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Guidelines for Prehospital Management of Traumatic Brain Injury 2nd Edition

CONTENTS

- S1 DISCLAIMER OF LIABILITY
S2 INTRODUCTION
S5 METHODS
ASSESSMENT
S8 I. Assessment: Oxygenation and Blood Pressure
S14 II. Assessment: Glasgow Coma Scale Score
S20 III. Assessment: Pupil Examination
TREATMENT
S23 IV. Treatment: Airway, Ventilation, and Oxygenation
S32 V. Treatment: Fluid Resuscitation
S37 VI. Treatment: Cerebral Herniation
DECISION MAKING
S42 VII. Decision Making Within the EMS System: Dispatch, Scene, Transportation, and Destination
APPENDICES
S48 Appendix A: Changes in Quality Ratings of Publications from the 1st Edition to the 2nd Edition
S49 Appendix B: Electronic Literature Searches
S51 Appendix C: Mixed Patient Samples
S52 Appendix D: Literature Search Yield

DISCLAIMER OF LIABILITY

The information contained in these Guidelines, which reflects the current state of knowledge at the time of completion of the literature search (July 2006), is intended to provide accurate and authoritative information about the subject matter covered. Because there will be future developments in scientific information and technology, it is anticipated that there will be periodic review and updating of these Guidelines. These Guidelines are distributed with the understanding that the Brain Trauma Foundation, the National Highway Traffic Safety Administration, and the other organiza-

tions that have collaborated in the development of these Guidelines are not engaged in rendering professional medical services. If medical advice or assistance is required, the services of a competent physician should be sought. The recommendations contained in these Guidelines may not be appropriate for use in all circumstances. The decision to adopt a particular recommendation contained in these Guidelines must be based on the judgment of medical personnel, who take into consideration the facts and circumstances in each case, and on the available resources.

INTRODUCTION

Worldwide, traumatic brain injury (TBI) is a leading cause of death and permanent disability. In the United States, there are approximately 1.4 million reported cases of TBI each year. The real incidence is difficult to determine, however, since many patients never seek medical care or go to an emergency department.⁷ Of the reported cases, roughly 50,000 patients die and 235,000 are hospitalized.^{6,7} Age categories most affected are patients less than 5 years of age, those between 15–24 years, and those over 70 years of age. TBI results in lifelong disabilities for more than 30,000 children each year.⁸ The mortality rate from blunt trauma without TBI is 1%; when TBI is involved, the mortality rate from severe blunt trauma is 30%.⁹

Half of those who die from TBI do so within the first 2 hours of injury. It is now known, however, that all neurological damage does not occur at the moment of impact (primary injury), but rather evolves over the ensuing minutes, hours, and days. This secondary brain injury can result in increased mortality and disability. Consequently, the early and appropriate management of TBI is critical to the survival of these patients.

Emergency Medical Services (EMS) personnel are often the first healthcare providers for patients with TBI. Thus, prehospital assessment and treatment is a critical link in providing appropriate care.¹ Treatment begins in the field and continues during transport by EMS providers who have varied skills, backgrounds, and qualifications. Over the past 30 years EMS has become progressively sophisticated, resulting in improved outcomes, particularly in cardiovascular¹⁰ and traumatic resuscitations. However, many challenges remain, especially in recognition and management of TBI in the prehospital setting.

Emergency medical care in the field is provided by a wide variety of personnel in the United States.¹⁷ The First Responder and EMT-Basic provide patient assessment and noninvasive intervention. However, a growing trend to offer additional training to the EMT-Basic now permits some of them to perform some invasive procedures, such as intravenous (I.V.) line placement and advanced airway interventions. EMT-Intermediate training includes invasive interventions, such as I.V. line placement, endotracheal intubation, and the administration of a limited list of resuscitation drugs. The EMT-Paramedic, who has the highest level of EMT

training, is allowed to perform advanced patient assessment as well as endotracheal intubation, ECG recognition, I.V. line placement, needle thoracostomy, and the administration of a comprehensive list of medications. In many countries, physicians in ambulances or helicopters respond to the call and care for the patient in the prehospital setting.¹⁰

This is the second edition of the evidence-based Guidelines for the Prehospital Management of Severe Traumatic Brain Injury, following the first edition in 2000. These Guidelines address key topics useful in the prehospital management of severe TBI. The following are notable changes from the first edition:

- In previous guidelines documents, Recommendations were assigned Levels (Standards, Guidelines, Options) based upon the degree of scientific confidence derived from the literature base (Strong, Moderate, and Weak, respectively). In this edition of the Prehospital Guidelines, recommendations are made without assigning Levels. However, at the end of each recommendation, the *Strength of the Recommendation* and the *Quality of Evidence* upon which the recommendation is made are clearly stated (refer to the Methods Section for a detailed description).
- The classifications of the quality of certain publications included in the previous edition have been changed. Publications are classified both by design and quality (see Methods section and Appendix A).
- All chapters are now presented in a new, uniform format. Each chapter was organized into the following chronological sections: Recommendations, Evidence Tables, Overview, Process, Scientific Foundations, Key Issues for Future Investigation, and References.
- A new 'Treatment: Cerebral Herniation' chapter was added in order to emphasize the unique considerations in the treatment of these patients.
- Discussion regarding the utilization of sedation, rapid sequence intubation, and lidocaine was moved to the 'Treatment: Airway, Ventilation, and Oxygenation' chapter.
- The topic of Brain Targeted Therapy was eliminated. The content was distributed across topics on Cerebral Herniation, Fluid Resuscitation, and Airway/Ventilation/Oxygenation.

- A new chapter, Decision Making Within the EMS System, is included and expands upon the "Hospital Transport Decisions" chapter from the previous edition. It addresses dispatch, level of care, transportation mode, and destination.
- Pediatric literature was added as a separate section for each topic.
- Publications cited in the text, but do not provide evidence for a recommendation, do not appear in the Evidence Tables.

Prevention: Although the treatment of TBI has improved considerably, it is clear that prevention must be a priority. EMS systems and providers are increasingly viewed as essential participants in injury prevention activities. EMS providers operate at the interface of public health, public safety, and individual patient care³ and interact daily with the public in a unique manner, as they are given entrée into homes, schools, and offices, affording opportunities to assess risk, capitalize on "teachable moments," collect data, provide community education, and function as advocates.^{12,21}

The National Highway Traffic Safety Administration (NHTSA) has identified injury prevention as an essential component for EMS education in its "EMS Education Agenda for the Future,"²⁰ and education in injury prevention is a part of the National Standard Curriculum (NSC) for paramedics.¹⁹ Combined with known successful prevention programs, such as helmet use,^{4,11,13,14} the nation's 800,000 prehospital providers¹⁸ have the possibility for profound impact in the realm of injury prevention.

To this end, many EMS systems have developed programs focused on injury prevention within their communities. These programs have targeted a variety of issues, including the proper use of child safety seats, fall prevention, and home safety inspections.⁵ However, to date there is limited evidence that specific injury prevention efforts undertaken by prehospital providers, including primary prevention programs, reduce the morbidity and mortality of specific injuries, including TBI.^{15,16} Therefore, the impact of the role of EMS provider and system injury prevention programs with respect to TBI cannot be determined by the available evidence. Thus, evidence-based guidelines for EMS injury prevention initiatives cannot be offered in this manuscript.

As it continues to expand, the field of EMS must continue to pursue the rigorous validation of specific interventions provided in the prehospital environment, including those that focus on injury prevention initiatives provided by EMS personnel. In the interim, EMS providers must continue to support the implementation of successful and validated individual and community based prevention efforts in the prehospital environment.

Though scientific evidence is insufficient to support a standard of care for many clinical practice parameters, this text has assembled the current scientific literature into a cohesive and comprehensive format in a manner that reflects the best evidence available to us. It is hoped that EMS personnel will find this information useful, and in turn, will use it for the benefit of patients with TBI.

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METHODS

I. TOPIC REFINEMENT

The Brain Trauma Foundation (BTF) and BTF Center for Guidelines Management (Center) convened a virtual meeting of previous participants in the development of guidelines for prehospital management of traumatic brain injury (TBI), as well as with colleagues new to the project. They specified topics for inclusion in the current update, and agreed to include pediatric literature as a separate section for each topic. Further refinement of topics and scope was accomplished in a subsequent work meeting of participants with BTF and Center staff. The group agreed to maintain the distinction between *Assessment* topics and *Treatment* topics, as follows:

| | |
|-------------------|--|
| <i>Assessment</i> | Oxygenation and Blood Pressure Glasgow Coma Scale Score Pupil Examination |
| <i>Treatment</i> | Airway/Ventilation/Oxygenation Fluid Resuscitation Cerebral Herniation Systems of Trauma Care and Hospital Transport Decisions |

The group further agreed to eliminate the topic of Brain Targeted Therapy, and distribute the content as follows:

Cerebral Herniation: This is a new chapter to include hyperventilation, mannitol, and hyperosmolar therapy.

Fluid Resuscitation: Hyperosmolar and non-hyperosmolar therapies are addressed in this chapter.

Airway/Ventilation/Oxygenation: Sedation is addressed in this chapter.

A preliminary search revealed an insufficient literature base to support a Prevention topic. Thus the group agreed to summarize the descriptive findings and discuss future research for Prevention in the Introduction section of the Guidelines.

Four participants were assigned to work on each topic – two for the adult section and two for the pediatric section. Participants finalized the scope of each topic and provided terms for the electronic literature search.

II. INCLUSION/EXCLUSION CRITERIA

Inclusion Criteria

- human subjects
- traumatic brain injury
- English language
- ≥ 25 subjects
- Randomized controlled trials (RCTs), cohort studies, case-control studies, case series, databases, registries

Exclusion Criteria

- sample contained >15% of pediatric patients, or >15% of patients with pathologies other than TBI AND the data were not reported separately (see Appendix C)
- wrong independent variable (e.g., the intervention was not specific to the topic)
- wrong dependent variable (e.g., outcomes were not mortality or morbidity, or did not associate with clinical outcomes)
- statistics used in the analysis were not appropriate to the research design, variables, and/or sample size
- case studies, editorials, comments, letters

III. LITERATURE SEARCH AND RETRIEVAL

Center staff worked with a doctoral-level research librarian to construct electronic search strategies for each topic from 1996 through April to August of 2005 (see Appendix B). They used strategies with the highest likelihood of capturing most of the targeted literature, which resulted in the acquisition of a large proportion of non-relevant citations. A set of abstracts was sent to the participants for each topic. Blinded to each others' work, they read the abstracts and eliminated citations using the criteria specified above.

Center staff compared the participants' selections, identified discrepancies, and worked with authors to resolve them. A set of full-text publications was sent to each participant. They read the publications and determined the final library of studies that would be used as evidence. Results of the electronic searches were supplemented by recommendations of peers and by reading reference lists of included studies.

A second search was conducted from 2005 through July of 2006 to capture any relevant Class I or II literature that might have been published since the first literature search in 2005. Relevant publications were added to those from the original search, constituting the final library of studies that were used as evidence in this document. The yield of literature from each phase of the search is presented in Appendix D.

IV. DATA ABSTRACTION AND SYNTHESIS

Remaining blinded to each other's work, participants read each publication and abstracted data using a predetermined format. They drafted chapters and the entire team gathered for a 2-day work session to discuss the literature base, and to achieve consensus on classification of quality of evidence, and strength of recommendations.

After the work meeting, participants revised each topic based on the group's recommendations. Virtual meetings were convened, during which a subset of approximately five members of the team edited each topic online. Final versions were circulated to the Review Committee. Critiques from the Review Committee were addressed by participants and incorporated, or not, based upon their accuracy and consistency with the pre-specified systematic process.

V. QUALITY ASSESSMENT AND CLASSIFICATION OF EVIDENCE

Different criteria are used to evaluate the quality of the evidence in assessment topics vs. treatment topics. Quality criteria for assessment topics are in Table 1, and those for treatment topics are in Table 2. These are based on criteria developed by the U.S. Preventive Services Task Force¹ the National Health Service Centre for Reviews and Dissemination (U.K.),² and the Cochrane Collaboration.³

Publications contained in the evidence tables was assessed by two epidemiologists who were blinded to each other's work as well as to the identification of the studies, authors, and journals They applied the criteria in Tables 1 and 2 to each study to provide the quality assessment and derive the classification of level of evidence.

VI. RECOMMENDATIONS

At the end of each recommendation section in this document, the recommendations are categorized in terms of *Strength* and *Quality of Evidence*. The strength of the recommendation is derived from the overall quality of the body of evidence used to assess the topic.

Strength of Recommendations

Consistent with methods generated by the Grades of Recommendation, Assessment, Development, and

TABLE 1. Quality assessment of diagnostic studies

| Criteria: | |
|--|---|
| • | Screening test relevant, available, adequately described |
| • | Study uses credible reference standard, performed regardless of test results |
| • | Reference standard interpreted independently of screening test |
| • | Handles indeterminate results in a reasonable manner |
| • | Spectrum of patients included in the study |
| • | Adequate sample size |
| • | Administration of reliable screening test |
| Class of evidence based on above criteria: | |
| Class I | Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease. |
| Class II | Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and with a "medium" spectrum of patients. A study may be Class II with fewer than 50 patients if it meets all of the other criteria for Class II. |
| Class III | Has fatal flaw such as: uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size of very narrow selected spectrum of patients. |

Evaluation (GRADE) working group, recommendations in this document are categorized as either *strong* or *weak*. As stated in the American Thoracic Society's official statement, in which they endorsed the GRADE methods for their guidelines endeavors, "The strength of a recommendation reflects the degree of confidence that the desirable effects of adherence to a recommendation outweigh the undesirable effects."⁴

Strong recommendations are derived from high quality evidence that provide precise estimates of the benefits or downsides of the topic being assessed. With weak recommendations, (1) there is lack of confidence that the benefits outweigh the downsides, (2) the benefits and downsides may be equal, and/or (3) there is uncertainty about the degree of benefits and downsides.

Quality of Body of Evidence

The underlying methods for assessing and classifying the quality of evidence of individual studies are represented in Tables 1 and 2. However, ultimately the individual studies must be considered in aggregate, whether through meta-analyses or through qualitative assessment. Thus, the strength of recommendations must be derived from the quality of the overall body of evidence used to address the topic.

The quality of the overall body of evidence for each recommendation in this document is classified as *high*, *moderate*, or *low*. Factors that may decrease the quality include potential bias, differing findings across studies,

TABLE 2. Quality assessment of treatment studies

| Class of Evidence | Study Design | Quality Criteria |
|-------------------|--|--|
| I | Good quality randomized controlled trial (RCT) | Adequate random assignment method. Allocation concealment. Groups similar at baseline. Outcome assessors blinded. Adequate sample size. Intention-to-treat analysis. Follow-up rate >85%. Differential loss to follow-up. Maintenance of comparable groups. |
| II | Moderate quality RCT | Violation of one or more of the criteria for a good quality RCT. ¹ |
| II | Good quality cohort | Blind or independent assessment in a prospective study, or use of reliable ² data in a retrospective study. Comparison of two or more groups must be clearly distinguished. Non-biased selection. Follow-up rate ≥85%. Adequate sample size. Statistical analysis of potential confounders. ³ |
| II | Good quality case-control | Accurate ascertainment of cases. Nonbiased selection of cases/controls with exclusion criteria applied equally to both. Adequate response rate. Appropriate attention to potential confounding variables. |
| III | Poor quality RCT | Major violations of the criteria for a good or moderate quality RCT. ¹ |
| III | Moderate or poor quality cohort | Violation of one or more criteria for a good quality cohort. ¹ |
| III | Moderate or poor quality case-control | Violation of one or more criteria for a good quality case-control. ¹ |
| III | Case Series, Databases or Registries | Prospectively collected data that is purely observational, and retrospectively collected data. |

¹ Assessor needs to make a judgment about whether one or more violations are sufficient to downgrade Class of study, based upon the topic, the seriousness of the violation(s), their potential impact on the results, and other aspects of the study. Two or three violations do not necessarily constitute a major flaw. The assessor needs to make a coherent argument why the violation(s) either do, or do not, warrant a downgrade.

