxygenation has been established, intravenous access and the administration of appropriate intravenous fluids are essential.

Assessment of the pediatric circulatory system must take into account the following. Shock in children may exist with a normal blood pressure. In children, cardiac output decreases in a linear fashion as blood volume decreases; however, blood pressure may remain unchanged. In the pediatric patient, stroke volume is fixed; thus, cardiac output in the face of hypovolemia is maintained by increasing the heart rate and peripheral vascular resistance. When cardiac reserve is exhausted, bradycardia indicates significantly decreased blood volume.

Intravenous access must be obtained while assessing the severity of injuries. With significant blood loss, the child's compensatory vasoconstriction can make IV access difficult. Attempts at IV access should be limited to 60–90 seconds, and if unsuccessful, the clinician should proceed to insertion of an intra-osseous needle. Be sure to avoid the leg with a suspected tibial/femoral fracture or vascular injury. All IV fluids should be warmed to 37° C.

Children have small blood volumes and cannot afford to lose large amounts of blood. Occult blood losses from the head (especially scalp) and neck region can result in significant hemodynamic instability. Aggressive control of bleeding is indicated. Remember, a hemodynamically unstable child should never be sent to CT scan to determine the site of bleeding. That child must be taken to the OR for surgical exploration. The choice of colloid over crystalloid for the initial resuscitation has been reported to increase the mortality by 4%. Crystalloids 20 ml/kg times 2 doses should be given and if no improvement in hemodynamics occurs, then administer blood 10ml/kg. Colloids should be given only as a temporizing measure while you are waiting for blood products.<sup>2</sup> Dextrose-containing fluids should be given only when there is laboratory evidence of hypoglycemia.

In the management of traumatic brain injury, the goal is maximizing cerebral perfusion pressure and reducing ICP. The early introduction of inotropes maintaining MAP of 70mmHg is recommended to avoid fluid overload.

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#### Early Care of the Pediatric Burn Patient

Gary F. Purdue, MD

Professor, Department of Surgery, UT Southwestern Medical Center, Dallas, Texas, USA

**Learning Objectives:** 1) to learn to recognize the elements of burn severity and understand the components of a major pediatric burn, 2) to recognize the different types of inhalation injury, and 3) to appreciate the special aspects of burn treatment, including thermal maintenance, airway protection, and fluid resuscitation.

Children are at special risk of burn injury, comprising one third of burn center admissions. A plan of initial burn assessment and therapy includes the care essential for all cases, specific treatments for minor burns, and the special requirements of major thermal trauma.

Rapid estimation of body surface area burned permits planning of immediate management and fluid therapy and dictates the needs for definitive care. Only second- and third-degree burns are tabulated with Lund-Browder or Berkow charts providing correction for age. The "Rule of Nine's" is not appropriate for children.

While depth of injury is important in determining the choice of care and ultimate outcome, initial evaluation is difficult. Characteristics will be discussed.

Burns of the face, hands, feet, and perineum/genitalia present special problems, while burned children <2 years have a much higher mortality and morbidity than similar burns in older children.

Pre-existing disease may cause the injury and profoundly affect care. Multiple trauma may be present, just as in the victim of any violent incident with abused children at special risk.

Immediate application of cool tap water provides pain relief, but thermal maintenance is critical. Covering with dry sterile sheets and warm blankets is the best treatment for patients with large burns. IV morphine relieves pain to permit adequate care.

Intravenous access is peripheral. Insertion through the burn is permitted. For very large burns, two large-bore peripheral IV lines may be required while central vessels are avoided. Urinary catheter and nasogastric tube are inserted. Periodic evaluations of the nose, pharynx, and lungs are performed to determine adequacy of the upper and lower airways.

The most important aspect of early care of a child with a major burn is fluid resuscitation. Children with burns of more than 10–20% TBSA require intravenous fluids for optimal management. While many methods of resuscitation are available, the Parkland formula using Ringer's lactate (4 ml/kg/% burn in the first day postburn) is most frequently used, with modifications for maintenance and glucose control.

"Inhalation injury" is two separate problems. Upper airway injury is caused by heat, which leads to upper airway obstruction by swelling. It is seen with significant burns of the face and neck and is heralded by changes in physical examination and laboratory studies until catastrophic airway closure occurs. Endotracheal intubation is both prophylaxis and therapy. Lower airway damage results from inhalation of smoke and its noxious products, usually becoming gradually apparent 24–48 hours after injury, identical to respiratory distress syndrome. Pulmonary toilet, mechanical ventilation, and prevention of infection are treatment.

Chemicals are treated with early dilution with large quantities of running water. Electrical burns in children are usually low voltage (110–220 volts). These are generally local injuries, often involving the mouth, without risk of deep muscle injury and myoglobinuria.

Severity is frequently underestimated by both caregiver and family. In the early stages after injury, the burn patient is uniquely stable and can be easily transferred long distances, provided adequate airway is maintained and appropriate fluid resuscitation begun and continued.

— Session B —

Prehospital Care

Co-Chair: Charles D. Deakin, MA MD MRCP FRCA, Southampton, UK  
 Co-Chair: Marvin A. Wayne, MD, FACEP, Bellingham, Washington, USA

Use of Capnography in Pre-Hospital Trauma Care

Dr. Charles D. Deakin

Consultant Anaesthetist, Southampton University Hospital, Southampton, UK

Learning Objectives:

- To understand the physiology of CO<sub>2</sub> production and excretion.
- To understand the techniques of measuring end-tidal CO<sub>2</sub>.
- To understand changes in end-tidal CO<sub>2</sub> in relation to pathophysiology.
- To understand predictive value of end-tidal CO<sub>2</sub> in relation to outcome.

**What is End-Tidal Carbon Dioxide?** Cellular metabolism results in carbon dioxide (CO<sub>2</sub>) formation as a by-product of adenosine triphosphate (ATP) production. CO<sub>2</sub> is excreted by the cell, and ultimately by the body, to maintain normal homeostasis. CO<sub>2</sub> diffuses out of the cell to enter the blood stream, where it is carried in the plasma or in erythrocytes. As blood flows through the lungs and the alveolar capillaries, a diffusion gradient causes CO<sub>2</sub> to diffuse from the blood into alveolar air spaces. The CO<sub>2</sub> is then excreted from the alveolar air spaces in expired air. The CO<sub>2</sub> in expired air can be measured using capnography. The peak CO<sub>2</sub> in expired air is maximal at end-expiration (end-tidal CO<sub>2</sub>; PetCO<sub>2</sub>) and equates approximately to arterial CO<sub>2</sub> (PaCO<sub>2</sub>).

**How is end-tidal carbon dioxide measured?** End-tidal CO<sub>2</sub> is measured directly from respiratory gases. There are two methods by which it can be measured:

- Colorimetric CO<sub>2</sub> detectors change colour when exposed to CO<sub>2</sub>.
- Electronic measurement. Uses spectrophotometry to give a real-time value of CO<sub>2</sub>.

**End-Tidal Carbon Dioxide and Cardiac Output.** In low cardiac output states, blood flow to the lungs is low, so that relatively few alveoli are perfused. Since tidal volumes delivered with a resuscitation bag tend to be large, many alveoli are ventilated that are not perfused and consequently the PetCO<sub>2</sub> is low. If the blood flow to the lungs improves, more alveoli are perfused and PetCO<sub>2</sub> will increase. Providing the lungs are ventilated at a fixed minute volume (rate x tidal volume), changes in PetCO<sub>2</sub> are proportional to changes in cardiac output.

Use of Capnography in Pre-Hospital Care

- Confirmation of endotracheal intubation. In a patient with a spontaneous cardiac output, correct endotracheal intubation will immediately show the presence of CO<sub>2</sub>, whereas oesophageal intubation results in absence of PetCO<sub>2</sub>. In the absence of cardiac output, PetCO<sub>2</sub> is minimal and correct endotracheal placement should be confirmed by other means.
- Operator fatigue. Because PetCO<sub>2</sub> is proportional to cardiac output, PetCO<sub>2</sub> is an indicator of the effectiveness of cardiac massage. Decreased PetCO<sub>2</sub> during cardiac massage may indicate operator fatigue.<sup>1</sup>
- Indication of the return of spontaneous cardiac activity. An increase in PetCO<sub>2</sub> is often the first indicator of the return of spontaneous circulation.<sup>1,2</sup>
- Indication of adequate ventilation. PetCO<sub>2</sub> is a marker of adequate ventilation because it approximates to arterial CO<sub>2</sub>. Ventilation of trauma patients using capnography results in more optimal PaCO<sub>2</sub> values.<sup>3</sup>
- Prediction of outcome. Patients suffering primary cardiac arrest in whom PetCO<sub>2</sub> has failed to rise above 1.4 kPa after 20 minutes of advanced life support are extremely unlikely to survive.<sup>4</sup> Only 5% trauma patients with PetCO<sub>2</sub> <3.2 kPa 20 min after pre-hospital intubation survive to discharge.<sup>5</sup>

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Selective Cervical Immobilization

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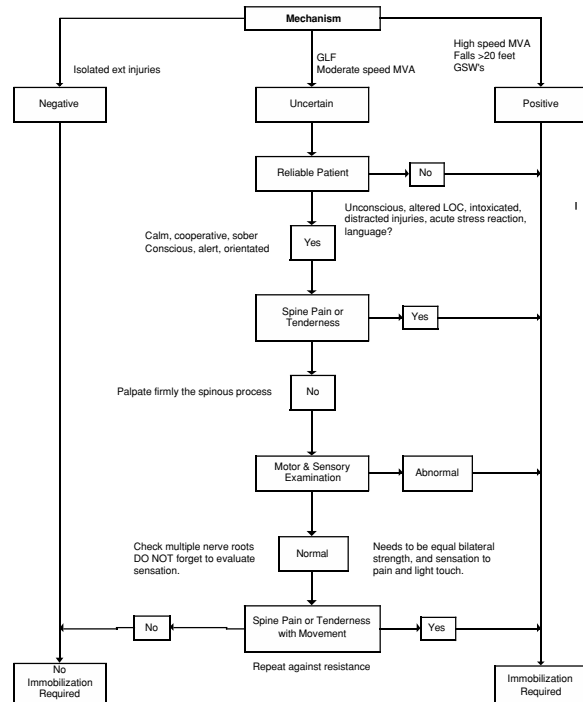
Medical Director EMS, Bellingham/Whatcom County Washington

**Learning Objectives:** 1) To review current EMS practice of cervical immobilization, 2) to discuss risks and benefits of current immobilization protocols, 3) to discuss literature and experience that suggest alternative "selective" immobilization, and 4) to list criteria for selective immobilization.

Regardless of trauma victims' presentation, the practice of EMS has been to place them into cervical immobilization and onto long backboards. While the safest thing to do, from a liability perspective, is it the best care? Immobilization is uncomfortable and takes time. Further, it increases the likelihood that the patient will be subjected to unnecessary X-rays and it can interfere with the ability to treat other injuries. If the patient vomits, it is difficult to maintain the airway; in the elderly and obese, immobilization can compromise breathing.

New research and the experience of some systems have shown that there are safe and effective means to determine who does and does not require spinal immobilization. Certain physical findings can be used to decide which trauma patients can safely be excluded from field cervical immobilization. These criteria include altered level of consciousness, midline cervical tenderness, evidence of intoxication, neurologic abnormality, and presence of painful distracting injury.

We review spinal injuries and discuss the implications of recent research, which has promoted the development of new "selective spinal immobilization" protocols. It also examines these protocols and determines how they can be implemented.



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Pre-Operative Fluid Resuscitation for Trauma Patients: Elemental or Detrimental?

Paul E. Pepe, MD, MPH, FACEP, FCCP, FACP, FCCM

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Learning Objectives:

- To understand the original rationale for our traditional approach to early management of post-traumatic hypotension and presumed shock.
- To appreciate that premature assumptions and inaccurate extrapolations may have been made regarding pre-hospital and emergency department "shock" management and that our current methods may not only be of little value, but, in fact, may actually be physiologically detrimental.
- To comprehend the value and limitations of the latest controlled, prospective, scientific studies that appear to be changing approaches to post-traumatic hypotension.
- To learn to delineate the differences between the various subsets of trauma and then consider appropriate management strategies and future directions in relevant research.
- To appreciate the potential of certain hypertonic solutions and hemoglobin-based oxygen carriers (HBOCs).

For the past three decades in North America, the standard approach to hypotensive injury patients has been to "re-perfuse" vital organs by augmenting central intra-vascular volume and systemic blood pressure mostly through rapid infusions of isotonic intravenous fluid (IVF) regardless of the injury mechanism or anatomic location. More importantly, such interventions have been provided, as early as possible, both prior to and following achievement of hemostasis. Despite the theoretical advantages of these interventions, no prospective controlled studies had ever clearly documented their efficacy in the clinical setting. Several new experimental studies now have demonstrated detrimental effects of aggressive

IVF resuscitation in certain uncontrolled hemorrhage models and one major clinical study has even shown the efficacy of withholding IVF infusions preoperatively in those patients with penetrating torso injuries (versus the standard rapid infusions of IVF in both the pre-hospital and emergency department settings). It is therefore speculated that BP elevation, prior to achievement of hemostasis, may actually increase mortality in certain subgroups of injury patients. The rationale, experimental evidence, scientific design, and limitations of these studies will be examined and qualified in this discussion. In addition, the concept of using hypertonic solutions and new hemoglobin-based oxygen carriers in such circumstances will be analyzed as well.

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#### Prehospital Use of Hypertonic Saline Derivatives

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**Learning Objectives:** 1) To understand the importance of correct assessment of the status of trauma cases in the prehospital setting and 2) to learn the use of small-volume hypertonic solutions in penetrating trauma for rapid fluid replacement, providing a modified systemic arterial pressure capable of maintaining vital functions while limiting the possibility of further hemorrhage.

Hypertonic saline solutions associated with colloids are particularly suitable for pre-hospital use in major trauma.

In European EMS systems, where physicians are involved in prehospital care, three steps of management are closely linked. First, the on-site evaluation of the patient is essential to assess the mechanism of the injuries and the respiratory and ventilatory status. Special care must be taken with penetrating trauma with hypotension or multiple blunt trauma with severe brain injury because the management of these patients is different.

Second, on-site respiratory management in order to provide efficient airway ventilation and oxygenation is the first priority of treatment. Stabilisation of respiratory status improves patient survival. Prehospital intubation is indicated in severe trauma patients who are unconscious (GCS <8) or hypotensive or when major analgesia is indicated. Intubation may be facilitated by rapid sequence induction. The decompression of tension pneumothorax as well as endotracheal intubation improves early survival of multiple blunt trauma patients.<sup>1</sup>

Third, the question of volume loading in prehospital setting; this is correctly regarded as a priority but is still a matter of discussion. However, it is now widely admitted that blood pressure targets must be adapted to the type of injuries. In the young patient with a specific cause of bleeding such as penetrating trauma, a blood pressure target of a SAP of 90 mmHg is suitable. Such permissive hypotension is well tolerated and useful, since it avoids unnecessary bleeding induced by the raise of blood pressure before surgical control of the hemorrhage. Consequently limited volume infusion is appropriate to this situation and reduces the risk of hemodilution and additional increase of bleeding.

On the other hand, a blood pressure target of SAP 120 mmHg is necessary for multiple trauma patients with severe brain injury in order to limit secondary injuries related to hypotension. Many experimental and clinical studies<sup>2</sup> confirm the importance of the control of blood pressure in this case. However, discussion on how to achieve this goal is still ongoing. Limitation of fluid infusion is one issue; the prehospital use of vasoconstrictors is another. Hypertonic saline + colloid solutions are particularly adapted to these cases. With a single bolus of 250 ml, the quick administration on scene associated with the small volume resuscitation time-saving and effective. The positive effect on blood pressure and the direct action of osmolarity on cerebral oedema are potential advantages. Several meta-analysis performed by Wade et al<sup>3</sup> on the cohort of patients included in all available clinical studies have shown that hypotonic saline with dextran improves survival in a subgroup of patients with penetrating injuries requiring emergency surgical procedures. Even more positive effects are observed in patients with severe traumatic brain injuries and hypotension, who are twice as likely to survive compared with patients receiving a standard crystalloid regimen.

Concerns about the possibility of adverse effects in uncontrolled hemorrhage have been raised. Some experimental models have been inappropriate (fatal hemorrhage, no surgical control). A more recent study<sup>4</sup> confirms that modified improvement of SBP (controlled hypotension) improves survival in penetrating trauma requiring emergency surgical procedures. Unfortunately the clinical experience with hypertonic saline + colloids is limited. This treatment is not currently used in North America and has been introduced only recently in Europe. The experience of a center using this procedure and the hemodynamic effects on patient with severe hypotensive traumatic shock is discussed.

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#### Prehospital Analgesia and Anesthesia

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**Learning Objectives:** 1) to understand the importance of early provision of analgesia and anesthesia in pre hospital emergency care and its use in France and 2) to learn methods of assessment and treatment of pain used in prehospital management

In mainland Europe, especially in France, prehospital EMS care is provided by physicians and anesthesiologists. The aim of prehospital treatment is to stabilize vital functions in order to avoid worsening of major injuries and to stabilize the patient before transportation to the hospital. A precise strategy is needed to provide analgesia, sedation, and anesthesia in prehospital care. Life-threatening problems must be diagnosed and controlled before giving analgesic drugs.