² Reliable data are concrete data such as mortality or re-operation.

³ Publication authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

the use of indirect evidence, or lack of precision. For example, if two or more Class I studies demonstrate contradictory findings for a particular topic, the overall quality most probably will be low because there is uncertainty about the effect. Similarly, Class I or II studies that provide indirect evidence may only constitute low quality evidence, overall.

Indirect Evidence

Well controlled studies conducted in the field are rare. One alternative is to apply evidence from studies conducted in other environments to field practice, or from other pathologies to TBI. In this document, indirect evidence from inhospital populations or from physiological studies was used, after careful consideration of the quality of the study for its own population, and then of its usefulness as indirect evidence. We used the following sequential process of questions:

1. To what extent does the physiology of the field application approximate the physiology of the in-hospital application?
2. What are the differences in patients, settings, treatments, and measurements between the field and in-hospital settings?

3. To what extent would those differences influence the physiology of the intervention?
4. To what extent and in what direction would those differences influence the observed effect?
5. What is the quality of the publication?
6. Consider all of the above (1) to determine if the publication can be used as indirect evidence, and if so, (2) to determine the quality of the evidence.

In this document, indirect evidence used to support a recommendation is identified as such.

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ASSESSMENT

I. ASSESSMENT: OXYGENATION AND BLOOD PRESSURE

I. RECOMMENDATIONS

Strength of Recommendations: Weak.
Quality of Evidence: Low, primarily from Class III studies and indirect evidence.

Adult

- A. Patients with suspected severe traumatic brain injury (TBI) should be monitored in the pre-hospital setting for hypoxemia (<90% arterial hemoglobin oxygen saturation) or hypotension (<90 mmHg systolic blood pressure [SBP]).
- B. Percentage of blood oxygen saturation should be measured continuously in the field with a pulse oximeter.
- C. Systolic (SBP) and diastolic blood pressure (DBP) should be measured using the most accurate method available under the circumstances.
- D. Oxygenation and blood pressure should be measured as often as possible, and should be monitored continuously if possible.

Pediatrics

- A. Pediatric patients with suspected severe TBI should be monitored in the prehospital setting for hypotension. Pediatric hypotension is defined as follows:

| | |
|--------------|------------------------|
| Age | SBP |
| 0 to 28 days | <60 mmHg |
| 1–12 months | <70 mmHg |
| 1–10 years | <70 + 2 × age in years |
| >10 years | < 90 mmHg |
- B. Percentage of blood oxygen saturation should be measured continuously in the field with a pulse oximeter using an appropriate pediatric sensor.
- C. SBP and DBP should be measured using an appropriately-sized pediatric cuff. When a blood pressure is difficult to obtain because of the child's age or body habitus, documentation of mental status, quality of peripheral pulses, and capillary refill time can be used as surrogate measures.
- D. Oxygenation and blood pressure should be measured as often as possible, and should be monitored continuously if possible.

II. EVIDENCE TABLES

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|---|--|------------|---|
| Chesnut <i>et al.</i> , 1993 ² | A prospective study of 717 severe TBI patients admitted consecutively to four centers investigated the effect on outcome of hypotension (systolic blood pressure (SBP) <90 mmHg) occurring from injury through resuscitation. | III | Hypotension was a statistically independent predictor of outcome. A single episode of hypotension during this period was associated with doubled mortality and also increased morbidity. Patients whose hypotension was not corrected in the field had a worse outcome than those whose hypotension was corrected by time of emergency department arrival. |
| Fearnside <i>et al.</i> , 1993 ⁶ | A prospective study of 315 severe TBI patients admitted consecutively to a single-center investigated prehospital and in-hospital predictors of outcome. | III | Hypotension (SBP < 90 mmHg) occurring at any time during a patient's course independently predicted worse outcome. |
| Gentleman, 1992 ⁸ | A retrospective study of 600 severe head injury patients in three cohorts evaluated regarding the influence of hypotension on outcome and the effect of improved prehospital care in decreasing its incidence and negative impact. | III | Improving prehospital management decreased the incidence of hypotension but its impact on outcome in patients suffering hypotensive insults maintained as a statistically significant, independent predictor of poor outcome. Management strategies that prevent or minimize hypotension in the prehospital phase improves outcome from severe head injury. |

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|---|---|------------|--|
| Hill <i>et al.</i> , 1993 ⁹ | Retrospective study of the prehospital and emergency department resuscitative management of 40 consecutive multitrauma patients. Hypotension (SBP \leq 80 mmHg) correlated strongly with fatal outcomes. Hemorrhagic hypovolemia was the major etiology of hypotension. | III | Improving the management of hypovolemic hypotension is a major potential mechanism for improving the outcome from severe head injury. |
| Marmarou <i>et al.</i> , 1991 ¹³ | From a prospectively collected database of 1030 severe head injury patients, all 428 patients who met intensive care unit monitoring criteria were analyzed for monitoring parameters that determined outcome and their threshold values. The two most critical values were the proportion of hourly intracranial pressure (ICP) readings greater than 20 mmHg and the proportion of hourly SBP readings less than 80 mmHg. | III | The incidence of morbidity and mortality resulting from severe head injury is strongly related to ICP and hypotension measured during the course of ICP management. |
| Stocchetti <i>et al.</i> , 1996 ²¹ | A prospective study of data collected at the accident scene from 50 severe TBI patients rescued by helicopter. SBP was classified as <60 mmHg, 60–80 mmHg, 81–99 mmHg, or >99 mmHg. Arterial oxygen saturation measured via pulse oximeter was classified as <60%, 60–80%, 81–90%, or >90%. | III | Low prehospital blood pressures or oxygen saturations were associated with worse outcomes. Arterial oxygen saturation of 80% or lower was associated with a 47% mortality compared with 15% mortality when oxygen saturation was greater than 80%. |
| Vassar <i>et al.</i> , 1993 ²³ | Prospective, randomized, controlled, multicenter trial comparing the efficacy of administering 250 mL of hypertonic saline vs. normal saline as the initial resuscitation fluid in facilitating the resuscitation and improving the outcome of hypotensive trauma patients. | II | <i>Post hoc</i> analysis of the severe TBI group revealed that the hypertonic saline group had a statistically significant improvement in survival to discharge. Raising the blood pressure in hypotensive severe TBI patients improves outcome in proportion to the efficacy of the resuscitation. |
| New Studies | | | |
| Davis <i>et al.</i> , 2004 ³ | Prospective observational study of 59 patients with suspected TBI who underwent paramedic RSI in the field and continuous oxygen saturation and ETCO ₂ monitoring. | III | Patients with pO ₂ < 70% and with ETCO ₂ < 27mmHg had significantly increased risk of death. |
| Dunford <i>et al.</i> , 2003 ⁴ | Prospective observational study of 54 patients with suspected TBI who underwent RSI with continuous oxygen saturation and pulse rate monitoring in the field. | III | 57% of patients had oxygen desaturation. Pulse rate decreases occurred in 61% of patients with desaturation and profound bradycardia in 19%. |
| Garner <i>et al.</i> , 2001 ¹⁷ | Retrospective review of 296 patients with severe TBI treated by paramedics or critical care transport teams in Australia. | III | There was a 16.2% incidence of hypotension upon first contact in the field. |
| Ochs <i>et al.</i> , 2002 ¹⁷ | Prospective observational study of 114 patients with TBI who underwent RSI by paramedics. Endpoints were successful intubation, measurement of oxygen saturation and CO ₂ levels on arrival to ED | III | Hypotension was encountered in 18.7% of patients upon first contact. Endotracheal intubation was accomplished successfully in 84%, Combitube rescue was performed in 15% and intubation failure occurred in one patient. |

EVIDENCE TABLE 2. Pediatrics

| Reference | Study Description | Data Class | Conclusion |
|---|---|------------|---|
| Kokoska <i>et al.</i> , 1998 ¹² | Retrospective review of 72 pediatric patients (age 3 mos–14 yrs) to evaluate hypotensive episodes and outcome. Hypotensive episode was defined as a blood pressure reading of less than the fifth percentile for age that lasted longer than 5 minutes. | III | Prehospital, ED and ICU hypotensive episodes were significantly associated with poor outcome. |
| Pigula <i>et al.</i> , 1993 ¹⁹ | 58 pediatric patients (<17 years old) with severe TBI were prospectively studied for the effect of hypotension (SBP <90 mmHg) on outcome. | III | An episode of hypotension decreased survival fourfold. |
| New Study | | | |
| Vavilala <i>et al.</i> , 2003 ²² | A retrospective review of the trauma registry for children under 14 years of age, isolated head injury (Abbreviated Injury Severity Scale < 2), and a GCS < 9. Demographics, assessment data, and risk factors were collected from the ED records (GCS, SBP, CT, coagulopathy). | III | Among children with SBP below the 75th percentile for age, 63% had poor outcome and 29% died. By comparison children with SBP > 75th percentile for age, 29% had poor outcome and 10% died. A systolic blood pressure less than the 75th percentile for age is associated with poor outcome and higher mortality rate. |

III. OVERVIEW

In severe TBI, secondary insults occur frequently and exert a profound negative influence on outcome. This influence appears to differ markedly from that of hypoxemic or hypotensive episodes of similar magnitude occurring in trauma patients who do not have neurologic involvement. Therefore, it is important to determine if evidence exists to support prehospital threshold values for oxygenation and blood pressure.

IV. PROCESS

For this update, Medline was searched from 1996 through July 2006 using the search strategy for this question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 28 potentially relevant publications, 4 were added to the existing table and used as evidence for this question. For pediatric studies, of 53 potentially relevant publications, one new study was included as evidence (see Evidence Tables).

V. SCIENTIFIC FOUNDATION

Adult

- A. Patients with suspected severe traumatic brain injury (TBI) should be monitored in the prehospital setting for hypoxemia (< 90% arterial hemoglobin oxygen saturation) or hypotension (<90 mmHg systolic blood pressure [SBP]).
- B. Percentage of blood oxygen saturation should be measured continuously in the field with a pulse oximeter.
- C. Systolic (SBP) and diastolic blood pressure (DBP) should be measured using the most accurate method available under the circumstances.
- D. Oxygenation and blood pressure should be measured as often as possible, and should be monitored continuously if possible.

Foundation. The deleterious influence of hypotension and hypoxemia on the outcome of patients with severe TBI was analyzed from a large (717 patients), prospectively collected dataset from the Traumatic Coma Data Bank (TCDB).^{2,13} The TCDB study demonstrated that prehospital hypotension (defined as a single observation of <90 mmHg SBP) and hypoxemia (defined as apnea, cyanosis, or a hemoglobin oxygen saturation <90% in the field or as a PaO₂ <60 mmHg by arterial blood gas analysis) were among the five most powerful predictors of outcome. These clinical findings were statistically independent of other major predictors, such as age, admission Glasgow Coma Scale (GCS) score, admission GCS motor score, intracranial diagnosis, and pupillary status. A single episode of hypotension was associated with a doubling of mortal-

ity and an increased morbidity when compared with a matched group of patients without hypotension. The TCDB study defined hypotension and hypoxemia as a single reported incident that met the definition of each and did not require a protracted duration for secondary insult.

A smaller Class III study from Australia corroborated the above findings; particularly with respect to the effects of hypotension on outcome.⁶ The clinical predictors of mortality derived from this study were identical. In both studies, the two predictors with the potential for being altered through clinical manipulations are hypotension and hypoxemia. These data are similar to those in other retrospectively analyzed in-hospital reports in adults.^{8-11,14-16,18,20,25}

The incidence of hypotension in patients with TBI upon first contact in the field was reported in a recent study from Australia to be 16% (48/296).⁷ Similarly, in a report from San Diego, initial hypotension (systolic BP <90 mm HG) was encountered in 19% of patients.¹⁷

A study from Italy²¹ of 50 patients with TBI transported by helicopter revealed that 55% had an oxygen saturation < 90% measured at the scene prior to intubation. Both hypoxemia and hypotension had significant negative impacts on outcome. Of the 28 patients who were hypoxemic, 13 did not have associated hypotension. There was a significant association between arterial desaturation and poor outcome ($p < 0.005$):

| Oxygen Saturation | Mortality | Severe Disability |
|-------------------|------------|-------------------|
| >90% | 14% (3/21) | 5% (1/21) |
| 60-90% | 27% (6/22) | 27% (6/22) |
| <60% | 50% (3/6) | 50% (3/6) |

The importance of frequent or continuous monitoring of oxygen saturation was recently documented in a study from San Diego of patients with suspected TBI who were undergoing rapid sequence intubation (RSI) in the pre-hospital setting.³ Each of the 59 study patients was matched to three historical non-intubated control patients. During the second half of the study, patients were monitored with a device which continuously recorded oxygen saturation (as well as end-tidal CO₂ [ETCO₂]) at 8 second intervals, thus allowing investigators to document the occurrence, timing, and duration of hypoxic episodes. Compared to historical controls, after controlling for other confounding factors, the authors reported that profound oxygen desaturations (SpO₂ <70%) during intubation and any oxygen desaturation (SpO₂ <90%) were associated with higher mortality (O.R. 3.89, 95% C.I. 1.12-13.52 and 3.86, 95% C.I. 1.18-12.61 respectively). Subgroup analysis from this study revealed that 31/54 (57%) patients had transient hypoxemia during the RSI attempt.⁴ In addition, the desaturation period lasted approximately 2.33 minutes.

Related Discussion. In-hospital studies provide important data that may be extrapolated to and representative of issues found in the prehospital setting. In a study of 107 patients with moderate or severe TBI (GCS < 13), the authors attempted to evaluate the effect of hypotension and hypoxia on the functional neurologic outcome of these patients by specifically quantifying the degree and duration of the secondary insult.¹ Any occurrence of hypotension was associated with an increased risk of 30 day in-hospital mortality (O.R. 3.39) and based upon the quantification analysis, moderate- and high-dose of hypotension were associated with progressively greater death rates (O.R. 3.14 and 12.55 respectively) and a strong trend towards poorer functional neurologic outcomes. In this study, there was no effect on patient outcome from hypoxia.

Another study involving a convenience sample of 50 patients with TBI who were undergoing transfer from an initial receiving hospital to a regional neurosurgical referral center revealed that upon arrival at the referral center, 6% of patients were hypoxic (O₂ saturation <95%) and 16% were hypotensive (systolic BP < 90 mmHg for adults and adjusted for age in children).⁵ The authors did not evaluate for effect on patient outcome. This study does demonstrate, however, that even after presumed resuscitation and stabilization, secondary insults are not uncommon and must be always be considered.