Prehospital pain management is now considered one of the major challenges for anesthesiologists outside the operating room and surgical department. There is no contraindication to treat acute pain in situ, but several factors are involved in the choice of the analgesic procedure adopted in the field. These include the general status of the patient and the location, type, and number of lesions. The French Society of Anesthesiology (SFAR) had proposed recommendations, including a decision tree, to manage pain in these settings. The progression from light sedation to general anesthesia should be considered a continuum depending generally on dose and association of drugs. A large number of drugs and techniques used for sedation and pain control in perioperative period can be transposed to prehospital care.

For the conscious patient, pain may be evaluated with the visual analog scale (VAS) or with a simple questionnaire (adjective rating scale [ARS]), but use of these tools is not simple in prehospital circumstances. The aim of analgesia is to obtain a VAS <30 mm or a ARS <2.

The relief of pain includes simple measures as rewarming, positive communication, splinting of fractures, oxygen supplementation, and pharmacologic agents administered systemically, either regionally or locally.

The two first levels of analgesic agents include paracetamol and nonsteroidal anti-inflammatory drugs (NSAID) administered by the intravenous route. Paracetamol is currently used for mild and moderate pain. NSAIDs decrease the levels of inflammatory generated by tissue injuries, but their adverse effects limit their use. Combined use with opioids enhances their efficacy. Opioid analgesics remain the cornerstone of pharmacological management of moderate to severe acute pain. Morphine is one of the oldest analgesic drugs and its use is safe when a titrated intravenous bolus injection is administered.

Epidural and spinal analgesia are contraindicated in prehospital care. Against this, peripheral nerves blocks have proven to be useful. Conscious patients with painful injuries may be treated by nerve blocks. Before any injection of local anesthetics is attempted, a precise neurological examination is necessary to rule out any unexpected neurological adverse effects that might occur later.

In the prehospital setting, many patients benefit from general anesthesia with endotracheal intubation instead of analgesia and spontaneous breathing. After endotracheal intubation with mechanical ventilation, patient comfort and safety are improved during painful mobilization with good toleration of the tube, removal of concern about respiratory depression, and protection from aspiration. General anesthesia provides deep sedation and as much analgesia required.

Prehospital pain management should now be approached with the same diligence as postoperative care. When used by a trained and experienced EMS care provider, familiar hospital techniques have been shown to be feasible and effective in the early management of trauma.

#### The Role of the Anesthesiologist in Civil Chemical and Biological Attack

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**Learning Objective:** To understand the role of the anesthesiologist at all stages in the management of casualties from terrorist CBW attack, including prehospital, emergency department, operating theatre, and intensive care unit.

The general public concern about the risks of civil attack by terrorists using chemical or biological agents has led to a reappraisal of the clinical approach to management of casualties. Traditionally, toxic exposure has been the domain of public health specialists and toxicologists, but the requirement for early life support has brought the role of the anesthesiologist, both in prehospital and hospital management, into focus. The specialty has an academic background in physiology, applied pharmacology, and pathophysiology and an everyday experience of management of airway and ventilation that makes it well prepared for the management of casualties who may be suffering from life-threatening assaults on vital somatic systems.

Despite widespread political and military rhetoric, chemical and biological agents are not necessarily 'weapons of mass destruction' in the same sense as nuclear weapons but are potentially weapons of mass injury. Early life support and appropriate antidote and antimicrobial therapy can break the link between mass injury and mass loss of life through a well-organised medical response.

In several European countries, anesthesiologists are part of the prehospital emergency response and are trained to be able to provide life support in a contaminated zone while wearing appropriate personal protective suits, an approach that has long been a part of military medical practice. Training, equipment, and exercises are essential for successful management at the prehospital level.

In the hospital, anesthesiologists have an important role in the continuing management of airway and ventilation. Some cases will require ICU care and longer term ventilation. In addition, supportive respiratory care may be required for large number of casualties where ordinary hospital beds may have to be converted to improvised intensive care beds through the provision of portable automatic ventilators. Chemical agents usually act with a short latency and casualties require early respiratory support, whereas biological agent attack (a deliberately induced epidemic) produces casualties that are under the care of specialised physicians and may require intensive care support at a later stage.

Many chemical agents and their antidotes have an effect upon the agents used in general anesthesia. Anesthesiologists therefore require good knowledge of CBW management as part of management of surgery for possible associated traumatic injuries. Although the possi-

ble range of chemical and biological agents regarded as hazards is wide, the number that pose real threats is limited, particularly when being deployed by terrorists. A study of agents that have been used such as sarin and anthrax, together with experience gained from civil accidental releases, provides a basis for anesthesiological training to provide an effective response.

**Terror-Induced, Multiple Casualty Events: Injury Patterns and Emergency Department Response**

*Amir Blumenfeld, Yabav Oron, Oleg Zaslavsky, Eitan Melamed, Ron Ben-Avraham, Guy Lin IDF Medical Corps Trauma Branch*

**Learning Objectives:** *To review and discuss the types of injuries caused by suicidal terrorist attacks and to consider the implications of these injury patterns on emergency medical systems.*

By September 2000, the Israeli-Palestinian conflict escalated by what was later known as the "Al-Aksa Intifada." It was a combination of civilian population riots and low-intensity military conflict between the Israeli army (IDF) and the Palestinian armed forces. Soon after these riots, which started in the west bank and Gaza strip, got into the hearts of the Israeli cities and towns and, by changing its nature to suicidal terrorist attacks, caused severe injuries and death among children, women, and men.

Up to December 2002, more than 5,000 civilians and security force personnel had been injured. About 700 people were killed, 370 of them in multiple casualty events (MCE) caused by explosives carried on suiciders' bodies or hidden in cars.

In order to define injury patterns and estimate the needs of the injured, we conducted a retrospective survey. Data were collected from EMS (operational and medical) records, police reports, ED records, trauma registry files, and specially designed questionnaires run among ED personnel.

MCE victims were divided into three groups by location of occurrence: open spaces (N=316), closed spaces (N=280), and buses (N=260). Injury severity as well as EMS and hospital resource utilization and patients' immediate outcomes were analyzed according to this division.

As a rule, an indoor blast magnifies both casualty generation and injury severity. Mortality rate, which ranged between 8% and 22%, was the highest among bus explosion victims. Severe injuries (ISS>16) rate ranges between 7% and 11.4%, while acute stress reaction is a common consequence (37% to 52%), especially among people injured in open spaces. Emergency interventions such as endotracheal intubation, chest drain insertion, and ED thoracotomy as well as operative procedures and ICU admission were needed much more frequently by victims injured in confined-space explosions. Though gathered experience improved hospitals' performance, there was still an "over-recruitment" phenomena of medical resources on both the prehospital and ED level.

The results and conclusions drawn from this study may serve as a basis for future planning of national emergency medical systems.

**— Session C —**

**CRNA Session**

*Chair: James M. Rich, MA, CRNA, Dallas, Texas, USA*

**Vascular Access for Trauma Anesthesia: Options, Risks, Benefits, and Complications**

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**Learning Objectives:** *1) To compare and contrast the classifications of shock, 2) to discuss the number, size, and location necessary for vascular access in trauma, 3) to understand the acute and chronic complications associated with vascular access, and 4) to discuss the options for vascular access for children younger than 5.*

Multiple trauma patients with hemorrhagic shock require rapid intravenous access after airway patency and ventilation are established. Timely restoration of intravascular volume improves systemic perfusion, alleviates tissue hypoxia and acidosis, and arrests cell death and progression to irreversible shock. Therapeutic goals include restoring volume deficits and preventing further loss.<sup>1</sup> The type and location of injury, duration and rate of blood loss, and classification of hemorrhagic shock (Table 1) will mandate the size, number, and location of intravenous catheters.

**Table 1. Classes of Shock<sup>2</sup>**

Class	Blood loss (mL)/% Total Blood Volume	Heart Rate	Blood	Pulse Pressure	Respirations/min Pressure
Class 1	<750 <15%	<100	Normal	Normal or increased	14–20
Class 2	750–1500 15–30%	>100	Normal	Decreased	20–30
Class 3	1500–2000 30–40%	>120	Decreased	Decreased	30–40
Class 4	>2000 >40%	>140	Decreased	Decreased	>35

ATLS protocol recommends insertion of two large-bore (16g or larger) IV catheters before insertion of a central venous catheter or venous cutdown in patients with severe injuries and hemorrhagic shock.<sup>3</sup> Classes 2, 3, and 4 shock warrant central venous access for fluid replacement and monitoring.

When considering a location for IV access, several factors are considered. Injuries below the diaphragm require one IV placed in a tributary of the superior vena cava because of possible disruption of the inferior vena cava. Patients with upper chest and neck injuries require access in lower extremities because superior vena cava disruption may be present. In multisystem trauma, large-bore IV access above and below the diaphragm is necessary.

Patients in hypovolemic shock need rapid administration of IV fluids through short large-bore catheters. Doubling internal diameter of the catheter increases flow 16-fold. Eight and nine French large-bore catheter introducers deliver flow rates nearly twice as fast as short 14g catheters and can be used in subclavian, internal and external jugular, femoral, and antecubital sites.<sup>4</sup>

Catheterization of large central veins provides access for rapid infusion and measurement of central venous pressure. Table 2 summarizes acute and chronic complications of subclavian and internal jugular catheters. Anesthesia providers must be aware of these complications, especially if the patient's condition does not improve or deteriorates during anesthesia.

**Table 2. Acute and Chronic Complications of Subclavian and Internal Jugular Catheters**

Acute Complications <sup>5,6</sup>	Late Complications <sup>5,6</sup>
Cardiac arrhythmias	Infection
Arterial puncture	Sepsis
Pneumothorax	Intravascular thrombosis
Hydrothorax	Pseudoaneurysm
Air embolism	Arteriovenous fistula formation
Hornor's Syndrome	
Thoracic duct injury	
Guidewire or catheter fragment embolization	
Cardiac tamponade	
Vessel perforation with hemorrhage	
Cerebral infarction	
Phrenic nerve injury	
Brachial plexopathy	

Intraosseous catheters can be used in children younger than 5 years of age because the cortical bone is softer. Specifically designed intraosseous needles are available and flow rates of 40 mL/min with crystalloids using pressure bags have been achieved.<sup>7</sup> Complications include disruption of the growth plate, cellulitis, osteomyelitis, fat embolism, and extravasation of fluids into the surrounding tissue.

Anesthesia providers must be skilled in each catheterization technique and utilize the technique with which they are most experienced. However, they should have the expertise to perform as many techniques as warranted by the situation. Diligent observation for possible complications should be an ongoing process during anesthesia. Successful vascular access is of prime importance in preventing morbidity and mortality in trauma.

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**Massive Volume Replacement in the Trauma Patient**

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**Learning Objective:** *To discuss the means of evaluating hemorrhagic blood loss and the appropriate replacement fluids in the trauma patient sustaining severe injuries.*

Hemorrhagic blood loss in the trauma patient leads to shock and increased mortality unless treated promptly and appropriately at the earliest possible time following initial injury. With an adequate understanding of the mechanism of injury, the anesthetist develops a high index of suspicion for potential high volume of blood loss in patients with significant thoracic, abdominal, and pelvic injuries. Additionally, conditions such as bilateral femoral fractures and major vascular injuries are also associated with substantial hemorrhage.

Initial Assessment and Management. In an ideal trauma system, intravenous fluids are initiated at the scene. Volume resuscitation is administered vigorously until the patient appears to normalize physiological parameters. Desirable endpoints include an adequate blood pressure, reasonable pulse rate, appropriate capillary refill, and 1-2 mL/kg urinary output per hour.

In the trauma center resuscitation area, several large-bore intravenous catheters are placed and blood is drawn for determination of a CBC, SMAC, coagulation panel, and toxicology screen. The establishment of venous access facilitates volume restoration and provides a route for intravenous drug administration. During CPR, peripheral lines are placed. Following restoration of spontaneous circulation, central venous lines are placed as indicated.

In life-threatening situations, type O-negative (or alternatively O-positive) blood is transfused without type and cross-matching. If time permits, generous volumes of crystalloid and colloid fluids are given with continuous evaluation of the patient's clinical presentation. Concurrently, hemoglobin and hematocrit values are determined to guide progress of resuscitation and the need for additional blood.

Management of major blood loss will include the placement of several large-bore intravenous catheters and placement of appropriate invasive physiological monitors. Liberal administration of balanced salt solution is used. Colloids are used to rapidly increase intravascular volume to aid in restoration of adequate blood pressure and appropriate pulse rate. During surgery, red blood cell salvaging is helpful in reducing the need for additional bank blood. Efficient fluid warming and adequate capacity to pump fluids at high flow rates are used to prevent hypothermia and to provide rapid fluid replacement. Initial comprehensive assessment and aggressive fluid resuscitation will often allow the anesthetist to avoid the need for ACLS drug interventions.

**Conclusions.** Fluid resuscitation of the trauma patient is a critical element in the over-

all anesthetic management. Early establishment of adequate venous access and administration of warmed crystalloid and colloid fluids and blood products are essential to initial resuscitation. Fluid management is based on careful assessment and monitoring of physiological and laboratory values. The principles of successful management of the trauma patient are based on organization and preparation, assessment of the patient's injuries, proper priority for therapeutic interventions, achievement and maintenance of a patent airway, fluid resuscitation, application of appropriate continuous invasive and noninvasive monitoring, correction of acid-base and electrolyte disturbances, and careful titration of anesthetic and adjunctive agents. The degree of functional outcome of trauma patients is largely dependent on the early involvement of sound principles of anesthesia care in the resuscitation and overall anesthetic management during the perioperative period. In a well-managed team approach, assessment and treatment are carried out in rapid succession or even simultaneously.

#### Suggested Readings

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#### Applying ATLS Guidelines to Trauma Care

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**Learning Objective:** To apply ATLS guidelines to management of the trauma patient in the critical care setting by CRNAs.

Assessment of the patient should begin with the airway.<sup>1</sup> Decisions should be made in the opening minutes of assessment to recognize pitfalls in establishing the airway, recognition of the incorrectly established airway, displacement of an ongoing airway, and the possibility of aspiration.

Problems that can occur early in assessment include several types of trauma: head trauma, neck trauma, and maxillofacial trauma that may influence the type of airway control used. The goal should be to provide airway support and deliver oxygen without causing further harm to patients (i.e., aspiration, further trauma).

Maxillofacial trauma patients should be assessed for their ability to breathe in supine position and for fractures to the trachea or oropharynx. Neck trauma patients may have penetrating injuries that cause displacement of the trachea and require tracheostomies. Associated laryngeal trauma may include a triad in the fracture of the larynx, including hoarseness, subcutaneous emphysema, and a palpable fracture.

In the initial assessment of the airway, look, listen, and feel for any abnormalities. Looking at the airway should include observation of obstruction, decreased air movement, retraction, deformity, and debris. Listening to the airway may reveal noisy speech, gurgle or stridor, or hoarseness requiring further intervention. Feeling the airway may reveal the location of the trachea, hematoma formation, or fracture locations.

Ventilation capabilities must be assessed for factors of the central nervous system that may impede the airway. These factors may include CNS depression, blunt chest trauma, spinal cord injury, and other problems.

Management of patients must always include immobilization of the neck at all times with traction on the head in a neutral position and care to avoid complicated fractures of the face and nasal area. Needs for definitive airways include the following types of patients: unconscious, severe maxillofacial trauma, and those at risk for obstruction or aspiration. Nasal tracheal intubation should be used only when clearly indicated. Airway algorithms should be followed to minimize poor decision making in choosing the next step in assisting the patient to ventilate. Jet ventilators or surgical cricothyrotomies may be used as a last resort in rescuing the airway.<sup>2,3</sup>

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#### Anesthetic Management of the Patient Sustaining Thoracic Trauma

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**Learning Objectives:** To understand manifestations and management of the life-threatening conditions that can result from blunt thoracic trauma.

Blunt thoracic trauma often results from the impact of drivers who are not wearing safety belts into the steering wheel during a motor vehicle crash. Penetrating and blunt trauma to the chest may injure several structures and thus compromise optimal resuscitation. These structures include the chest wall, the lungs and airways, the heart and pericardium, and the great vessels of the thorax. Injuries to these structures also compromise anesthesia care by affecting gas exchange and cardiac output.

Several life-threatening conditions require immediate interventions in patients with chest injuries. A tension pneumothorax develops when the pleural cavity is punctured, creating a one-way valve that controls the flow of air into this cavity. With each breath, more air becomes trapped in this space, increasing intrapleural pressure to the point that it eventually exceeds all other intrathoracic pressures. The enlarging pleural cavity then collapses the ipsilateral lung and shifts structures of the mediastinum (e.g., trachea, great vessels, heart) into the opposite hemithorax, thereby compressing the contralateral lung. The size of a pneumothorax rapidly increases during positive-pressure ventilation, especially if nitrous oxide is used in the field for analgesia or during anesthesia in the trauma facility. Patients with a pneumothorax often present with hypotension, subcutaneous emphysema of the neck or chest, unilateral decrease in breath sounds, diminished chest wall motion, hyper-resonance

to percussion of one hemithorax, distended neck veins, or tracheal shift. An upright expirational chest radiograph provides definite information if the problem is significant. However, if the trauma patient is unstable, a large-bore intravenous catheter is inserted into the superior portion of the second intercostal space along the midclavicular line.