The value of 90-mmHg systolic pressure to delineate the threshold for hypotension arose arbitrarily, and is more a statistical than a physiologic parameter. In considering the evidence concerning the influence of cerebral perfusion pressure (CPP) on outcome, it is possible that systolic pressures significantly >90 mmHg would be desirable during the prehospital and resuscitation phase, but no studies have been performed to corroborate this. The importance of mean arterial pressure (MAP), as opposed to systolic pressure, should also be stressed, not only because of its role in calculating [CPP] = [MAP - intracranial pressure (ICP)], but because the lack of a consistent relationship between the systolic and mean pressures makes calculations based on systolic values unreliable. It may be valuable to maintain mean arterial pressures considerably above those represented by systolic pressures of 90 mmHg throughout the patient's course.

No Class I study has directly addressed the efficacy of preventing or correcting early hypotension in the prehospital setting to improve outcome. However, a subgroup of severe TBI patients was subjected to *post hoc* analysis in a randomized, placebo controlled, multicenter trial that compared the efficacy of administering 250 mL of hypertonic saline versus normal saline as the initial resuscitation fluid in hypotensive trauma patients.²³ In that trial, the hypertonic saline group had improved blood pressure re-

sponses, decreased overall fluid requirements, and associated improvements in survival. The investigators retrospectively reviewed the records of the subgroup of patients with severe TBI and found that this group had statistically significant improvement in survival to discharge. Although this was a *post hoc* analysis of Class II data, it suggests that elevating the blood pressure in severe TBI patients with hypotension improves outcome.

Pediatrics

1. Pediatric patients with suspected severe TBI should be monitored in the prehospital setting for hypotension. Pediatric hypotension is defined as follows:

| Age | SBP |
|--------------|-------------------------|
| 0 to 28 days | <60 mmHg |
| 1-12 months | <70 |
| 1-10 years | < 70 + 2 × age in years |
| >10 years | <90 |

2. Percentage of blood oxygen saturation should be measured continuously in the field with a pulse oximeter using an appropriate pediatric sensor.
3. SBP and DBP should be measured using an appropriately sized pediatric cuff. When a blood pressure is difficult to obtain because of the child's age or body habitus, documentation of mental status, quality of peripheral pulses, and capillary refill time can be used as surrogate measures.
4. Oxygenation and blood pressure should be measured as often as possible, and should be monitored continuously if possible.

Foundation. The deleterious influence of hypotension and hypoxemia on the outcome of children with severe TBI is similar to that seen in adults. There are a very limited number of Class III pediatric studies and most were hospital-based data. There is no Class I or II evidence that addresses the value of either prehospital assessment or intervention on the outcome of severe TBI in children.

Pigula and colleagues prospectively evaluated the effect of hypotension (SBP <90 mmHg) and hypoxia (PaO₂ < 60 mmHg) on outcome in 170 patients with a GCS < 8.¹⁹ In the pediatric group age < 17 years they noted that the overall mortality rate in children was better than adults (29% vs. 48%). Children with both hypoxia and hypotension had a higher mortality rate (67%) compared to normotensive children without hypoxia (16%).

Another retrospective study examined the effect of hypotension on outcome of 72 children with a GCS of 6-8.¹² Hypotension was defined hypotension as SBP <5th percentile for age lasting for longer than 5 minutes. Eighty-nine percent of the patients were intubated in

the field and the remaining 11% were intubated in the emergency department. There were 62 hypotensive episodes and 9 patients were hypoxic. The majority of these episodes occurred in the emergency department or intensive care unit. Patients with poor outcome had more hypotensive episodes compared to those with good outcome.

Related Discussion. One retrospective study of ICU patients noted survival improved 19-fold in children age 0–17 years with GCS <8 when the maximum SBP was >135 mmHg.²⁴ Vavilala and colleagues examined the association between age adjusted SBP percentile and outcome after severe TBI. Using the age-adjusted SBP values published by the BTF in 2000 the author reported that a SBP less than the 75th percentile for age was associated with poor outcome.²²

VI. KEY ISSUES FOR FUTURE INVESTIGATION

Clinical trials are needed in the following areas:

1. Do prospective data correlate magnitude and duration of hypotensive and hypoxic episodes to outcome?
2. Is mean arterial pressure a more accurate indicator of hypotension than systolic blood pressure?
3. How accurate are devices that measure systolic, diastolic, and mean blood pressures during transportation?
4. A similar assessment to that outlined in (2) above is needed for arterial oxygen saturation.
5. Prospective studies on the above four points are needed for the pediatric population.

The two major areas needing investigation are (1) the critical values for duration and magnitude of hypotensive and hypoxemic episodes and how they affect neurological outcome, and (2) the optimal resuscitation protocol (fluid type, route of administration, etc.) for resuscitating the patient with severe TBI. The former question is not a subject for a controlled trial for ethical reasons, and therefore is best undertaken using a prospective study with the precise collection of prehospital blood pressure and oxygenation data, which is then correlated with outcome. The latter question can be studied in prospective, randomized investigations, several of which are presently underway.

The pediatric TBI population has needs similar to that of adults. Specifically research in the following areas is needed:

1. The correlation between prehospital SBP and pulse oximeter measurement and outcome.
2. The impact of prehospital intervention on outcome (fluid resuscitation and maintaining airway/ventilation).
3. The reliability of other hemodynamic stability parameters, such as peripheral perfusion, capillary

refill time, mental status, and the quality of peripheral pulses as prehospital surrogates to obtaining blood pressure in young children.

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II. ASSESSMENT: GLASGOW COMA SCALE SCORE

I. RECOMMENDATIONS

Strength of Recommendations: Weak.

Quality of Evidence: Low, primarily from Class III studies and indirect evidence.

Adult

- A. Prehospital measurement of the Glasgow Coma Scale (GCS) is a significant and reliable indicator of the severity of traumatic brain injury (TBI), and should be used repeatedly to identify improvement or deterioration over time.
- B. The GCS must be obtained through interaction with the patient (i.e., by giving verbal directions or, for patients unable to follow commands, by applying a painful stimulus such as nail bed pressure or axillary pinch).
- C. The GCS should be measured after airway, breathing, and circulation are assessed, after a clear airway is established, and after necessary ventilatory or circulatory resuscitation has been performed.
- D. The GCS should be measured preferably prior to administering sedative or paralytic agents, or after these drugs have been metabolized.
- E. The GCS should be measured by prehospital providers who are appropriately trained in how to administer the GCS.

Pediatrics

- A. The GCS and the pediatric GCS (P-GCS, Table 1) are reliable indicators of the severity of TBI in children and should be used repeatedly to identify improvement or deterioration over time.

- B. The adult protocol for standard GCS measurement should be followed in children over 2 years of age. In pre-verbal children, the P-GCS should be employed, with a full verbal score of 5 assigned to infants cooing or babbling.
- C. Prehospital providers should determine the GCS or P-GCS after airway, breathing, and circulation are assessed and stabilized.
- D. The GCS and P-GCS should be measured preferably prior to administering sedative or paralytic agents, or after these drugs have been metabolized.

EVIDENCE TABLE 1. Comparison of Pediatric GCS with GCS

| GCS | | P-GCS | |
|----------------------|---|-------------------------------|---|
| Eye Opening | | Eye Opening | |
| - Spontaneous | 4 | - Spontaneous | 4 |
| - Speech | 3 | - Speech | 3 |
| - Pain | 2 | - Pain | 2 |
| - None | 1 | - None | 1 |
| Verbal response | | Verbal response | |
| - Oriented | 5 | - Coos, Babbles | 5 |
| - Confused | 4 | - Irritable cries | 4 |
| - Inappropriate | 3 | - Cries to pain | 3 |
| - Incomprehensible | 2 | - Moans to pain | 2 |
| - None | 1 | - None | 1 |
| Motor response | | Motor response | |
| - Obey command | 6 | - Normal spontaneous movement | 6 |
| - Localize pain | 5 | - Withdraws to touch | 5 |
| - Flexor withdrawal | 4 | - Withdraws to pain | 4 |
| - Flexor posturing | 3 | - Abnormal flexion | 3 |
| - Extensor posturing | 2 | - Abnormal extension | 2 |
| - None | 1 | - None | 1 |

II. EVIDENCE TABLES

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion | | | | |
|------------------------------|---|------------|------------|------------|--------|-----|-----------|
| Baxt, 1987 ² | Review of 128 patients treated and transported by ground ambulance and 104 patients treated and transported by rotorcraft air ambulance | III | Field GCS | Mortality | | | |
| | | | | | Ground | Air | |
| | | | | 3 | 75% | 68% | |
| | | | | 4 | 60% | 23% | |
| | | | | 5 | 35% | 36% | |
| | | | | 6 | 8% | 13% | |
| Servadei, 1998 ¹⁶ | Prospective study of 65 patients with acute posttraumatic subdural hematoma, comparing the need for surgical evacuation with GCS change from the field to the ED, as well as CT scan findings including size of hematoma and amount of midline shift. | III | GCS | Evacuation | Field | ED | Mortality |
| | | | | Yes | 8.4 | 6.7 | 56% |
| | | | | No | 7.2 | 7.2 | 20% |

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion | | |
|------------------------------|--|------------|---|---------------|----------------|
| Winkler, 1984 ²⁰ | Prospective study of field vs. ED GCS in 33 patients with field GCS <8 and TBI, grouped by outcome (I = no deficit, II = minor deficit, III = major deficit, IV = died) | III | <u>Mean Field GCS</u> | <u>ED GCS</u> | <u>Outcome</u> |
| | | | 4.14 | 9.43 | I |
| | | | 4.67 | 7.33 | II |
| | | | 4.45 | 6.27 | III |
| | | | 4.33 | 5.17 | IV |
| New Studies | | | | | |
| Bazarian, 2003 ³ | Prospective observational study of field versus emergency physician GCS score in convenience sample of 60 patients with TBI. | III | Significant linear relationship between field and ED GCS scores (field providers usually scored patients approximately 2 points lower than emergency physician). | | |
| Horowitz, 2001 ⁸ | Retrospective chart review of 655 patients with transient loss of consciousness and field GCS of 14 or 15, to determine if patients needed direct transport to a trauma center. | III | Overall, 2.9% of patients met the predefined criteria for trauma center treatment. If the need for emergency neurosurgical operation was the only criterion, 0.2% of patients required the trauma center. | | |
| Lane, 2003 ¹⁰ | Prospective study of prehospital providers (EMTs, RNs) to determine the effect of instructional video training on GCS scoring ability using 4 prepared case scenarios. | II | Training in GCS scoring using a video resulted in significantly improved scoring results. | | |
| Winchell, 1997 ¹⁹ | Retrospective registry review of patients with TBI and GCS < 9 to determine the effect of endotracheal intubation on patient outcome with data available for mortality based upon field GCS. | III | Patients with a field GCS score of 3 had an overall mortality of 54.5% and discharge to home rate of 35%. Patients with a GCS of 4-8 had an overall mortality of 13.1% and discharge to home rate of 42%. | | |

EVIDENCE TABLE 2. Pediatrics

| Reference | Study Description | Data Class | Conclusion | | | | |
|------------------------------|---|------------|---|--------------------------|---------------|-------------------|--|
| Massagli, 1996 ¹² | Retrospective review of 33 children admitted to level I trauma center after severe TBI, comparing early and late outcomes to various injury indices. | III | <u>Field GCS</u> | <u>Good Outcome</u> | | | |
| | | | | <u>Early</u> | <u>Late</u> | | |
| | | | 3-5 | 6% | 12% | | |
| | | | 6-15 | 67% | 33% | | |
| New Studies | | | | | | | |
| Holmes, 2005 ⁷ | Prospectively enrolled 2,043 patients age 0-18 years, of whom 327 were under 2 years of age. Pediatric GCS scores were assigned to the younger cohort, with GCS on those over 2 years of age. Outcome measures were TBI on head CT scan, or TBI with need for acute intervention. | II | <u>Pediatric GCS</u> | <u>Standard GCS</u> | | | |
| | | | <u>Age < 2 years</u> | <u>2 years and Older</u> | | | |
| | | | <u>Area Under the Curve and 90% Confidence Interval</u> | | | | |
| | | | Eye opening | 0.66 (0.53,0.79) | | 0.77(0.71,0.82) | |
| | | | Verbal | 0.70 (0.55,0.85) | | 0.77 (0.71,0.82) | |
| | | | Motor | 0.60 (0.48,0.72) | | 0.71 (0.65,0.77) | |
| | | | Total GCS | 0.72 (0.65, 0.87) | | 0.82 (0.76, 0.87) | |
| Johnson, 1997 ⁹ | Retrospective review of 1,320 pediatric patients admitted to Level I trauma center, 127 with moderate injury and 94 severe injury. Of the severe TBI patients, 56 were transported by EMS and 42 by interfacility transport. | III | GCS | EMS | Interfacility | | |
| | | | 3-8 | 26.8% | 1.7% | | |
| | | | 9-12 | 50.0 | 2.3% | | |
| | | | 13-15 | 0% | 0% | | |
| White, 2001 ¹⁸ | Retrospective review of 136 patients in the pediatric ICU. Evaluated admission GCS and 6-hours GCS as predictors of outcome. | III | GCS | Mortality | | | |
| | | | 3 | 75% | | | |
| | | | 4 | 18% | | | |
| | | | 5 | 0% | | | |
| | | | 6 | 6% | | | |

III. OVERVIEW

Teasdale and Jennett¹⁷ developed the GCS in 1974 as an objective measure of the level of consciousness after TBI. It has since become the most widely-used clinical

measure of the severity of TBI. The GCS permits a repetitive and moderately reliable standardized method of reporting and recording ongoing neurologic evaluations even when performed by a variety of health care providers. The GCS evaluates three

independent responses: eye opening, motor response, and verbal response.

Authors stated that for patients unable to follow commands, the motor response is scored on the best-observed response to a standardized stimulus.¹⁷ The stimulus can be blunt pressure applied to the nail bed using a pencil, or a pinch of the patient's anterior axillary skin.

The GCS score, however, can be affected by pre- and post-traumatic factors that may impair neurologic response and that field providers can recognize and treat immediately. Reversible conditions such as hypoglycemia or narcotic overdose should be determined and treated with intravenous glucose or naloxone. Hypoxia and/or hypotension are common complications in trauma patients and have been shown to negatively affect GCS scoring. Therefore, the airway, breathing and circulation should be assessed and stabilized first prior to measuring the GCS or P-GCS.

Another GCS scoring difficulty involves preverbal children. The American College of Emergency Physicians, and the American Academy of Pediatrics in its 1998 publication *APLS—The Pediatric Emergency Medicine Course*,¹ agreed that for children under the age of 2 years, a modified GCS that assigns a full verbal score (5) for crying after stimulation, is appropriate.

A number of studies confirmed a moderate degree of inter- and intra-rater reliability in scoring the GCS, including GCS scores that prehospital Emergency Medical Services providers obtain.^{4,6,13}

IV. PROCESS

For this update Medline was searched from 1996 through July 2006 using the search strategy for this question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 105 potentially relevant publications, 4 were added to the existing table and used as evidence for this question. For pediatric studies, of 42 potentially relevant publications, 3 new studies were used as evidence for this question (see Evidence Tables).

V. SCIENTIFIC FOUNDATION

Adult

- A. Prehospital measurement of the Glasgow Coma Scale (GCS) is a significant and reliable indicator of the severity of traumatic brain injury (TBI), and should be used repeatedly to identify improvement or deterioration over time.