Many thoracic injuries can be life threatening. Massive hemothorax, which can be caused by bleeding from the heart and great vessels, must be treated immediately. Adequate fluid resuscitation is accomplished before placement of chest tubes. Chest tubes allow drainage of blood from the pleural cavity but can lead to more extensive bleeding and hypotension. Pericardial tamponade that restricts filling of the cardiac chambers during diastole and produces a fixed low cardiac output is also a life-threatening emergency that requires immediate correction with pericardiocentesis. Patients with cardiac rupture without pericardial tamponade seldom survive because exsanguination is extremely rapid in this situation. Traumatic aortic rupture, if complete, is usually fatal, but with an intimal tear with a dissecting aneurysm, the patient can be saved if the diagnosis and repair are performed promptly during well-managed fluid resuscitation and anesthesia care. Management of these cases requires rapid and accurate assessment and appropriate surgical and anesthesia intervention. Partial disruption of the trachea or major bronchi can be handled in many cases through securing of the airway (by intubation or tracheostomy) and surgical correction. Total disruption of the trachea is commonly fatal unless rapid surgical retrieval of the distal disrupted airway segment is accomplished; this measure allows life-saving mechanical ventilation.

Diagnosis of stable chest injuries is frequently enhanced by computed tomography (CT), angiography, and other radiologic studies.

#### Anesthetic Management of the Trauma Patient in the Rural Health Care Setting

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**Learning Objective:** To discuss the anesthetic considerations unique to the rural health care trauma patient as they relate to the area of shock.

The rural health patient presents many challenges to the anesthetic care provider in resources and in the management and treatment of shock. Recognition of the signs and symptoms of shock is the key to successful intervention and treatment of trauma patients.

Shock is defined as both inadequate tissue/organ perfusion and a lack of tissue oxygenation. Knowledge of cardiac output and stroke volume is necessary to evaluate the patient who presents in shock. Cardiac output is the volume of blood pumped per minute as a result of heart rate and stroke volume. Stroke volume is the amount of blood pumped by the heart as determined by preload, myocardial contractility, and afterload.<sup>1</sup>

Early changes of blood loss include tachycardia, progressive vasoconstriction, release of histamine, and bradykinin. Initial goals include restoring cardiac output via volume repletion with isotonic solutions.<sup>1</sup> Vasopressors may be contraindicated at this time due to the need for volume replacement and the additional stress placed on the heart muscle.

Recognition of shock includes tachycardia, vasoconstriction, decreased cardiac output, a narrowing pulse pressure, decreasing mean arterial pressures, and decreased blood flow. Tachycardia varies by patient age group, and normal values should be taken into consideration while assessing the patient.<sup>1</sup>

Pitfalls in assessment of the shock patient include extremes of age, athletes, pregnant patients, medications ingested by the patient prior to arrival, and misleading hemoglobin and hematocrit values resulting from fluid resuscitation.

Types of shock include hemorrhagic, cardiogenic, neurogenic, and some types of septic shock. Class I, II, III, and IV types of hemorrhagic shock can start as "minor" emergencies and quickly turn into the loss of patient life. Initial assessment of the patient and rapid allocation of equipment and personnel may yield the difference in outcome to the patient in the rural health setting.<sup>1</sup>

Equipment such as a large-volume rapid infusion system, forced-air warmer, intravenous fluid warmer may be utilized to reverse hypothermia and offset blood loss quickly.<sup>2</sup> Lab personnel and nursing staff are essential to respond rapidly to the patient's changing condition. ATLS( guidelines and practice trauma drills are helpful in training the trauma team to respond successfully to trauma patients and assist practitioners in the "rules of engagement" for highly successful outcomes.

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#### Airway Management in Trauma Patients

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**Learning Objective:** Upon completion of this lecture, the participant will be able to list the four anatomic variants associated with a potential difficult airway.

Airway management and fluid resuscitation are the two most important priorities of the trauma patient, if there is to be any chance of viable survival without significant disability. This lecture will cover important aspects of airway management for the trauma patient.

Airway anatomy, evaluation, and assessment of the airway with recognition of airway distortion caused by either blunt or penetrating trauma are crucial to develop an appropriate plan of care. Remembering the "four Ds" will aid in airway assessment, i.e., disproportion, distortion, decreased range of motion, and dental overbite.<sup>1</sup>

In order to provide rapid correction of the "Crash Airway" patient, a quick method for recognizing this situation is crucial. Application of Mason's PU-92 concept accomplishes this.<sup>2,3</sup>

Rational selection of an appropriate airway technique to include aspiration prophylaxis and protection of suspected or evident cervical spine injuries is paramount. Populations that require special consideration in trauma include obstetrical patients, pediatric patients, patients with a traumatized airway, and patients with suspected or evident cervical spine injuries. Methods to secure the airway in these populations will be discussed.<sup>4</sup>

When airway difficulty is suspected, the practitioner must decide to either temporarily avoid tracheal intubation through use of a non-intubation airway technique with or without application of a minimally invasive airway option. It is also crucial in the face of potential intubation difficulty that consideration be given to a technique that allows spontaneous ventilation versus apnea secondary to use of neuromuscular blocks.

The choice of rapid-sequence intubation (RSI) should be reserved for patients with no

signs of predicted difficulty. RSI should be avoided if rescue ventilation options are not available to treat a failed airway.<sup>7</sup>

A failed intubation strategy should include use of bag-valve-mask ventilation (BVMV) with cricoid pressure as well as the use of a Combitube, LMA, or LMA-Fastrach (ILMA) to provide life-saving ventilation and oxygenation as well as the potential for tracheal intubation (i.e., LMA-Fastrach [ILMA]). The Combitube offers aspiration prophylaxis similar to that of an endotracheal tube. The LMA protects from aspiration much better than BVMV.<sup>2,6,8</sup>

If rescue ventilation does not attain or maintain an acceptable SpO<sub>2</sub> ( $\geq 92\%$ ), then a cricothyrotomy option should be immediately applied; however, the use of rescue ventilation will greatly decrease the need for transtracheal jet ventilation, percutaneous dilational cricothyrotomy, or surgical cricothyrotomy.<sup>9</sup>

Confirmation of tracheal intubation is a central aspect of airway management. The best method to confirm endotracheal intubation is to use capnography in a patient with a beating heart and good pulmonary vascular blood flow and to use an esophageal detector device in patients with cardiac arrest or severe low flow states.<sup>10</sup> In addition to the use of a near-fail-safe device, the patient's chest should also be auscultated along the mid-axillary lines and over the abdomen.

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#### Anesthetic Management of Patients with Abdominal Trauma

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**Learning Objectives:** 1) To state the indications for emergency exploratory laparotomy, 2) to determine appropriate intraoperative monitoring, 3) to determine "safe" drugs, 4) to recognize transfusion complications, and 5) to determine when abbreviated damage control surgery is appropriate.

Exsanguinating hemorrhage is the major acute cause of death following abdominal trauma.<sup>1–3</sup> Initial focus is on controlling hemorrhage, limiting contamination, rapid assessment, and treatment of blunt and penetrating abdominal trauma.

First priority is securing the airway, then IV access, resuscitation, and identification and stabilization of life-threatening injuries. A decision is then made to proceed with surgical intervention or perform more diagnostic evaluation.

Initial laboratory and diagnostic studies are based on the patient's stability. Indications for emergency exploratory laparotomy<sup>4</sup> are listed below:

1. Penetrating or blunt trauma with hypotension
2. Uncontrolled hemorrhage
3. Signs of peritonitis
4. GSW to abdomen
5. Positive objective study (CT, Sonogram, DPL)
6. Ruptured diaphragm
7. Pneumoperitoneum on admission chest film
8. Evisceration of bowel or omentum
9. Herniation of abdominal contents
10. Significant bleeding from NG tube, rectum
11. Ongoing bleeding from unknown source
12. Stab wounds with known vascular, biliary, or colonic injury

Minimum noninvasive monitors include EKG, automated B/P, pulse oximetry, core temperature probe with stethoscope, and capnography. A Foley catheter with urometer, radial or brachial arterial catheter for monitoring and frequent lab analysis during trauma laparotomy. Two large-bore peripheral catheters must be established with central venous access in cases involving large blood loss or transfusion. Blood must be available, often infusing prior to opening the abdomen in severely hypotensive patients.

Early goals include re-establishment and maintenance of normal hemodynamics. Correct size and number of IV lines is accomplished before incision. Hypotension from drug effect, suppression of endogenous catecholamines, and initiation of positive-pressure ventilation will dictate the need for immediate surgical incision upon induction. Following incision, tamponade of abdominal bleeding is lost, and copious blood loss may precipitate.

Etomidate (0.2 mg/kg), normally cardiac neutral, is well tolerated in awake traumatized patients. Ketamine can promote greater hypotension in a patient with poor sympathetic tone. In unstable hypotension, oxygen with a muscle relaxant is required until return of hemodynamics allow additional anesthetic drugs. When anesthesia needs to be withheld, scopolamine may be given for amnesia.

Periodic measurement of laboratory values is essential. Central venous pressure, urine output and hemodynamics aid in calculation of fluid volumes. Cell saver blood should be given for noncontaminated intra-abdominal blood loss.

The following complications can arise from massive transfusions<sup>5,6</sup>: coagulopathy,

hypothermia, hypocalcemia, hyperkalemia, and hemolysis.

With a pH <7.10, temperature <34 C, SBP <70 mmHg, and Injury Severity Score >25, 98% of patients develop life-threatening coagulopathy.<sup>7</sup> Factors increasing morbidity and mortality include hypothermia.<sup>2,5,6,8,9</sup> Combating hypothermia, all fluids must be warmed, OR temperature kept between 21 and 25 C, and forced air warmers used.

During trauma laparotomy, muscle relaxation should be complete. Drugs releasing histamine should be avoided. The bowel should always be decompressed by an NG or OG tube and nitrous oxide should not be used.

Abbreviated damage control surgery is appropriate in severely injured patients with metabolic derangements in whom prolonged initial operations would be dangerous.<sup>2</sup> Shorter operative times increase survival and decrease morbidity.<sup>10,11</sup>

To minimize anesthetic risk, we should strive to know the mechanism of injuries, resuscitation status, and present co-morbidity. Use only hemodynamically stable anesthetic agents with invasive monitoring. Fluid management is challenging because of rapid, unpredictable changes in volume status. Possible complications must be anticipated, and the appropriate therapeutic options instituted. Anesthesia providers must maintain a high index of suspicion, avoiding complacency, even when the patient appears stable.

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#### Anesthetic Management of the Acute Spinal Cord Injured Patient

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**Learning Objectives:** To review 1) the assessment of patients with suspected spinal cord injury, including the likelihood of such injury, 2) protective and stabilizing measures for patients being evaluated for spinal cord injury, and 3) anesthetic techniques used during the management of patients with suspected or documented spinal cord injury.

More than 11,000 spinal cord injuries (SCIs) occur each year in the United States. Approximately 4200 of people with such injuries die before they can be transported to a treatment facility, and another 1150 die during hospitalization. Eventual outcome after an acute SCI depends on three factors: 1) the severity of the acute injury, 2) the prevention of exacerbation of the injury during rescue, transport, and hospitalization; and (3) the avoidance of hypoxia and systemic hypotension, which can further compromise neural function.

Assessment for spinal cord injury is conducted in the traumatized individual. The mechanism of injury usually helps in the diagnosis of possible SCI. If an individual has been thrown from an automobile, a 1 in 13 chance exists that a cervical fracture has been sustained. If the victim remains in the car, the chances of such an injury improve to 1 in 436. Cervical SCI should be assumed to be present in any patient who has sustained trauma to the head or face, in any unconscious trauma patient, and in any patient who complains of pain before or after careful palpation of the cervical spine.

If SCI is suspected, care should be taken to prevent further extension of the injury. A properly fitted cervical collar should be carefully placed before the patient is moved or extricated. Precautions are taken to prevent further extension of actual or potential neurologic deficits. Spinal immobilization is completed before the patient is moved. The head is stabilized in neutral alignment with no extension, flexion, or rotation. Stabilization is accomplished by placing a cervical collar on the patient, splinting, and/or sandbagging the head in neutral alignment. The patient is placed on a long spinal back board before movement and transport.

If the patient with an SCI is breathing spontaneously on arrival at the treatment facility, the anesthetist evaluates the adequacy of ventilation. If the patient is not able to protect his or her airway (because he or she is unconscious or semiconscious; has an absent or diminished gag reflex or cough; or has intraoral or facial injuries with significant edema, or bleeding, or both), rapid intubation is needed. If ventilation appears to be reasonable, chest and cervical spine radiographic evaluation and neurologic examinations can be started while an arterial blood gas determination is completed. A lateral view of the cervical spine quickly obtained and it generally reveals most unstable fractures. For a complete evaluation of the cervical spine, multiple films or CT scanning may be required. An adequate evaluation must include all seven cervical vertebrae; C–7 is the most common site of injury. In the stable cooperative patient with an SCI, awake nasal intubation is the method of choice. The nasal intubation can be accomplished blindly with the use of an Endotrach tube, which has a trigger device that allows the tip of the endotracheal tube to be positioned with relative ease. The tube can also be guided by use of a direct fiberoptic laryngoscope. In children and uncooperative adults or in patients in whom awake intubation fails, a carefully selected dose of thiopental and a neuromuscular blocking agent is used for inducing general anesthesia for oral intubation. If there is a delay in establishing the airway, the patient is ventilated by mask while cricoid pressure is maintained until the airway is secured.

**Uncertain  
pathogen?**

**Until you  
know its name,  
trust ours.\***

\*For infections due to susceptible strains of indicated organisms.

.....  
Careful inquiry should be made concerning previous hypersensitivity reaction, as serious and occasionally fatal anaphylactic reactions have been reported in patients receiving therapy with penicillins. ZOSYN is contraindicated in patients with a history of these reactions to any of the penicillins, cephalosporins, or  $\beta$ -lactamase inhibitors.

While ZOSYN possesses the characteristic low toxicity of the penicillin group of antibiotics, periodic assessment of organ system functions, including renal, hepatic, and hematopoietic, during prolonged therapy is advisable.

During clinical trials, pseudomembranous colitis has been rarely reported (<1%).

The most commonly reported adverse events in clinical trials, irrespective of relationship to therapy, included diarrhea (11.3%), headache (7.7%), constipation (7.7%), nausea (6.9%), and insomnia (6.6%).

***Please see adjacent brief summary of Prescribing Information.***

**ZOSYN<sup>IV</sup>**  
(piperacillin sodium/tazobactam sodium)

**EMPIRIC THERAPY FOR SERIOUS INFECTIONS**



## ZOSYN® (Piperacillin and Tazobactam for Injection) Brief Summary

### See package insert for full prescribing information.

**INDICATIONS AND USAGE** For the treatment of patients with moderate to severe infections caused by piperacillin-resistant, piperacillin/tazobactam-susceptible,  $\beta$ -lactamase producing strains of the designated microorganisms in the specified conditions listed below:

Appendicitis (complicated by rupture or abscess) and peritonitis caused by *Escherichia coli* or the following members of the *Bacteroides fragilis* group: *B. fragilis*, *B. ovatus*, *B. thetaioaomicron*, or *B. vulgatus*. The individual members of this group were studied in less than 10 cases.

Uncomplicated and complicated skin and skin structure infections, including cellulitis, cutaneous abscesses, and ischemic/diabetic foot infections caused by *Staphylococcus aureus*.

Postpartum endometritis or pelvic inflammatory disease caused by *Escherichia coli*.

Community-acquired pneumonia (moderate severity only) caused by *Haemophilus influenzae*.

Nosocomial pneumonia (moderate to severe) caused by *Staphylococcus aureus*. (See Full Prescribing Information—**DOSAGE AND ADMINISTRATION**.)

Infections caused by piperacillin-susceptible organisms, for which piperacillin has been shown to be effective, are also amenable to ZOSYN treatment due to its piperacillin content. Treatment of mixed infections caused by piperacillin-susceptible organisms and piperacillin-resistant,  $\beta$ -lactamase producing organisms susceptible to ZOSYN should not require the addition of another antibiotic. ZOSYN is useful as presumptive therapy in the indicated conditions prior to the identification of causative organisms because of its broad spectrum of bactericidal activity against gram-positive and gram-negative aerobic and anaerobic organisms. Appropriate cultures should usually be performed before initiating antimicrobial treatment in order to isolate and identify the organisms causing infection and to determine their susceptibility to ZOSYN.

**CONTRAINDICATIONS** ZOSYN is contraindicated in patients with a history of allergic reactions to any of the penicillins, cephalosporins, or  $\beta$ -lactamase inhibitors.