- B. The GCS must be obtained through interaction with the patient (i.e., by giving verbal directions or, for patients unable to follow commands, by applying a painful stimulus such as nail bed pressure or axillary pinch).
- C. The GCS should be measured after airway, breathing, and circulation are assessed, after a clear airway is established, and after necessary ventilatory or circulatory resuscitation has been performed.
- D. The GCS should be measured preferably prior to administering sedative or paralytic agents, or after these drugs have been metabolized.
- E. The GCS should be measured by prehospital providers who are appropriately trained in how to administer the GCS.

Foundation. Baxt² compared advanced prehospital care provided by aeromedical scene responders to ground transport providers using less sophisticated medical interventions. He obtained the mortality rates for GCS scores performed in the field by the flight team. The predictive value for mortality of a GCS of 3 to 5 was 50% and 61% for helicopter and ground transport patients, respectively. The predictive value for a GCS of 6 to 8 was 14.5% and 15.3% respectively. In addition, the predictive value for a bad outcome (dead, vegetative, or severely disabled) for GCS of 3 to 5 was 81.6% and 84% for helicopter and ground transported patients, respectively, and for a GCS of 6 to 8, it was 34.5% and 40.7%, respectively. The study is limited by the fact that the GCS for ground transported patients was not calculated in the field by the paramedics, but rather on arrival in the ED.

A retrospective study designed to evaluate the effect of endotracheal intubation on the outcome of patients with TBI provided overall mortality data stratified by initial field GCS score.¹⁹ Of 351 patients with isolated TBI, patients with a GCS score of 3 had a 54.5% mortality compared to 13.1% for those patients with a GCS score of 4–8. In addition, of those patients with a GCS score of 3, 35% were able to be discharged to home compared to 42% of patients with a GCS score of 4–8.

Horowitz *et al*⁸ performed a retrospective chart review to evaluate whether or not patients with a field GCS score of 14 or 15 and a history of loss of consciousness after trauma required transport to a trauma center, based upon meeting any one of the following criteria: admission to a surgical or neurosurgical ICU, positive CT scan, hospital length of stay greater than 3 days, or need for non-orthopedic emergency surgery within 6 hours of hospital arrival. Of 655 patients included in the study, 19 (2.9%) met the criteria and one patient (0.2%) required emergent neurosurgical intervention. The authors suggested that patients with a brief loss of consciousness who have a GCS score in the field of 14 or 15 do not need transport directly to a trauma center

but rather can be taken to a local facility with appropriate CT scan capabilities, and then undergo transfer to a trauma center if necessary.

Winkler²⁰ evaluated 33 consecutive TBI patients, comparing the field GCS to the GCS score obtained on arrival in the emergency department (ED). Patients were grouped according to their final outcome (no deficits, minor deficits, major deficits, or dead). All four groups had similar GCS scores in the field. However, those who ultimately were discharged with no or minor deficits had significant improvements (> 2 points) in the GCS score at the time of their ED assessment. In contrast, those who had significant deficits or died showed little or no improvement in the GCS score when assessed in the ED.

Servadei¹⁶ used change between the prehospital setting GCS score and the ED score as one criterion to determine the need for operative evacuation of post-traumatic subdural hematomas. For example, a patient whose GCS was unchanged or improved was often a candidate for nonoperative management. On the other hand, if the GCS score deteriorated from the field to the ED, there was a significant likelihood of the need for surgical intervention. Other criteria involved in the decision to operate included the size of the hematoma and the amount of midline shift. Patients treated surgically in this study had an average 2 point decrease in the GCS, whereas those treated expectantly did not change significantly.

Many emergency medical systems often do not record the GCS in TBI patients.¹⁵ This may explain the dearth of prehospital studies on the use of the GCS in the field setting and its correlation to patient outcome. Despite the paucity of prehospital data, the GCS measured in the hospital has been shown to have a significant correlation with patient outcome following severe TBI, either as a sum score or simply the motor component. In a prospective study by Narayan,¹⁴ a positive predictive value of 77% for a poor outcome (dead, vegetative, or severely disabled) was measured for patients with a GCS of 3 to 5 and 26% for those with a GCS of 6 to 8. In a study from Australia,⁵ a significant inverse correlation was found between the initial GCS in the hospital (obtained 6-48 hours after injury) and mortality.

In another series of patients with TBI entered into the U.S. Traumatic Coma Data Bank, mortality rates for patients with initial GCS scores of 3, 4, or 5 were 78.4%, 55.9%, and 40.2%, respectively.¹¹ Of note, however, is that 4.1%, 6.3%, and 12.2% of the three groups, respectively, had good outcome.

The ability of Emergency Medical Care providers to obtain the GCS score reliably was evaluated by Menegazzi¹³ who used videotaped scenarios of patients with severe, moderate, and mild/no alteration of level of consciousness in a classroom setting to compare the inter- and intra-rater GCS scoring reliability of paramedics and emergency physicians. He demon-

strated moderate agreement between physicians and paramedics in measuring the GCS score.

In a similar fashion, Lane *et al*¹⁰ conducted a prospective study of 75 EMS providers of all levels (EMT-B, EMT-I, EMT-P, RN) who were asked to calculate the GCS of 4 scripted TBI patient scenarios. Prior to viewing the video, 14.7% of participants correctly scored all 4 cases. By comparison, 64% correctly scored the cases after reviewing a training video.

In a followup study, 46 EMT-B providers were randomly divided into two groups. One group one received a standard GCS scoring reference card, the other did not. Both groups received standardized video training. Of those EMTs using a reference card, 50% scored all 4 cases correctly prior to training and 100% scored them all correctly after the training. Without a reference card, 8% of the providers scored the cases correctly before the training, compared to 77% after the training. Although this study did not examine long-term retention of GCS scoring, formal training improved the overall scoring by EMS providers of all types.

Bazarian *et al*³ conducted a prospective observational study involving 60 patients with TBI and a field GCS score of 8-13 in which he compared the field score to the score obtained by emergency physicians upon arrival of the patient to the hospital. The authors documented that there is a significant linear relationship between the field GCS score and the emergency physician score. However the field GCS scores were usually approximately 2 points lower than the emergency physician score. The linear relationship suggests that, assuming most GCS scores improve from field to ED, there is concordance between EMS and physicians in assessment of TBI patients using the GCS.

Pediatrics

- A. The GCS and the pediatric GCS (P-GCS, Table 1) are reliable indicators of the severity of TBI in children and should be used repeatedly to identify improvement or deterioration over time.
- B. The adult protocol for standard GCS measurement should be followed in children over 2 years of age. In pre-verbal children, the P-GCS should be employed, with a full verbal score of 5 assigned to infants cooing or babbling.
- C. Prehospital providers should determine the GCS or P-GCS after airway, breathing, and circulation are assessed and stabilized.
- D. The GCS and P-GCS should be measured preferably prior to administering sedative or paralytic agents, or after these drugs have been metabolized.

Foundation. A GCS score of 12-15 reflects the presence of higher integrative brain function. These higher

functions are difficult to assess in the young child due to central nervous system immaturity. Maturation of the central nervous system is a continuum from intrauterine development to adolescence. Therefore, especially in young children, the GCS should reflect the expected normal verbal and motor responses for developmental stage. The GCS in its standard form is not applicable to infants and preverbal children. As stated earlier, the American College of Emergency Physicians and the American Academy of Pediatrics in its 1998 publication *APLS—The Pediatric Emergency Medicine Course* agreed that for preverbal children, a modified GCS (Pediatric Glasgow Coma Scale) that assigns a full verbal score (5) for spontaneous cooing should be used.

The relationship of outcome to GCS has also been demonstrated in children in hospital-based studies. In a study of 109 children who sustained TBI, Massagli, using only the motor component of the GCS and a dichotomized outcome of good (moderate, no disability) vs. bad (dead, vegetative, or severely disabled), revealed that the GCS motor component alone was indicative of outcome.¹²

White examined survival among 137 children with severe TBI. A higher GCS at 6 hours after admission to the pediatric intensive care unit was a better predictor of survival (odds ratio 4.6 and 95% CI 2.06,11.9). All patients with a GCS > 8 at 6 hours survived.¹⁸

Johnson compared mortality rate among 98 children with severe TBI; 56 children were transferred directly from the scene and 42 were transferred between facilities.⁹ Mortality rates were significantly higher (50%) in children with a GCS between 3 and 8 when they were transferred from other facilities, compared to 27% for patients transported from the field.

The basic principle for measuring the pediatric GCS follows the same guidelines as adults. Holmes and colleagues evaluated 2,043 children with TBI, 16% of whom were under 2 years of age.⁷ The pediatric GCS accurately predicted 97% of these infants needing acute intervention. Acute intervention was defined as one of the following proximal outcomes: need for a neurosurgical procedure, requiring an anticonvulsant medication for more than one week, longer than 2 days of hospitalization, or having a persistent neurological deficit until hospital discharge.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

The following questions require study to evaluate the role of the GCS score in the prehospital setting:

1. What is the ability of the initial field GCS score to predict outcome, compared with the post-resuscitation score, or compared with any improvement or deterioration in score during the prehospital phase?
2. How does the presence of central nervous system depressants affect the field measurement of the GCS and its predictive value?
3. Is the motor score alone, obtained in the prehospital setting, a reliable indicator and predictor of outcome?
4. What mechanisms, such as training or educational programs, improve the reliability of GCS scoring?
5. What is the appropriate coma scale to be used by prehospital providers in pre-verbal children?
6. What is the reliability/validity of GCS/Pediatric GCS (PGCS) as measured by prehospital providers?
7. What is the correlation between the initial field GCS/PGCS and the emergency department GCS/PGCS?
8. What is the impact of prehospital interventions on the GCS/PGCS and outcome?
9. What strategies can be employed to improve pre-hospital documentation of the GCS?

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III. ASSESSMENT: PUPIL EXAMINATION

I. RECOMMENDATIONS

Strength of Recommendations: Weak.
Quality of Evidence: Low, from Class III studies and indirect evidence.

Adult and Pediatrics

- A. Pupils should be assessed in the field for use in diagnosis, treatment, and prognosis.
- B. When assessing pupils:
 - Evidence of orbital trauma should be noted.

- Pupils should be measured after the patient has been resuscitated and stabilized
- Left and right pupillary findings should be identified
 - Unilateral or bilateral dilated pupil(s).
 - Fixed and dilated pupil(s).

Asymmetry is defined as > 1 mm difference in diameter
A fixed pupil is defined as < 1 mm response to bright light

II. EVIDENCE TABLES

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|-------------------------------|--|------------|---|
| Chesnut, 1994 ³ | Retrospective review of 608 patients from 1983-1988 with GCS < 8 to evaluate pupil asymmetry as localizing predictor of intracranial lesion. | III | > 1mm anisocoria: 40% sensitive, 67% specific. All anisocoria: 25% sensitive, 92% specific. Pupil size did not predict mass or location. Pupil asymmetry was less predictive in children than in adults. |
| Jiang, 2002 ⁶ | Retrospective review of 846 patients to determine factors affecting prognosis, including GCS, age, pupil response, hypoxia, hyperthermia and elevated ICP. | III | Bilateral pupil abnormalities: 62% mortality. Bilateral normal pupils: 17% mortality. |
| Mamelak, 1996 ⁷ | Retrospective review of 672 patients with GCS < 8 on admission and remained comatose > 6 hours Logistic regression of factors affecting outcome on admission and at 24 hours (age, pupil exam, motor exam). | III | Age was the most important independent predictor of outcome. Predictive strength of motor exam was greater than pupil exam. |
| Schreiber, 2002 ¹⁵ | Retrospective review of prospective databank of Level I trauma center from 1994 to 2000 from 418 consecutive patients age 13-88 years using univariate logistic regression to evaluate factors determining mortality, including BP, midline shift, elevated ICP, nonreactive pupil on one side, and GCS. | III | Independent risk factors for mortality: hypotension and intracranial hypertension. GCS and age together were significant predictors of mortality. Data not broken down by age. |
| Signorini, 1999 ¹⁶ | Retrospective review of 372 consecutive moderate and severe TBI patients from 1989-1991, age > 14 years (mean age 42). Multiple logistic regression analysis of 5 factors (age, GCS, ISS, pupil exam and CT scan) on 1 year outcome. | III | Bilateral blown pupils: 40% survival. Bilateral reactive pupils: 90% survival. Data not classified by age. |
| Chan, 2005 ² | Prospective study of 265 patients aged 2-18 years admitted from 1998 to 2001 with minor TBI to two trauma centers to evaluate differences in the two populations (urban and rural) that affected patient outcomes using multiple logistic regression | III | Clinical predictors of intracranial injury were headache (OR 20.8, CI 3.9-25.2), unequal pupils (OR 8.4, CI 4.3-17.9) and GCS=13 (OR 3.8, CI 1.9-6.8). Detailed clinical exam was of no diagnostic value in detecting injuries found on CT. |
| Halley, 2004 ⁵ | Prospective descriptive study of 98 isolated TBI patients aged 2-16 years in 1-year period, with loss of consciousness or amnesia, that received CT scans to evaluate the diagnostic value of CT. | III | 13 % had CT abnormality. 33% with CT abnormality had normal neurologic exam. |
| Massagli, 1996 ⁸ | Retrospective review of 33 patients < 17 years to determine predictors of outcome at hospital discharge, and 5 and 7 years post discharge | III | Pupillary response was significantly associated GOS scores at 5-7 years (p = .001). |
| McCabe, 2001 ⁹ | Retrospective review of 30 consecutive patients with "shaken baby syndrome" aged 1-39 months, to determine prognostic indicators including pupil response, midline shift, and ventilatory requirements | III | 8 of 30 patients (27%) had bilateral fixed pupils on arrival with 100% mortality for those patients. |

III. OVERVIEW

The pupillary exam is an essential component of the post-traumatic neurological exam. It consists of assessment of the size, symmetry and reaction to light of both pupils. The light reflex depends on a properly functioning lens, retina, optic nerve, brain stem, and oculomotor nerve (cranial nerve III). The direct pupil response assesses unilateral function of the III nerve; the consensual response assesses the function of the contralateral III nerve. Absence or asymmetry of these reflexes may indicate a herniation syndrome or ischemia of the brain stem.

Pupillary asymmetry less than 1 mm is normal and has no pathologic significance.¹⁰ In one study of 310 healthy volunteers with 2,432 paired measurements using advanced technology, asymmetry of pupillary size greater than 0.5 mm was seen in less than 1% of patients and was rarely seen in TBI patients unless the ICP exceeded 20 mm Hg.¹⁷

Increased intracranial pressure resulting in uncal herniation compresses cranial nerve III, resulting in a reduction of parasympathetic tone to the pupillary constrictor fibers, producing a dilated pupil with decreased reactivity. Destruction of the nerve also results in a dilated and fixed pupil. Bilaterally dilated and fixed pupils are consistent with direct brain stem injury, as well as with marked elevation of ICP. Metabolic or cardiovascular disturbances including hypoxemia, hypotension, and hypothermia are associated with dilated pupils and abnormal reactivity, making it necessary to resuscitate and stabilize the patient before assessing pupillary function.^{11,13}

Direct trauma to cranial nerve III in the absence of significant intracranial injury or herniation may result in pupillary abnormalities usually associated with ocular motor deficits. Asymmetric pupillary constriction can make the contralateral pupil appear dilated. Following trauma, as the result of a carotid dissection, sympathetic chain function may be impaired, resulting in Horner's syndrome.⁴ These patients also have ptosis associated with the miotic eye, with the contralateral "dilated" pupil having a normal brisk constriction to light. This assessment may be difficult in the field.

Pupillary function may be an indicator of brain injury after trauma, but it is neither a specific indicator of injury severity or involved anatomy. Nevertheless, studies support the assessment of pupillary functions in the acute setting of trauma as both a guide to immediate medical decision making, and as a long term prognosticator.^{2,6,9,16,7}

IV. PROCESS

For this update Medline was searched from 1996 through July 2006 using the search strategy for this

question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 24 potentially relevant publications, 5 were used as evidence for this topic. For pediatric studies, of 9 potentially relevant publications 4 were used as evidence for this topic. (Note: In the previous edition of these guidelines, there were no evidence tables for this topic.)

V. SCIENTIFIC FOUNDATION

- A. Pupils should be assessed in the field for use in diagnosis, treatment, and prognosis.
- B. When assessing pupils:
 - Evidence of orbital trauma should be noted.
 - Pupils should be measured after the patient has been resuscitated and stabilized
 - Left and right pupillary findings should be identified
 - Unilateral or bilateral dilated pupil(s).
 - Fixed and dilated pupil(s).

Asymmetry is defined as > 1 mm difference in diameter
A fixed pupil is defined as < 1 mm response to bright light

Adult

Foundation. The relationship of pupillary findings in the field to outcome has not been studied. Though there are no prehospital data, studies from in-hospital settings support a relationship between pupillary findings and outcome.^{1,12,14} There is a strong correlation between fixed, dilated pupils and ultimate mortality.^{6,9,16} Also, in-hospital studies suggest that the pupillary findings have prognostic value, especially when combined with other physical findings.^{1,12,14,15}

Chesnut *et al.* retrospectively analyzed data from 608 patients with severe TBI to assess the reliability of pupillary asymmetry in predicting the presence and location of intracranial mass lesions.³ Pupillary asymmetry had a positive predictive value of 30% with almost 80% of those patients having a contralateral lesion to the pupil finding. Anisocoria had a sensitivity of 40% and a specificity of 67%; even when the pupils were different by more than 3 mm there was a 43% positive predictive value. Thus, a single measurement of pupillary asymmetry is neither a sensitive nor specific finding in either identifying or localizing an intracranial mass lesion.

Mamelak *et al.* studied 672 TBI patients aged 0 - 80+ years. They found that age was the most important predictor of outcome, followed by initial motor exam and then by pupil response, demonstrating some correlation between pupillary response and outcome.⁷

Pediatrics

Foundation. There are few studies that specifically address the pupillary assessment in children following TBI. A prospective study of 98 pediatric patients found that 33% of those with a CT scan abnormality had a normal neurologic exam.⁵ In a prospective study of 265 pediatric patients the clinical predictors of intracranial injury were evaluated. Headache, pupillary response and initial GCS all indicated intracranial injury. However, a detailed clinical exam had no diagnostic value in detecting lesions found on head CT, supporting the poor sensitivity of pupil findings found in the first study.²

Massagli *et al.* studied 33 pediatric TBI patients and found that severity score and initial pupillary response were significantly related to long term outcome after 5-7 years, measured by the GOS (Glasgow Outcome Scale).⁸ McCabe *et al.* evaluated 30 pediatric patients diagnosed with "shaken baby syndrome" and found a 100% mortality for the 8 with bilateral fixed pupils on arrival.⁹

VI. KEY QUESTIONS FOR FUTURE INVESTIGATION

The prehospital and in-hospital environments are significantly different. In the field pupillary exam is difficult to perform and is less reliable than when performed in the hospital. Given that prehospital providers are increasingly involved in decision making regarding therapeutic interventions and transport destinations, it is important to further investigate methods of enhancing accuracy of assessment measures such as pupillary examination. The following key questions need to be addressed:

1. Can prehospital providers accurately assess pupil size and light reactivity in the prehospital environment?
2. Are there ways to improve reliability of the pupillary exam in the field?
3. Is there acceptable interobserver reliability in the prehospital pupil examination?
4. Are pupil findings in the field predictive of patient outcome in both adult and pediatric TBI patients?
5. Does the common practice of performing serial pupillary examinations improve prognostic capa-

bility? The frequency at which examinations are performed needs to be determined.

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TREATMENT

IV. TREATMENT: AIRWAY, VENTILATION, AND OXYGENATION

I. RECOMMENDATIONS

Strength of Recommendations: Weak.
Quality of Evidence: Low, primarily from Class III studies.

Adult

- A. In ground transported patients in urban environments, the routine use of paralytics to assist endotracheal intubation in patients who are spontaneously breathing, and maintaining an SpO₂ above 90% on supplemental oxygen, is not recommended.

Adult and Pediatrics

- A. Hypoxemia (oxygen saturation [SpO₂] < 90%) should be avoided, and corrected immediately upon identification.
B. An airway should be established, by the most appropriate means available, in patients who

have severe traumatic brain injury (TBI) (Glasgow Coma Scale [GCS] < 9), the inability to maintain an adequate airway, or hypoxemia not corrected by supplemental oxygen.

- C. Emergency Medical Service (EMS) systems implementing endotracheal intubation protocols including the use of rapid sequence intubation (RSI) protocols should monitor blood pressure, oxygenation, and when feasible, ET/CO₂.
D. When endotracheal intubation is used to establish an airway, confirmation of placement of the tube in the trachea should include lung auscultation and end-tidal CO₂ (ET/CO₂) determination.
E. Patients should be maintained with normal breathing rates (ET/CO₂ 35–40 mmHg), and hyperventilation (ET/CO₂ < 35 mmHg) should be avoided unless the patient shows signs of cerebral herniation.¹

II. EVIDENCE TABLES

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|--------------------------------|--|------------|--|
| Chesnut, 1993 ⁸ | Prospective study of 717 multicenter severe TBI patients investigated the effect on outcome of hypotension (SBP < 90 mmHg) occurring from injury through resuscitation. | III | Hypotension was a statistically independent predictor of outcome. A single episode of hypotension during this period doubled mortality and increased morbidity. Patients with hypotension not corrected in the field had a worse outcome than those whose hypotension was corrected by time of emergency department arrival. |
| Hsiao, 1993 ²² | Retrospective trauma registry-based study of 120 patients with a GCS < 14 evaluated the need for emergency intubation in the field or ED and compared to CT scan findings. | III | The patients in GCS group 3–5 were all intubated, 73% had abnormal CT scans; 73% of patients with GCS 6–7 were intubated, 36% had abnormal CT scans; 62% of patients with GCS 8–9 were intubated, 62% had abnormal CT scans; 20% of patients with GCS 10–13 required intubation, 23% had abnormal CT scans. |
| Silverston, 1989 ³¹ | Study of 25 consecutive trauma patients, including head injury; evaluated the use of noninvasive pulse oximetry in the field and in a moving ambulance. | III | Sixteen percent of patients had O ₂ saturation < 75%, and an additional 28% were between 75 and 90%. There were no demonstrated difficulties using the pulse oximeter in the field or ambulance. |

(Continued on next page)

¹Refer to Chapter VI, Cerebral Herniation

EVIDENCE TABLE 1. Adult (Continued)

| Reference | Study Description | Data Class | Conclusion |
|--------------------------------|--|------------|---|
| Stocchetti, 1996 ³⁴ | Cohort study of 50 trauma patients transported from the scene by helicopter evaluated the incidence and effect of hypoxemia and hypotension on outcome. | III | 55% of patients were hypoxemic (SpO ₂ < 90%) and 24% had hypotension. Both hypoxemia and hypotension negatively affected outcome; however, the degree to which each independently affected the outcome was not studied. |
| Winchell, 1997 ⁴⁰ | Retrospective case control study of 1,092 patients with severe TBI with pre-hospital GCS <9 and head or neck AIS > 4. Compared patients who underwent prehospital endotracheal intubation with those who did not. | III | For patients with GCS < 9 there was a 74% survival for patients receiving prehospital endotracheal intubation vs. 64% for those who did not. For patients with isolated severe TBI there was a 77% survival for patients receiving prehospital endotracheal intubation vs. 50% for those who did not. |
| New Studies | | | |
| Bochicchio, 2003 ³ | Retrospective review of a prospectively collected data base of 191 patients with TBI. Compared patients intubated in the field to those intubated after arrival to the trauma center. Evaluated overall mortality, hospital and ICU length of stay, days on a ventilator and incidence of pneumonia. | III | Patients intubated in the field had a higher mortality, longer stay in the ICU and overall hospital, more ventilator days, and a higher incidence of pneumonia. This study included a mixed group of blunt and penetrating injury and it is not clear if the two study groups were similar. Groups are not equivalent, i.e., prehospital group was probably sicker. Hospital group had a shorter transport time. |
| Bulger, 2005 ⁵ | Retrospective review of 2,012 TBI patients intubated with and without the use of neuromuscular blocking agents. (NMBAs) | III | 17% of 920 patients with mild TBI were intubated. Patients not receiving NMBAs were more likely to be hypotensive, higher AIS, in cardiopulmonary arrest and transported by HEMS. Mortality was 25% vs. 37% in intubated patients with NMBA. Potential selection bias, i.e. sicker patients did not get NMBA. |
| Davis, 2003 ¹³ | Prospective observational study of 209 suspected TBI patients who underwent RSI after failed endotracheal intubation attempts; compared to 627 matched controls who did not undergo intubation. GCS, pO ₂ , and presence of gag reflex were used in decision making to intubate using RSI. Air transport excluded. | III | Patients who underwent RSI had higher mortality rate and worse neurologic outcomes than patients who did not undergo intubation. Higher rate of inadvertent hyperventilation in the RSI group. Transient hypoxia developed in >50% of patients undergoing ETCO ₂ monitoring, many with concurrent bradycardia. Scene times were longer, arrival PO ₂ values higher, and arrival PCO ₂ lower in RSI cohort. Hyperventilated group had higher mortality. 67 of the 209 patients intubated using RSI had either a minor concussion or no TBI. |
| Davis, 2003 ¹⁴ | Prospective observational study measuring success rate for Combitube insertion after unsuccessful orotracheal intubation. Of 420 patients with suspected TBI and GCS < 8, 61 were not orotracheally intubated after 3 attempts. In these 61 patients, the Combitube was used as a salvage device. | III | Of 61 Combitube insertion attempts, 58 (95%) were successful. Patients undergoing Combitube insertion had higher face AIS scores and were more likely to have oropharyngeal secretions or blood. No mortality differences between patients with Combitube insertion versus orotracheal intubation. |
| Davis, 2003 ¹² | Prospective observational study of 249 suspected TBI patients who underwent intubation including RSI after failed endotracheal intubation attempt. Compared to 189 historical controls. Determined the overall success rate for intubation (defined as placement of either an endotracheal tube or Combitube as a rescue airway) after implementation of the RSI protocol. | III | Implementation of an RSI protocol improved intubation success rates from 39% in historical controls to 85% including 99% of patients who underwent RSI. Mean time at scene for RSI patients was 28 minutes. Paramedics were unable to intubate 15% of patients after RSI (needed Combitube). |
| Davis, 2004 ¹⁰ | Prospective observational study of 355 suspected TBI patients who underwent intubation including use of RSI after failed endotracheal intubation attempts. 144 patients received ETCO ₂ monitoring; 149 did not. Considered the efficacy of using a continuous quantitative ETCO ₂ monitor to prevent inadvertent hyperventilation. | III | 8 patients with monitoring (5.6%) had severe hyperventilation (pCO ₂ < 25 mm Hg) compared to 20 patients without monitoring (13.4%) (OR = 2.64; 95% CI, 1.12-6.20; p = 0.035). There was no significant difference in mortality between groups. Sub-analysis indicated significantly higher mortality for patients with severe hyperventilation than for those without (OR = 2.9; 95% CI, 1.13-6.6; p = 0.016). |
| Davis 2004 ¹¹ | Prospective observational study of 59 intubated TBI patients with GCS ≤8 and 177 matched historical non-intubated controls. Compared ETCO ₂ and SpO ₂ in relation to mortality. TBI patients were intubated using RSI after unsuccessful attempts to intubate without medications. | III | Lowest and final ETCO ₂ values were independently correlated with increased mortality. Patients with the lowest ETCO ₂ between 20-27 mmHg and those with ETCO ₂ < 20 mmHg had higher mortality (OR 3.38 and 3.64) Patients with final ETCO ₂ < 4 mmHg had higher mortality (OR 3.86). Hypoxia after intubation, both 90%-95% and <90% were associated with higher mortality (OR 3.23 and 3.86). |

(Continued on next page)

EVIDENCE TABLE 1. Adult (Continued)

| Reference | Study Description | Data Class | Conclusion |
|-------------------------------|--|------------|---|
| Deitch, 2003 ¹⁵ | Prospective observational study of 36 patients monitoring blood pressure before and after the use of etomidate for RSI. | III | Hypotension was noted in 9% of patients. Study patients were not consecutive; algorithm for etomidate use unclear. |
| Dunford, 2003 ¹⁶ | Prospective observational study of 54 patients with suspected TBI who underwent RSI after failed intubation attempts. Patients were monitored during the RSI procedure for oxygen saturation and effect on heart rate. | III | 57% of RSI patients had a period of oxygen desaturation. 19 / 31 (61%) had a pulse decrease of > 20 per minute including 19% with bradycardia less than 50 beats per minute. 26 of the 31 events of desaturation occurred in patients whose initial SpO ₂ was greater than or equal to 90%; it is unclear why these patients were intubated; 5 patients had uncorrectable hypoxia before intubation. It is unclear why so many patients desaturated, especially if they were properly preoxygenate vs. other factors. In addition, 26/31 (85%) of the intubations were described as "easy". |
| Grmec, 2004 ¹⁹ | Prospective observational study of 81 patients (58 TBI, GCS < 9) who underwent endotracheal intubation in the field and evaluation for correct placement of the tube using auscultation and capnometry. | III | Auscultation alone mis-identified 8 (10%) cases with 4 false negatives and 4 false positives. Capnometry correctly identified tube placement in all cases. |
| Helm 2002 ²¹ | Prospective observational study of 127 patients with TBI who were intubated in the field and placed onto a portable transport ventilator. Patients were assessed upon arrival to the hospital for adequacy of oxygenation and hypo or hyperventilation | III | Optimal oxygenation (PaO ₂ >100 mm Hg) was found in 85% of patients; hypoxemia (PaO ₂ < 60 mm Hg) was found in 2.5%. Hypoventilation (PaCO ₂ > 45 mm Hg) was noted in 16.4% and hyperventilation (PaCO ₂ < 35 mm Hg) in 41% of patients. In a subset of 38 patients with isolated TBI, 45% (17) had hypocapnia (PaCO ₂ < 35 mmHg) on hospital arrival; 2 were hypercapnic ((PaCO ₂ > 45 mmHg) on hospital arrival. |
| Helm, 2003 ²¹ | Prospective study of 97 trauma patients, of whom 71 had TBI, in which patients were randomized to permit or not permit visualization of a continuous ETCO ₂ monitor applied in the prehospital setting. Patients were evaluated upon arrival to the hospital for hypo- or hyperventilation. | II | Patients with a visible ETCO ₂ monitor were found to be hypoventilated in 5.3% of cases and hyperventilated in 32%. Patients without visible ETCO ₂ readings were found to be hypoventilated in 38% of cases and hyperventilated in 43% |
| Katz, 2001 ²⁴ | Prospective observational study of patients intubated in the field by paramedics. Upon ED arrival, tube placement was checked by capnometry, auscultation, and direct laryngoscopy | III | 108 intubated patients; 25% (27/108) were found to have improperly placed endotracheal tube: 18 in the esophagus and 9 above the cords. Study cannot demonstrate whether the ET tube was initially misplaced in the esophagus or if it became dislodged during transport; therefore, the study does not answer whether this is an intubation skill problem or a postintubation monitoring problem |
| Murray, 2000 ²⁸ | Retrospective review comparing patients who were intubated in the field (N = 81) to patients who were not (N = 714). | III | ISS, GCS, mechanism of injury, and distribution of head AIS score were less severe in the non intubated patients. Patients who had prehospital intubation did not have better survival than matched patients. Intubation was attempted if respiratory effort was present but appeared labored and did not improve with BVM, or apnea. Most common reasons for failed intubation were clenched teeth or intact gag. |
| Ochs, 2002 ²⁹ | Prospective study to evaluate the ability of paramedic RSI to facilitate intubation of 114 patients with severe TBI | III | Paramedics received a 7-hour course. 84% success rate, i.e. 16% failure with RSI. (vs. 63% success rate reported by Wang in study not using paralytics ¹⁴). RSI added 15 minutes to the field time. |
| Silvestri, 2005 ³² | Prospective observational study evaluating the association between out of hospital use of continuous ETCO ₂ monitoring and unrecognized misplaced intubations within a regional EMS system. | III | 153 intubations: 93 had continuous ETCO ₂ monitoring and 60 did not. The rate of unrecognized misplaced intubations in the ETCO ₂ monitored group was 0%, and the rate in the non monitored group was 23%. Use of monitoring was at the discretion of the EMS unit, therefore, the study suffers from selection bias in that those paramedics using ETCO ₂ monitoring were most likely more compulsive in airway management. No randomization; findings depended on self reporting. No report of number of initial esophageal intubations that were recognized or number of complications during intubation. |