**WARNINGS** SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTIC/ANAPHYLACTOID) REACTIONS (INCLUDING SHOCK) HAVE BEEN REPORTED IN PATIENTS RECEIVING THERAPY WITH PENICILLINS INCLUDING ZOSYN. THESE REACTIONS ARE MORE LIKELY TO OCCUR IN INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY OR A HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS. THERE HAVE BEEN REPORTS OF INDIVIDUALS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE REACTIONS WHEN TREATED WITH CEPHALOSPORINS. BEFORE INITIATING THERAPY WITH ZOSYN, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OR OTHER ALLERGENS. IF AN ALLERGIC REACTION OCCURS, ZOSYN SHOULD BE DISCONTINUED AND APPROPRIATE THERAPY INSTITUTED. **SERIOUS ANAPHYLACTIC/ANAPHYLACTOID REACTIONS (INCLUDING SHOCK) REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE, OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, SHOULD ALSO BE ADMINISTERED AS INDICATED.**

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including ZOSYN, and may range in severity from mild to life-threatening. Consider this diagnosis in patients who present with diarrhea after antibacterial agent administration.** Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, initiate therapeutic measures. Mild cases usually respond to drug discontinuation alone. In moderate to severe cases, fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis may be necessary.

**PRECAUTIONS** General: Bleeding manifestations have occurred in some patients receiving  $\beta$ -lactam antibiotics, including piperacillin. These reactions have sometimes been associated with coagulation test abnormalities such as clotting time, platelet aggregation, and prothrombin time and are more likely to occur in renal failure patients. If bleeding manifestations occur, discontinue ZOSYN and institute appropriate therapy.

The possibility of the emergence of resistant organisms that might cause superinfections should be kept in mind. If this occurs, appropriate measures should be taken.

As with other penicillins, patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).

ZOSYN is a monosodium salt of piperacillin and a monosodium salt of tazobactam, containing 2.35 mEq (54 mg) of Na<sup>+</sup> per gram of piperacillin; consider this when treating patients requiring restricted salt intake. Perform periodic electrolyte determinations in patients with low potassium reserves; the possibility of hypokalemia should be kept in mind with patients who have potentially low potassium reserves and who are receiving cytotoxic therapy or diuretics.

As with other semisynthetic penicillins, piperacillin has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

In patients with renal insufficiency or in hemodialysis patients, the intravenous dose should be adjusted to the degree of renal function impairment.

**Laboratory Tests:** Perform periodic assessment of hematopoietic function, especially with prolonged therapy, ie,  $\geq 21$  days. (See **ADVERSE REACTIONS—Adverse Laboratory Events**.)

**Drug Interactions:** *Aminoglycosides*—The mixing of ZOSYN with an aminoglycoside in vitro can result in substantial inactivation of the aminoglycoside. (See Full Prescribing Information—**DOSAGE AND ADMINISTRATION—Compatible Intravenous Diluent Solutions**.)

When ZOSYN was co-administered with tobramycin, the area under the curve, renal clearance, and urinary recovery of tobramycin were decreased by 11%, 32%, and 38%, respectively. Pharmacokinetic alterations of tobramycin when administered with ZOSYN may be due to in vivo and in vitro inactivation of tobramycin in the presence of piperacillin/tazobactam. The inactivation of aminoglycosides in the presence of penicillin-class drugs has been recognized. It has been postulated that microbiologically inactive penicillin-aminoglycoside complexes of unknown toxicity form. In patients with severe renal dysfunction (ie, chronic hemodialysis patients), tobramycin pharmacokinetics are significantly altered when administered with piperacillin. The alteration of tobramycin pharmacokinetics and the potential toxicity of the penicillin-aminoglycoside complexes in patients with mild to moderate renal dysfunction who are administered an aminoglycoside with ZOSYN are unknown.

*Probenecid*—Probenecid administered with ZOSYN prolongs the half-life of piperacillin by 21% and of tazobactam by 71%.

*Vancomycin*—No pharmacokinetic interactions with ZOSYN have been noted.

*Heparin*—Coagulation parameters should be tested more frequently and monitored regularly during simultaneous administration of high doses of heparin, oral anticoagulants, or other drugs that may affect the blood coagulation system or the thrombocyte function.

*Vecuronium*—Piperacillin used with vecuronium has been implicated in the prolongation of the neuromuscular blockade of vecuronium. ZOSYN could produce the same phenomenon if given with vecuronium. Due to their similar mechanism of action, the neuromuscular blockade produced by any of the non-depolarizing muscle relaxants could be prolonged in the presence of piperacillin. (See package insert for vecuronium bromide.)

*Methotrexate*—Piperacillin may reduce the excretion of methotrexate; therefore, serum levels of methotrexate should be monitored in patients to avoid drug toxicity.

**Drug/Laboratory Test Interactions:** As with other penicillins, ZOSYN may result in a false-positive reaction for glucose in the urine using a copper-reduction method (CLINITEST<sup>®</sup>). Glucose tests based on enzymatic glucose oxidase reactions (such as DIASTIX<sup>®</sup> or TES-TAPE<sup>®</sup>) are recommended.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Long term carcinogenicity studies in animals have not been conducted with piperacillin/tazobactam, piperacillin, or tazobactam. Piperacillin/tazobactam was negative in the following mutagenicity tests/assays up to the concentrations noted: microbial mutagenicity assay (14.84/1.86  $\mu$ g/plate), unscheduled DNA synthesis (UDS) test (5689/711  $\mu$ g/mL), mammalian point mutation (Chinese hamster ovary cell HPRT) assay (8000/1000  $\mu$ g/mL), and a mammalian cell (BALB/c-3T3) transformation assay (8/1  $\mu$ g/mL). In vivo, piperacillin/tazobactam did not induce chromosomal aberrations in rats dosed I.V. with 1500/187.5 mg/kg; this dose is similar to the maximum recommended human daily (MRHD) dose on a body-surface-area basis (BSA) (mg/m<sup>2</sup>).

Piperacillin was negative in the following mutagenicity tests/assays up to the concentrations noted: microbial mutagenicity assays (50  $\mu$ g/plate), UDS test (10,000  $\mu$ g/mL), and a cell (BALB/c-3T3) transformation assay (3000  $\mu$ g/mL). There was no DNA damage in bacteria (Rec assay) exposed to piperacillin at concentrations up to 200  $\mu$ g/disk. In a mammalian point mutation (mouse lymphoma cells) assay, piperacillin was positive at concentrations  $\geq 2500$   $\mu$ g/mL. In vivo, piperacillin did not induce chromosomal aberrations in mice at I.V. doses up to 2000 mg/kg/day or rats at I.V. doses up to 1500 mg/kg/day. These doses are half (mice) or similar to (rats) the MRHD dose based on BSA (mg/m<sup>2</sup>). In another in vivo test, there was no dominant lethal effect when piperacillin was administered to rats at I.V. doses up to 2000 mg/kg/day, which is similar to the MRHD dose based on BSA (mg/m<sup>2</sup>). When mice were administered piperacillin at I.V. doses up to 2000 mg/kg/day, which is half the MRHD dose based on BSA (mg/m<sup>2</sup>), urine from these animals was not mutagenic when tested in a microbial mutagenicity assay. Bacteria injected into the peritoneal cavity of mice administered piperacillin at I.V. doses up to 2000 mg/kg/day did not show increased mutation frequencies.

Tazobactam was negative in the following mutagenicity assays up to the concentrations noted: microbial mutagenicity assays (333  $\mu$ g/plate), UDS test (2000  $\mu$ g/mL), mammalian point mutation (Chinese hamster ovary cell HPRT) (5000  $\mu$ g/mL), a cell (BALB/c-3T3) transformation assay (900  $\mu$ g/mL). In another mammalian point mutation (mouse lymphoma cells) assay, tazobactam was positive at concentrations  $\geq 3000$   $\mu$ g/mL. In an in vitro cytogenetics (Chinese hamster lung cells) assay, tazobactam was negative at concentrations up to 3000  $\mu$ g/mL. In vivo, tazobactam did not induce chromosomal aberrations in rats at I.V. doses up to 5000 mg/kg, which is 23 times the MRHD dose based on BSA (mg/m<sup>2</sup>).

**Pregnancy: Teratogenic effects—Pregnancy Category B:** Piperacillin/tazobactam: Reproduction studies in rats have revealed no evidence of impaired fertility due to piperacillin/tazobactam administered up to a dose which is similar to the MRHD dose based on BSA (mg/m<sup>2</sup>).

Teratology studies in mice and rats have revealed no evidence of harm to the fetus due to piperacillin/tazobactam administered up to a dose which is 1 to 2 times and 2 to 3 times the human dose of piperacillin and tazobactam, respectively, based on BSA (mg/m<sup>2</sup>). Piperacillin and tazobactam cross the placenta.

Piperacillin: Reproduction and teratology studies in mice and rats have revealed no evidence of impaired fertility or fetal harm due to piperacillin administered up to a dose which is half (mice) or similar to (rats) the MRHD dose based on BSA (mg/m<sup>2</sup>).

Tazobactam: Reproduction studies in rats have revealed no evidence of impaired fertility due to tazobactam administered at doses up to 3 times the MRHD dose based on BSA (mg/m<sup>2</sup>).