(Continued on next page)

EVIDENCE TABLE 1. Adult (Continued)

| Reference | Study Description | Data Class | Conclusion |
|----------------------------|---|------------|--|
| Sloane, 2000 ³³ | Retrospective review of aeromedically transported trauma patients comparing those who underwent RSI in the field with those who received it in the hospital. Subgroup analysis of 75 TBI patients was performed. | III | There were no differences in hospital or ICU length of stay or in final outcome based upon mortality or discharge site between the 2 groups. Groups not similar and reviewer not blinded. Patients intubated by physicians or flight nurses. |
| Wang, 2004 ³⁷ | Retrospective trauma registry review of 4,098 adult patients with TBI comparing those who were intubated in the field (n = 1,797) with those who underwent intubation in the ED (n = 2,301). Evaluated mortality and functional neurologic outcome. | III | Patients who were intubated in the field had a higher mortality (OR 3.99) and higher incidence of poor neurologic outcome. Patients not matched; field intubation group was more severely injured. |

EVIDENCE TABLE 2. Pediatrics

| Reference | Study Description | Data Class | Conclusion |
|------------------------------|--|------------|---|
| New Studies | | | |
| Cooper, 2001 ⁹ | Retrospective National Pediatric Trauma Registry study of 578 children with TBI comparing those treated with endotracheal intubation to those treated with bag-valve-mask (BVM). Evaluated overall mortality as well as functional independence. | III | 479 received endotracheal intubation; 99 managed with bag mask ventilation. No differences in mortality or functional independence scores between groups. |
| Gaushe, 2000 ¹⁸ | Prospective study in which 830 patients ≤12 years were randomized on an alternating day basis to airway management with either an endotracheal tube or bag-valve-mask (BVM). Subgroup analysis for TBI patients (BVM n = 27, ETI n = 36) | II | No significant difference between groups in mortality (OR 0.71, CI 0.23–2.19) or neurological outcome (OR 1.44, CI 0.24–8.52). |
| Meyer, 2000 ²⁶ | Prospective observational study of 188 children with TBI who underwent endotracheal intubation. Patients were evaluated for success rate of intubation, complications and hypo- and hyperventilation. | III | The overall success rate for intubation was 78% (98% in comatose patients). Hyperventilation occurred in 10 patients and hypoventilation in 2. |
| Suominen, 2000 ³⁵ | Retrospective review comparing children with TBI who underwent endotracheal intubation in the field with those who received the procedure in the initial receiving hospital or at the referral trauma center. | III | No significant difference in survival. 59 patients intubated in the field had a higher ISS. |

III. OVERVIEW

Airway management and normal oxygenation in the patient with traumatic brain injury (TBI) are two of the most important management issues in the prehospital period, and have been an important research focus in prehospital care since the Guidelines⁴⁷ were originally written. Key issues are management of oxygenation and ventilation, including the identification of patients who will benefit from endotracheal intubation.

Hypoxemia is a strong predictor of outcome in the TBI patient.^{8,25} Consequently, the primary goal in field management is assessing the airway and ensuring adequate oxygenation. Class III evidence suggests that comatose patient with persistently low oxygen saturation despite O₂ therapy benefit from intubation.⁴⁰

Prehospital airway management studies relate to assessment, technique, and performance skills. These include whether endotracheal intubation skills can be taught and safely maintained by prehospital providers with minimal complications. Corollaries to this question include recognition of an esophageal intubation

in the field, and the degree to which prehospital providers are able to manage difficult or failed airways. Additionally, medication adjuncts to prehospital airway intubation have been studied, as have methods of oversight, monitoring, and quality improvement processes.

These management issues are dependent upon the properly identifying the patients who need intubation. Ultimately, the goal of these studies is to ascertain the conditions in which field endotracheal intubation results in improved neurologic outcomes and decreased mortality.

IV. Process

For this update Medline was searched from 1996 through July 2006 using the search strategy for this question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 55 potentially relevant publications, 18 were added to the existing table and used as evidence for this question. For pediatric studies, of 62 potentially relevant

publications, 4 were used as evidence for this question (see Evidence Tables).

V. SCIENTIFIC FOUNDATION

Adult

- A. In ground transported patients in urban environments, the routine use of paralytics to assist endotracheal intubation in patients who are spontaneously breathing and maintaining an SpO₂ >90% on supplemental oxygen is not recommended.

Foundation. Recent studies suggest that pre-hospital intubation of TBI patients may not be beneficial in patients able to maintain a SpO₂ > 90% with supplemental oxygen alone.^{10,11,13} Studies which reported worse or equivocal outcomes in patients intubated in the field must be viewed with caution since intubated patients were usually more severely injured.^{3,28,37}

Rapid sequence intubation (RSI), has been used in the pre-hospital setting. The use of lidocaine, fentanyl, and/or esmolol as premedication has not been demonstrated to decrease morbidity or mortality.²³ There is insufficient evidence to advocate for or against the use of premedications in the field. In addition, there is little focused research on the best induction agents to employ for prehospital RSI.

A series of studies from San Diego shows an overall improvement in intubation success rate, from 39% in historical controls (non-RSI group) to approximately 85% in the study groups using RSI.^{12,15,29} Entry criteria in these studies were a GCS < 9 with suspected TBI, transport time from the scene to the receiving hospital > 10 minutes, and inability to intubate without RSI due to either a clenched jaw, active gag or combativeness obviating easy intubation. Study patients were then matched to historical controls who did not undergo endotracheal intubation. In this series of studies, it is not clear what fraction of patients were unable to oxygenate and/or ventilate, compared to those who were intubated out for airway protection. Thirty-two percent of the patients who were intubated did not have a TBI. These studies report a higher mortality rate in the RSI group: 41% compared to 30% for those patients not intubated (O.R. 1.6; 95% C.I. 1.1-2.3) and a lower incidence of good neurologic outcome in the RSI group, 37% vs. 49% (O.R. 1.6; 95% C.I. 1.1-2.3).^{10,13,16} On arrival to the hospital, patients in the RSI group had severe hyperventilation (PaCO₂ < 25 mmHg) in 15% of cases compared with 8% of non-intubated controls. Patients who were not hyperventilated (PaCO₂ > 32 mmHg) had a predicted mortality of 23% and an actual mortality of 26% whereas patients with a pCO₂ < 32mmHg had a predicted mortality of 27% but an actual mortality of 39%. Patients with a single intubation attempt had a higher mortality rate than

patients requiring multiple attempts, as did those needing intubation *en route* or those whose airway was managed with a Combitube because of a failed endotracheal intubation.

Challenging the findings from San Diego is a retrospective analysis of 2,012 TBI patients from the Seattle, Washington EMS system.⁵ This system ensures that each paramedic performs at least 12 intubations per year or returns to the operating room for additional training. The authors of this study concluded that paralytic use improved outcome for TBI patients. However, the retrospective design of the study limits its strength. A second study also supported the prehospital use of paralytics.³³ However, physicians or flight nurses performed the intubation in this study.

Thus, the safety and efficacy of RSI in the prehospital setting remains undetermined. The above studies suggest that even though RSI may improve intubation success *per se*, it might actually contribute to worse outcomes. Potential reasons for this include an increased incidence of inadvertent hypoxia and bradycardia, prolonged scene time, and inadvertent hyperventilation after successful intubation. However, all provided Class III evidence, rendering the findings questionable.

In summary, these studies suggest the need for aggressive airway management in hypoventilated or hypoxemic TBI patients, either by endotracheal intubation or by bag mask ventilation. However, in those patients with a SpO₂ > 90% with supplemental oxygen, paramedic use of RSI in ground transport units in urban settings does not appear to be of benefit and may be detrimental.

Adult and Pediatrics

- A. *Hypoxemia (oxygen saturation [SpO₂] < 90%) should be avoided and corrected immediately upon identification.*

Foundation. The detrimental effect of hypoxemia on the outcome of patients with TBI has been demonstrated in several studies.^{8,34} The largest study, involving 717 patients admitted to 4 centers, showed that hypoxemia (an apneic or cyanotic episode in patients in the field, and SpO₂ < 60 mmHg on arterial blood gas in patients in the emergency department) has a detrimental effect on patient outcome, particularly when associated with hypotension.⁸ Mortality was 26.9% if neither hypoxemia nor hypotension occurred, 28% for hypoxemia alone, and 57.2% if both were noted (p = 0.013).

In a second study of 50 patients with TBI who were transported by helicopter, 55% had oxygen saturation less than 90% measured at the scene prior to intubation.³⁴ That study indicated that both hypoxemia and hypotension had a negative impact on outcome. Of the 28 patients who were hypoxemic, 13 had no associated hypotension (see Table A). There was a significant association between arterial desaturation and poor outcome (p < 0.005).

Hypoxemia can be corrected using supplemental oxygen and varying combinations of bag mask ventilation, endotracheal intubation, and other airway adjuncts including Combitubes and laryngeal mask airways. Consequently, studies have evaluated the ability of prehospital providers to perform endotracheal intubation, and whether endotracheal intubation impacts outcome.¹³ Only one study has looked at whether bag mask ventilation is comparable to endotracheal intubation in the prehospital environment.³¹

B. An airway should be established in patients who have severe TBI [Glasgow Coma Scale (GCS) < 9], the inability to maintain an adequate airway, or hypoxemia not corrected by supplemental oxygen by the most appropriate means available.

Foundation. In studies of general trauma patients, establishment of an artificial airway is recommended in patients unable to oxygenate or ventilate normally, unable to protect their airway, or in patients whose predicted clinical course is such that the benefit of securing the airway is thought to outweigh its risks.³⁶ Failure of oxygenation, ventilation, and airway protection can be assessed by physical exam and by physiologic monitoring. The clinical course may be difficult to predict and so a low threshold for securing the airway has been practiced. However, this practice of securing an airway in an adequately oxygenated patient may not be beneficial when transport times are short.

A low GCS score in the pre-hospital environment has been correlated with an increased incidence of an acute intracranial lesion on head CT in the trauma center.²² One retrospective case-control study of 1,092 patients with severe TBI (GCS < 9 and a head or neck Abbreviated Injury Score [AIS] equal to or greater than 4) compared those patients who underwent prehospital endotracheal intubation with those who did not.⁴⁰ EMS providers intubated patients only if they were apneic, unconscious with ineffective ventilation, and without a gag reflex. The study protocol required that no medications be used for intubation and a maximum of three intubation attempts were permitted. Prehospital endotracheal intubation was associated with significantly improved survival with an overall survival rate of 74% for intubated patients versus 64% for those not intubated. Patients with isolated TBI had a survival rate of 50% in the non-intubated group compared to a 77% survival rate in the intubated group.

C. EMS systems implementing endotracheal intubation protocols, including the use of RSI protocols, should monitor blood pressure, oxygenation, and, when feasible, ETCO₂.

Foundation. Because both hypoxia and hypotension have been associated with poor outcomes in TBI patients, careful monitoring of both blood pressure and oxygen saturation, and the correction of abnormalities when identified, are indicated. There are limitations to SpO₂ monitoring. In non-TBI studies, nail polish, hy-

potension, severe anemia, and vasoconstriction have all been reported to give false low oxygen saturation readings.² Despite these limitations, oxygen saturation monitors have been reported to provide a reliable measurement of hemoglobin oxygen saturation in the field, with both TBI and non-TBI patients.^{16,31}

In one observational study, 54 patients with suspected TBI were monitored during RSI for SpO₂ and effect on heart rate.¹⁶ Fifty-seven percent of RSI patients had a period of oxygen desaturation, 61% of whom had a pulse decrease of > 20 beats per minute including 19% with bradycardia less than 50 beats per minute. Twenty-six of the 31 events of desaturation occurred in patients whose initial SpO₂ was greater than or equal to 90%, i.e., only 5 patients had uncorrectable hypoxia before intubation. One of the concerns raised by this study is why so many patients desaturated, especially in light of the report that 26/31 (85%) of the intubations were described as "easy".

Hyperventilation with hypocapnia may worsen outcome in TBI patients.^{10,13} Therefore, monitoring of ETCO₂ is emerging as a fundamental component of TBI management not only in the hospital but also in the pre-hospital arena. After TBI, there may be a period of prolonged hypoperfusion with cerebral blood flow (CBF) reduced by as much as two-thirds of normal. Hyperventilation can further decrease the CBF, potentially causing cerebral ischemia or infarction. Evidence from hospital-based studies indicates that prophylactic early hyperventilation can seriously compromise cerebral perfusion and worsen patient outcome.^{27,30} Inadvertent hyperventilation during pre-hospital transport is associated with increased mortality.¹¹

The ETCO₂ level has been shown in hospital-based studies to be well correlated with the PaCO₂ levels in healthy patients.^{7,17,38,39,41} However, ETCO₂ technology has limitations. A significant difference in PaCO₂ and ETCO₂ measurements has been reported in patients with multiple trauma, severe chest trauma, hypotension, and heavy blood loss.²⁰ This difference is due to increased dead space secondary to decreased alveolar perfusion or disruptions in pulmonary blood flow.²¹

Several studies have demonstrated the incidence of induced hypocapnia during the field management of adult^{10,11} and pediatric²⁶ TBI patients. In a retrospective study from San Diego, 59 adult severe TBI patients who were unable to be intubated without RSI were matched to 177 historical non-intubated controls.¹¹ The study utilized ETCO₂ monitoring and found an association between hypocapnia and mortality and a statistically significant association between ventilatory rate and ETCO₂. Both the lowest and final ETCO₂ readings were associated with increased mortality vs. matched controls.

In another analysis of the same registry, ETCO₂ monitoring was used in 144 patients (compared to 149 patients without monitoring), to assess whether closer monitoring would result in a lower rate of inadvertent severe hyperventilation (defined as ETCO₂ < 25 mmHg).¹⁰ Patients with ETCO₂ monitoring had a lower incidence of severe hyperventilation (5.6% vs. 13.4%; $p = 0.035$). There was no significant difference in mortality between these groups. A sub-analysis showed that patients who were severely hyperventilated had a higher mortality rate than those who were not (56% vs. 30%; $p = 0.016$).

D. When endotracheal intubation is used to establish an airway, confirmation of placement of the tube in the trachea should include lung auscultation and end-tidal CO₂(ETCO₂) determination.

Foundation. The discussion of endotracheal intubation includes both whether prehospital providers can be taught the skill, and also if they can identify and correct an error when it occurs. From studies conducted in general trauma patients, the success rate of intubation by prehospital providers ranged from 50% to 100%.^{4,24} Major complication rates ranged from 2–17% in pediatric groups⁴ and as high as 25% in adults.²⁴ Thus, confirmation of correct endotracheal tube placement is critical.

In studies cited previously, paramedics intubated successfully 84% of the time; 16% of these patients required a rescue device to secure the airway.^{13,14} These studies stress both the critical importance of CO₂ detection protocols in any prehospital system using endotracheal intubation and the imperative for these systems to have airway rescue devices available in case of a failed intubation.

In a study from the Orlando Florida EMS system, Katz and Falk reported 28/107 (25%) patients who had a prehospital intubation arrived in the ED with an unrecognized misplaced endotracheal tube, 18 in the esophagus and 9 above the vocal cords.²⁴ In a follow-up study, Silvestri *et al.* reported that the missed esophageal rate dropped to zero with the utilization of ETCO₂ monitoring in the field.³² Likewise, Grmec *et al.* studied 81 patients (58 with severe TBI) who underwent prehospital intubation by emergency physicians, comparing auscultation to capnometry with capnography for confirmation of proper endotracheal tube placement.¹⁹ Successful intubation was observed in 73 patients, however, 8 patients were intubated into the esophagus as shown by capnometry. Of those, four were incorrectly thought to be in the trachea based upon auscultation. In a prospective study from San Diego, with the use of auscultation, pulse oximetry, colorimetric capnometry, and syringe aspiration there were 96 endotracheal intubations with no unrecognized esophageal intubations.²⁹

E. Patients should be maintained with normal breathing rates (ETCO₂ 35–40 mmHg), and hyperventilation (ETCO₂

< 35 mmHg) should be avoided unless the patient shows signs of cerebral herniation.²

Foundation. There is a growing body of evidence that hyperventilation with an associated hypocapnia (PaCO₂ < 35 mmHg) is associated with worse outcomes in TBI patients.^{10,11} Consequently there is an increased emphasis on ensuring that the ventilation promotes eucapnia during transport, i.e., ETCO₂ of 35–40.

Adequacy of ventilation is dependent not only on the ventilation rate, but also on the tidal volume of oxygen delivered, and the pressure under which the tidal volume is delivered. Continuous capnometry is the best way to monitor ventilation. In the absence of capnometry, adequacy of ventilation is promoted by monitoring the airway seal and chest rise. The 2005 CRR/ECC Guidelines recommend 10–12 breaths per minute (6–7 mL/kg) delivered over 1 sec in order to minimize gastric inflation.¹

In one prehospital study, 38 intubated patients with isolated TBI were placed on a ventilator with a tidal volume of 10 mL/kg at a rate of 10 breaths per minute: 17 (45%) were found to have hypocapnia (PaCO₂ < 35 mm Hg) upon arrival to the hospital (an additional 2 patient were found to be hypercapnic (PaCO₂ > 45 mmHg) upon arrival.²¹ The challenge of achieving eucapnia is compounded in patients with polytrauma, especially with lung injury. In a second prehospital study by the same group of investigators, that included non-TBI patients, the use of capnography with ventilator adjustments during transport significantly decreased the incidence of hypocapnia upon arrival at the trauma center.²⁰

Pediatrics—Additional Considerations

There is no evidence to support the superiority of out of hospital endotracheal intubation over bag valve mask ventilation in pediatric patients with TBI.

Foundation. One small retrospective study reported no statistically significant difference in survival in children with TBI who were intubated in the field compared with those who were not.³⁵ Two large pediatric studies questioned the superiority of field intubation, with or without RSI, over bag mask ventilation.^{9,18} Cooper *et al.*, in a retrospective study of the National Pediatric Trauma Registry compared children with severe TBI defined as an AIS score ≥ 4 who underwent intubation in the field with those treated with bag-valve-mask (BVM) ventilation.⁹ Of the 578 patients included in the study, 99 (17%) received BVM ventilatory assistance while 479 (83%) were intubated. Both the overall mortality rate for the two groups (48%) and the functional outcome as measured by the Functional Independence Measure (score < 6) in children > 7 years were statistically similar (ETI 67%, BVM 65%). The rate of other organ system

²Refer to Chapter VI, Cerebral Herniation

complications was lower in children who were intubated (58%) when compared to those treated with BVM (71%, $p < 0.05$). Of note, children who underwent intubation were older than those receiving BVM and more often received intravenous fluids, medications, and helicopter transport.

In a prospective, randomized trial that provides Class II evidence, Gausche *et al.* compared survival and outcome after either prehospital intubation (ETI) or ventilation with bag-valve-mask (BVM) in children using an even-odd day randomization protocol.¹⁸ A total of 830 patients were entered; 420 received ETI, 410 received BVM. A small subset of patients had TBI (36 and 27 patients in the 2 groups, respectively). There was no significant difference in outcomes between groups. Survival for TBI patients who underwent ETI was 25% compared with 32% in the BVM group (O.R. 0.71; 95% C.I. 0.23–2.19). Good neurologic outcome, defined as no or mild disability, was 11% in the ETI patients and 8% in BVM treated group (O.R. 1.44; 95% C.I. 0.24–8.52). Although no difference in outcomes was found for the small subgroup of TBI patients, the findings from the larger group of general trauma patients indicated fewer complications with BVM.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

1. How do other airway management devices available for field use by EMTs with basic training com-

TABLE A. Oxygen saturation prior to intubation vs. mortality and severe disability outcomes in TBI patients transported by helicopter³⁴

| Oxygen Saturation | Mortality | Severe Disability |
|-------------------|--------------|-------------------|
| > 90% | 14.3% (3/21) | 4.8% (1/21) |
| 60–90% | 27.3% (6/22) | 27.3% (6/22) |
| <60% | 50% (3/6) | 50% (3/6) |

TABLE B. Prehospital endotracheal intubation and outcome in severe TBI patients (Winchell³)

| | Intubated | Not Intubated |
|------------------------|-----------|---------------|
| All Patients-Mortality | 26% | 36.2% |
| Isolated TBI-Mortality | 22.8 | 49.6 |

TABLE C. Field GCS score and the need for prehospital endotracheal intubation in TBI patients²²

| | GCS score | | | |
|------------------|-----------|-----|-----|-------|
| | 3–5 | 6–7 | 8–9 | 10–13 |
| Field intubation | 27% | 27% | 8% | 2% |
| ED intubation | 73% | 45% | 53% | 18% |
| CT scan positive | 73% | 36% | 62% | 23% |

TABLE D. Outcome of patients intubated in the field compared to non-intubated controls and effect of hypoxia and hyperventilation¹¹

| Measurement | Mortality | | | |
|---------------------------|-----------|----------|------------|------------|
| | RSI | Controls | Odds Ratio | 95% CI |
| Lowest SpO ₂ | | | | |
| <70% | 44% | 17% | 3.89 | (1.1–13.5) |
| Lowest ET/CO ₂ | | | | |
| >27 mm Hg | 22% | 17% | 1.43 | (0.4–5.4) |
| 20–27 mm Hg | 47% | 21% | 3.38 | (1.1–10.2) |
| <20 mm Hg | 47% | 20% | 3.64 | (1.1–11.8) |

pare to each other, and to endotracheal intubation? In particular, studies should focus on maintaining adequate oxygen saturation, how this would affect outcomes in TBI patients.

2. What is the effect on outcome of early short-term hyperventilation after TBI, beginning in the prehospital setting? Studies need to consider extremely variable prehospital times, for example, the short prehospital time in urban areas that permit only a brief period of hyperventilation.
3. Objective measures of the degree and effectiveness of hyperventilation in the prehospital setting should be developed.
4. Does the hypotensive effect of various RSI medications affect outcomes of TBI patients?
5. Is there a subset of patients with TBI who benefit from RSI? Specifically, when RSI is performed under carefully monitored conditions that ensure oxygenation and prevent hypocapnia, are outcomes improved?
6. Does the use of capnometry improve outcomes by decreasing inadvertent hypo- or hypercapnia?
7. A large, well-designed trial is needed to compare no intubation, non-pharmacologically-assisted intubation, and RSI for maintaining adequate prehospital oxygenation.

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V. TREATMENT: FLUID RESUSCITATION

I. RECOMMENDATIONS

Strength of Recommendations: Weak
 Quality of Evidence: Low, from Class III studies, or
 Class II studies with contradictory findings.

Adult

- A. Hypotensive patients should be treated with isotonic fluids.

- B. Hypertonic resuscitation is a treatment option for TBI patients with a Glasgow Coma Scale Score (GCS) < 8.

Pediatrics

- A. For the pediatric TBI patient, hypotension should be treated with isotonic solutions.

II. EVIDENCE TABLES

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|-----------------------------|---|------------|--|
| Chesnut, 1993 ³ | A prospective study of 717 consecutive severe head injury patients admitted to four centers investigated the effect on outcome of hypotension occurring from injury through resuscitation | III | Hypotension was a statistically independent predictor of outcome. A single episode of hypotension during this period doubled mortality and also increased morbidity. Patients without correction of hypotension in the field had a worse outcome than those whose hypotension was corrected by ED arrival. |
| Luerssen, 1988 ⁹ | Prospective series of 8,814 adult and pediatric TBI patients admitted to 41 metropolitan hospitals in NY, TX and CA in 1980–81. 22% pediatric patients (1,906 < 15 yr); adult TBI patients (6,908 > 15 yr). Measures: age, sex, admission vital signs, injury mechanism, GCS post resuscitation, pupillary response, associated injury/AIS, "major symptoms", and brain injury by imaging or at surgery, and mortality prior to hospital discharge. Hypoxia not studied. Profound hypotension: systolic BP 30 mmHg below median for age. Analysis: Two by two tables by Pearson's chi-square test with Yates correction. Ordered contingency tables by Mantel-Haentzel. Logistic regression for age vs. survival. | III | Both hypotension and hypertension were associated with higher adult mortality. Only hypotension was associated with higher mortality in children. Children with severe hypertension had the lowest mortality rate. Pediatric mortality was significantly lower than adult mortality, with notable exceptions of children with profound hypotension (33.3% < 15 yr vs. 11.8% > 15 yr) or subdural hematoma (40.5% < 15 yr vs. 43.9% > 15 yr). |
| Vassar, 1993 ¹⁵ | A randomized, double-blind, multicenter trial comparing the efficacy of administering 250 mL of hypertonic saline vs. normal saline as the initial resuscitation fluid in 194 hypotensive trauma patients over a 15-month period. 144 (74%) had severe TBI (defined as an AIS for the head of 4–6). | II | No significant increase in the overall survival of patients with severe TBI, however, the survival rate in the hypertonic saline group was higher than that in the normal saline group for the cohort with baseline GCS score of 8 or less. |
| Vassar, 1990 ¹⁶ | Randomized, double-blind, clinical trial of 106 patients over an 8-month period. Intracranial hemorrhage was present in 28 (26%). | II | No adverse effects of rapid infusion of 7.5% NaCl or 7.5% NaCl/6% dextran 70 were noted. No beneficial effects were noted. No evidence of potentiating intracranial bleeding. |
| Vassar, 1991 ¹⁷ | Randomized, double-blind, multi-center clinical trial of 166 hypotensive patients over a 44-month period. 53 (32%) had severe TBI (defined as an abbreviated injury score for the head of 4, 5, or 6). Compared survival to discharge for patients receiving hypertonic saline/dextran (HSD) with those receiving normal saline (LR). | II | The rate of survival to hospital discharge in patients with severe TBI was significantly higher in those patients who received hypertonic saline/dextran (HSD) (32% of patients with HSD vs. 16% in patients with LR). |
| Vassar, 1993 ¹⁸ | Randomized, double-blind, clinical trial of 258 hypotensive patients over 31 months at a university-based trauma center. 27 (10%) had severe TBI. Administered 7.5% NaCl (HS) and 7.5% NaCl/6% dextran 70 (HSD). | II | HS and HSD caused no neurological abnormalities. Both were associated with decreased mortality in patients with initial GCS < 8 and in those with anatomic confirmation of severe cerebral damage. |

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|---------------------------|---|------------|---|
| Wade, 1997 ¹⁹ | Retrospective analysis of individual patient data from previously published randomized double-blind trials of hypertonic saline/dextran in patients with TBI and hypotension. TBI was defined as AIS for the head of > 4. 1,395 data records were analyzed from six separate studies. 233 patients were included. 80 patients were treated in the ED, 143 were treated in the pre-hospital phase. | III | Logistic regression analysis was performed on patients with TBI showing an odds ratio of 1.92 for 24-hr survival and 2.12 for survival until discharge. Thus, patients with TBI in the presence of hypotension who received hypertonic saline/dextran were approximately twice as likely to survive as those who received saline ($p = 0.048$). |
| Cooper, 2004 ⁴ | New Study Double blind randomized controlled trial of 229 patients with TBI who were comatose (GCS < 9) and hypotensive (systolic blood pressure < 100 mmHg). Studied between 1998 and 2002. Patients were randomized to rapid perfusion of either 250 mL of 7% saline or 250 mL of Ringer's lactate. | II | Survival to hospital discharge and survival at 6 months were equal in the 2 groups. No significant difference between groups in the GOS at 6 months or in any other measure of post-injury neurologic function. |