Teratology studies in mice and rats have revealed no evidence of fetal harm due to tazobactam administered at doses up to 6 and 14 times, respectively, the human dose based on BSA (mg/m<sup>2</sup>). In rats, tazobactam crosses the placenta. Concentrations in the fetus are less than or equal to 10% of those found in maternal plasma. There are no adequate and well-controlled studies with the piperacillin/tazobactam combination or with piperacillin or tazobactam alone in pregnant women. Use this drug during pregnancy only if clearly needed.

**Nursing Mothers:** Piperacillin is excreted in low concentrations in human milk; tazobactam concentrations in human milk have not been studied. Exercise caution when ZOSYN is administered to a nursing woman.

**Pediatric Use:** Safety and efficacy in pediatric patients have not been established.

**Geriatric Use:** Patients over 65 years are **not** at an increased risk of developing adverse effects solely because of age. However, dosage should be adjusted in the presence of renal insufficiency.

**ADVERSE REACTIONS** During the initial clinical investigations, 2621 patients worldwide were treated with ZOSYN in phase 3 trials. In the key North American clinical trials (n=830 patients), 90% of the adverse events reported were mild to moderate in severity and transient in nature. However, in 3.2% of the patients treated worldwide, ZOSYN was discontinued because of adverse events primarily involving the skin (1.3%), including rash and pruritus; the gastrointestinal system (0.9%), including diarrhea, nausea, and vomiting; and allergic reactions (0.5%).

Adverse local reactions that were reported, irrespective of relationship to ZOSYN therapy, were phlebitis (1.3%), injection site reaction (0.5%), pain (0.2%), inflammation (0.2%), thrombophlebitis (0.2%), and edema (0.1%). In the completed study of nosocomial lower respiratory tract infections, 155 patients received ZOSYN 3.375 g every 4 hours in combination with an aminoglycoside. In this trial, 88.5% of the adverse experiences reported were mild to moderate in severity and transient in nature. In this trial, ZOSYN was discontinued in four patients (2.6%) due to adverse experiences: thrombocytopenia and pancreatitis in one patient; fever in one patient; fever and eosinophilia in another patient; and diarrhea and elevated liver enzymes in the fourth patient.

**Adverse Clinical Events:** Based on patients from the North American trials (n=1063), the events with the highest incidence in patients, irrespective of relationship to ZOSYN therapy, were diarrhea (11.3%); headache (7.7%); constipation (7.7%); nausea (6.9%); insomnia (6.8%); rash (4.2%), including maculopapular, bullous, urticarial, and eczematoid; vomiting (3.3%); dyspepsia (3.3%); pruritus (3.1%); stool changes (2.4%); fever (2.4%); agitation (2.1%); pain (1.7%); moniliasis (1.6%); hypertension (1.6%); dizziness (1.4%); abdominal pain (1.3%); chest pain (1.3%); edema (1.2%); anxiety (1.2%); rhinitis (1.2%); and dyspnea (1.1%). Based on patients in the completed study of nosocomial lower respiratory tract infections (n=155), using every-4-hour dosing and aminoglycoside therapy, the events with the highest incidence in patients, irrespective of relationship to ZOSYN and aminoglycoside therapy, were diarrhea (20%); constipation (8.4%); agitation (7.1%); nausea (5.8%); headache (4.5%); insomnia (4.3%); oral thrush (3.9%); erythematous rash (3.9%); anxiety (3.2%); fever (3.2%); pain (3.2%); pruritus (3.2%); hiccough (2.6%); vomiting (2.6%); dyspepsia (1.9%); edema (1.9%); fluid overload (1.9%); stool changes (1.9%); anorexia (1.3%); cardiac arrest (1.3%); confusion (1.3%); diaphoresis (1.3%); duodenal ulcer (1.3%); flatulence (1.3%); hypertension (1.3%); hypotension (1.3%); inflammation at injection site (1.3%); pleural effusion (1.3%); pneumothorax (1.3%); rash, not otherwise specified (1.3%); supraventricular tachycardia (1.3%); thrombophlebitis (1.3%); and urinary incontinence (1.3%).

Additional adverse systemic clinical events reported in 1.0% or less of the patients in the initial North American trials and/or in the patients administered ZOSYN 3.375 g every 4 hours plus an aminoglycoside in the nosocomial lower respiratory tract study are listed below within each body system (bracketed events occurred only in the nosocomial pneumonia trial): *Autonomic nervous system:* hypotension, ileus, syncope. *Body as a whole:* rigors, back pain, malaise, [asthenia, chest pain]. *Cardiovascular:* tachycardia, including supraventricular and ventricular; bradycardia; arrhythmia, including atrial fibrillation, ventricular fibrillation, cardiac arrest, cardiac failure, circulatory failure, myocardial infarction, [angina]. *Central nervous system:* tremor, convulsions, vertigo, [aggressive reaction (combative)]. *Gastrointestinal:* melena, flatulence, hemorrhage, gastritis, hiccough, ulcerative stomatitis, [fecal incontinence, gastric ulcer, pancreatitis]. Pseudomembranous colitis was reported in one patient during the clinical trials. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment. (See **WARNINGS**.) *Hearing and vestibular system:* tinnitus, [deafness, earache]. *Hypersensitivity:* anaphylaxis. *Metabolic and Nutritional:* symptomatic hypoglycemia, thirst, [gout, vitamin B<sub>12</sub> deficiency anemia]. *Musculoskeletal:* myalgia, arthralgia. *Platelets, Bleeding, Clotting:* mesenteric embolism, purpura, epistaxis, pulmonary embolism, [ecchymosis, hemoptysis]. (See **PRECAUTIONS—General**.) *Psychiatric:* confusion, hallucination, depression. *Reproductive, Female:* leukorrhea, vaginitis, [perineal irritation/pain]. *Reproductive, Male:* [balanoposthitis]. *Respiratory:* pharyngitis, pulmonary edema, bronchospasm, coughing, [atelectasis, dyspnea, hypoxia]. *Skin and Appendages:* genital pruritus, diaphoresis, [conjunctivitis, xerosis]. *Special senses:* taste perversion. *Urinary:* retention, dysuria, oliguria, hematuria, incontinence, [urinary tract infection with trichomonas, yeast in urine]. *Vision:* photophobia. *Vascular (extracardiac):* flushing, [cerebrovascular accident].

Additional adverse events reported from worldwide marketing experience with ZOSYN, where causal relationship to ZOSYN is uncertain: *Gastrointestinal:* hepatitis, cholestatic jaundice. *Hematologic:* hemolytic anemia, anemia, thrombocytosis, agranulocytosis, pancytopenia. *Immune:* hypersensitivity reactions, anaphylactic/anaphylactoid reactions (including shock). *Infections and Infestations:* candida superinfections. *Renal:* rarely, interstitial nephritis, renal failure. *Skin and Appendages:* erythema multiforme and Stevens-Johnson syndrome, rarely reported; toxic epidermal necrolysis.

**Adverse Laboratory Events (Seen During Clinical Trials):** Of the studies reported, including that of nosocomial lower respiratory tract infections in which a higher dose of ZOSYN was used in combination with an aminoglycoside, changes in laboratory parameters, without regard to drug relationship, include: *Hematologic:* decreases in hemoglobin and hematocrit, thrombocytopenia, increases in platelet count, eosinophilia, leukopenia, neutropenia. The leukopenia/neutropenia appears to be reversible and most frequently associated with prolonged administration, ie,  $\geq 21$  days of therapy. These patients were withdrawn from therapy; some had accompanying systemic symptoms (eg, fever, rigors, chills). *Coagulation:* positive direct Coombs' test, prolonged prothrombin time, prolonged partial thromboplastin time. *Hepatic:* transient elevations of AST (SGOT), ALT (SGPT), alkaline phosphatase, bilirubin. *Renal:* increases in serum creatinine, blood urea nitrogen. *Urinalysis:* proteinuria, hematuria, pyuria. Additional laboratory events include abnormalities in electrolytes (ie, increases and decreases in sodium, potassium, and calcium), hyperglycemia, decreases in total protein or albumin, blood glucose decreased, gamma-glutamyltransferase increased, hypokalemia, and bleeding time prolonged. The following adverse reaction has also been reported for PIPRACIL<sup>®</sup> (sterile piperacillin sodium): *Skeletal:* prolonged muscle relaxation. (See **PRECAUTIONS—Drug Interactions**.)

Piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

**OVERDOSAGE** There have been post-marketing reports of overdose with piperacillin/tazobactam. The majority of those events experienced including nausea, vomiting, and diarrhea have also been reported with the usual recommended dosages. Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure). Treatment should be supportive and symptomatic according to the patient's clinical presentation. Excessive serum concentrations of either piperacillin or tazobactam may be reduced by hemodialysis. (See Full Prescribing Information—**CLINICAL PHARMACOLOGY**.)

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