EVIDENCE TABLE 2. Pediatrics

| Reference | Study Description | Data Class | Conclusion |
|-----------------------------|---|------------|--|
| Johnson, 1995 ⁶ | Retrospective medical record and imaging review of 28 children with confirmed child abuse with significant TBI. | III | Apnea was present in majority of patients and 50% of children were also hypotensive. No patient with clinical evidence of cerebral hypoxia and/or ischemia had a good outcome. |
| Kokoska, 1998 ⁷ | Retrospective chart review, 1990–95 measuring presence of hypoxia, hypotension, or hypercarbia during transport, ED, OR, and first 24 hours in PICU. | III | Early hypotension linked to prolonged length of stay and worse 3 month GOS. |
| Levin, 1992 ⁸ | Prospective data bank cohort study of 103 children (< 16 years) with severe TBI (GCS < 9). | III | Outcome was poorest in 0-4 year age group, which had an increased incidence of evacuated subdural hematomas (20%) and hypotension (32%). 14-21% in all age ranges were hypoxic. |
| Luerssen, 1988 ⁹ | Prospective series of 8,814 adult and pediatric TBI patients admitted to 41 metropolitan hospitals in NY, TX and CA in 1980–81. 22% pediatric patients (1,906 < 15 yr); adult TBI patients (6,908 > 15 yr). | III | Only hypotension was associated with higher mortality in children. Children with severe hypertension had the lowest mortality rate. |
| Mayer, 1985 ¹⁰ | Prospective study (1978–1981) of 200 consecutive children (3 wk–16 yr, mean 5.6 yr) with severe TBI (GCS < 8). | III | Mortality 55% with any hypotension, hypercarbia or hypoxia vs. 7.7% without. |
| Michaud, 1992 ¹¹ | Retrospective study of prospectively collected Trauma Registry data in 75 children presenting to Harborview Medical Center with severe TBI (GCS 8 or less) between January 1, 1985 and December 31, 1986. Assessed fatality rate in system with advanced EMS and regional trauma center (83% received EMS field care). Identified factors predictive of survival and/or disability. GOS at discharge from acute care hospital measured. | III | Mortality increased if hypotension or abnormal pupils noted in the field. ED $pO_2 > 350$ better outcome; pO_2 105–350 same outcome as hypoxic group. |
| Ong, 1996 ¹² | Prospective cohort study of 151 consecutive children (< 15 yr) admitted within 24 hr of TBI (GCS < 15) from 1993–1994 in Kuala Lumpur. Follow-up GOS at discharge and 6 months. | III | Hypoxia increased poor outcome by 2 to 4 fold in severe TBI. |
| Pigula, 1993 ¹³ | Five-year prospective cohort study of 58 children (< 17 yr) and a matched set of 112 adults with severe TBI (GCS < 8). Group I – normal BP and PaO_2 . Group II – hypotension or hypoxia or both. Adults compared to this subgroup. | III | Hypotension with or without hypoxia causes significant mortality in children to levels found in adults. Adequate resuscitation probably the single most critical factor for optimal survival. Survival fourfold higher with neither hypoxia nor hypotension compared with either hypoxia or hypotension ($p < 0.001$). |

III. OVERVIEW

Hemorrhage following trauma decreases cardiac preload. When compensatory mechanisms are overwhelmed, this hypovolemia leads to decreased peripheral perfusion and oxygen delivery. Fluid therapy is used to replete preload, supporting cardiovascular function and peripheral oxygen delivery. This is particularly important in patients with TBI, as decreased cerebral perfusion can increase the extent of primary neurological injury. Specifically, hypotension has been shown to produce significant secondary brain injury and substantially worsen outcome.

In adults, hypotension is defined as a systolic blood pressure (SBP) < 90 mmHg. In children, hypotension is defined as SBP less than the 5th percentile for age or by clinical signs of shock. Usual values are:

- <60 mmHg in term neonates (0 to 28 days)
- <70 mmHg in infants (1 month to 12 months)
- <70 mmHg + 2 X age in years in children 1 to 10 years
- <90 mmHg in children > 10 years

To date, crystalloid fluid has been used most often to augment cardiac preload, maintain cardiac output, and support peripheral oxygen delivery in trauma patients. The recommendation for adults is to rapidly infuse two liters of Ringer's lactate or normal saline as the initial fluid bolus.¹ In children, fluid resuscitation is indicated for clinical signs of decreased perfusion even when an adequate blood pressure reading is obtained.

The goal of prehospital fluid resuscitation is to support oxygen delivery and optimize cerebral hemodynamics. Crystalloid fluid is most often used, although other options such as hyperoncotic and hypertonic fluids as well as hemoglobin substitutes have been used. If hypotension does occur, blood pressure and oxygen delivery should be promptly restored to avoid secondary brain injury. Ideally, this infusion should be accomplished without causing secondary blood loss or hemodilution.

IV. PROCESS

For this update Medline was searched from 1996 through July 2006 using the search strategy for this question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 15 potentially relevant publications, 1 was added to the existing table and used as evidence for this question. For pediatric studies, of 23 potentially relevant publications, no new studies were included (see Evidence Tables).

V. SCIENTIFIC FOUNDATION

Adult

A. Hypotensive patients should be treated with isotonic fluids.

Foundation. The deleterious effects of hypotension in both adult and pediatric patients with TBI have been documented. Early hypotension has been shown to be a statistically significant and independent factor associated with worsening outcome from TBI.^{3,5,9,20} From the report on prediction of outcome from TBI,² hypotension was one of the five factors found to have a 70% or greater positive predictive value for mortality. Despite the solid evidence of the negative influence of early hypotension on outcome from TBI in adults, there is much less evidence that reducing or preventing this secondary insult improves outcome.

Because the underlying cause of hypotension in these patients is almost always blood and/or fluid losses, intravascular volume repletion is the most effective way of restoring blood pressure. In contrast, data indicate that early restoration of blood pressure in patients with penetrating torso trauma worsens outcome. The relationship between these data and outcome in patients with TBI is unknown.

Specific evidence indicating that pre-hospital protocols prevent or minimize hypotensive insults and improve outcome is minimal. Despite the use of multivariate analysis to control for confounding variables, the possibility remains that some, most, or all secondary insults occurring during the pre-hospital period that are associated with poor recovery are simply manifestations of the severity of injury and not treatable entities.

B. Hypertonic resuscitation is a treatment option for TBI patients with a Glasgow Coma Scale Score (GCS) < 8.

Foundation. Isotonic crystalloid solution is the fluid most often used in the prehospital resuscitation of TBI patients. However, little data have been published to support its use.

Wade reviewed a set of studies containing data for patients with TBI who received hypertonic saline.¹⁹ Survival to discharge was 38% for patients treated with hypertonic saline and 27% for standard therapy ($p = 0.08$). When logistic regression analysis was performed comparing hypertonic with isotonic fluids, the odds ratio was 1.92 for 24-hour survival and 2.12 for survival to discharge ($p = 0.048$).

Vassar *et al.* published four randomized, double-blind trials of hypertonic saline.^{15,16,17,18} In the first, comparing two groups of TBI patients receiving either hypertonic or normal saline, no differences in outcome were found.¹⁶ Additionally, intracranial bleeding did not increase with either therapy. In a later study comparing hypertonic saline with Ringer's lactate in 166 patients, (32% with severe TBI) logistic regression analysis showed the hypertonic saline group to have improved

survival.¹⁷ A third study of 258 patients (10% with severe TBI) compared hypertonic saline with hypertonic saline and dextran.¹⁸ In patients with a GCS less than 8 or with severe anatomic cerebral damage, survival with either fluid was greater than predicted by the Trauma Related Injury Severity Score (TRISS). In 1993, Vassar published a multi-center trial of 194 patients, 74% had severe TBI.¹⁵ Although there was no overall effect on survival, patients in the hypertonic saline group with an initial GCS < 8 had better survival.

More recently, Cooper *et al.* reported a randomized double blind trial of hypertonic saline or standard fluid therapy in 229 patients with severe TBI and hypotension.⁴ Multi-trauma patients were included but patients with comorbid conditions, peripheral edema or close proximity to the hospital were excluded. Following an initial fluid bolus of 250 mL, patients received standard resuscitation, both in the field and in the hospital. There were no differences in outcomes between the two groups.

Pediatrics

A. For the pediatric TBI patient, hypotension should be treated with isotonic solutions.

Foundation. The negative impact of hypotension with or without hypoxia and hypercarbia in patients with severe TBI has been demonstrated repeatedly in studies of mixed adult and pediatric populations.^{2,3,5,14} In these studies, hypoxia, hypercarbia, and hypotension were all commonly observed.

In a prospective study of 200 children, Mayer¹⁰ found that mortality was 55% in the presence of hypoxia, hypercarbia or hypotension and only 7.7% without any of these factors present ($p < 0.01$). In a prospective cohort study by Ong¹² in Kuala Lumpur, the presence of hypotension increased the probability of a poor outcome. In the setting of abusive TBI, Johnson⁶ found that apnea was present in the majority of patients and 50% were also hypotensive. It was concluded that cerebral hypoxia and/or ischemia was more strongly associated with poor outcome than mechanism of injury.

Pigula *et al.*¹³ analyzed the influence of hypotension on mortality from severe TBI (GCS ≤ 8) in two prospectively collected pediatric (age ≤ 16 years) databases. The participating centers were well developed pediatric trauma centers. They reported an 18% incidence of hypotension (defined as either a systolic blood pressure (SBP) ≤ 90 mmHg or a SBP less than the fifth percentile for age) on arrival to the emergency department. A mortality rate of 61% was observed with hypotension on admission versus 22% among patients without hypotension. When hypotension was combined with hypoxia, the mortality rate was 85%. Hypotension was a statistically significant predictor of outcome with a PPV of 61% for mortality. Early hypotension negated the improvement in survival from severe TBI that is generally afforded by youth.

Kokosa *et al.*⁷ performed a retrospective chart review of all pediatric patients admitted to a single Level I trauma center over a 5 year period. Limiting the patient population to children with non-penetrating TBI with post-resuscitation age-adjusted GCS scores between 6–8 ($n = 72$), they indexed secondary insults occurring during transport to the emergency department up through the first 24 hours in the ICU. Hypotension was defined as five or more minutes at or below the fifth percentile for age according to the Task Force on Blood Pressure Control in Children.¹ The majority of hypotensive episodes occurred during resuscitation in the ED (39%) and the PICU (37%). Patients with residual moderate and severe disability had experienced significantly more hypotensive episodes than those with good outcomes.

Michaud¹¹ found that hypotension in the field and emergency department was significantly related to mortality in children. In a data bank study from four centers,⁸ Levin found that outcome was poorest in patients 0–4 year olds, which was the group that demonstrated high rates of hypotension (32%).

In a prospective series of 6,908 adults and 1906 children less than 15 years of age at 41 centers, Luerssen *et al.*⁹ found that hypotension was significantly associated with higher mortality in children. They reported a greater deleterious effect of hypotension in children than adults. Notably, children with severe hypertension had the lowest mortality rate.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

Studies of fluid resuscitation in the prehospital setting are needed. Few data exist to guide endpoints of therapy. The current concern that raising blood pressure may increase secondary blood loss after certain types of trauma, thus worsening cerebral hemodynamics, needs to be validated in humans. Additional investigation to determine the most effective fluid for resuscitation, and the role of “newer” fluid regimens including various hypertonic solutions, mannitol, and synthetic colloids needs to be performed.

There is a lack of studies in children that assess whether prehospital protocols directed at minimizing or preventing hypotension actually improve outcome from TBI. This issue may be approached using large, prospectively collected observational databases that allow analysis of blood pressure and volume status while controlling for confounding variables. It has been suggested that supranormal blood pressures may be acceptable or even associated with improved outcome in children with severe TBI.²⁰ Further investigation in this area is needed.

The following specific questions need to be studied in the prehospital arena for both adults and children:

1. What is the optimal target blood pressure for resuscitation in patients with either isolated TBI or those with multiple injuries including TBI?

2. Is mean arterial blood pressure a better endpoint than systolic blood pressure?
3. Is there a subgroup of brain injured patients in whom a lower volume of resuscitation fluid should be used?
4. What is the ideal resuscitation fluid in the prehospital setting?
5. Is there a role for large particle colloids in the prehospital setting?
6. What is the role of hemoglobin substitutes in the prehospital setting?
7. Can noninvasive field technology identify and help titrate therapy in the prehospital setting of patients with severe TBI?

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VI. TREATMENT: CEREBRAL HERNIATION

I. RECOMMENDATIONS

Strength of Recommendations: Weak
Quality of Evidence: Low, primarily from Class III studies and indirect evidence.

Adult and Pediatrics

- A. Mild or prophylactic hyperventilation (PaCO₂ < 35 mmHg) should be avoided. Hyperventilation therapy titrated to clinical effect may be necessary for brief periods in cases of cerebral herniation or acute neurologic deterioration.³
- B. Patients should be assessed frequently for clinical signs of cerebral herniation. The clinical signs of cerebral herniation include dilated and unreactive pupils, asymmetric pupils, a motor exam that identifies either extensor posturing or no response, or progressive neurologic deterioration (decrease in the Glasgow Coma Scale

[GCS] Score of more than 2 points from the patient's prior best score in patients with an initial GCS < 9).

- C. In patients who are normoventilated, well oxygenated, and normotensive – and still have signs of cerebral herniation – hyperventilation should be used as a temporizing measure, and discontinued when clinical signs of herniation resolve.

Hyperventilation is administered as:

- 20 breaths per minute in an adult
- 25 breaths per minute in a child
- 30 breaths per minute in an infant less than 1 year old

The goal of hyperventilation is ETCO₂ of 30-35 mmHg. Capnography is the preferred method for monitoring ventilation.

³Duplicated from Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents.¹

II. EVIDENCE TABLE

EVIDENCE TABLE 1.

| Reference | Study Description | Data Class | Conclusion |
|--|---|------------|--|
| Cooper, 2004 ⁸ | Double blind randomized controlled trial of 229 patients with TBI who were comatose (GCS < 9) and hypotensive (systolic blood pressure < 100 mmHg). Studied between 1998 and 2002. Patients were randomized to rapid perfusion of either 250 mL of 7% saline or 250 mL of Ringer's lactate. | II | Survival to hospital discharge and survival at 6 months were equal in the 2 groups. No significant difference between groups in the GOS at 6 months or in any other measure of post-injury neurologic function. |
| Davis <i>et al.</i> , 2004 ¹⁰ | A retrospective linear regression analysis of the impact of hypocapnia and decreased oxygen saturation during pre-hospital rapid sequence intubation (RSI) on patient mortality. Patients undergoing rapid sequence intubation were matched with historical controls. | III | Hyperventilation and severe hypoxia during paramedic RSI were associated with an increase in mortality. |
| Muizelaar <i>et al.</i> , 1991 ²⁴ | Sub-analysis of an RCT of THAM in which 77 adults and children with severe TBI were enrolled. | II | Patients with an initial GCS motor score of 4–5 that were hyperventilated to a PaCO ₂ of 25 mm Hg during the first 5 days after injury had significantly worse outcomes 6 months after injury than did those kept at a PaCO ₂ of 35 mm Hg. |
| Qureshi <i>et al.</i> , 1999 ²⁷ | Retrospective analysis comparing continuous administration of 3% sodium chloride/acetate solution at 75-150 mL/hr (N = 30) or 2% solution (N = 6) to NS maintenance in 82 TBI patients with GCS ≤ 8. | III | More penetrating TBI and mass lesions in HS group. HS group had a higher in-hospital mortality. Patients treated with HS were more likely to receive barbiturate treatment. |

EVIDENCE TABLE 1.

| Reference | Study Description | Data Class | Conclusion |
|---|--|------------|---|
| Schwartz <i>et al.</i> , 1984 ³³ | Randomized trial comparing mannitol with barbiturates for ICP control. Crossover permitted. Sequential analysis n=59. | III | Pentobarbital was not significantly better than mannitol. Mannitol group had better outcome mortality 41% vs. 77%. CPP much better with mannitol than barbiturates (75 mmHg vs. 45 mmHg) |
| Shackford <i>et al.</i> 1998 ³⁴ | Randomized controlled trial comparing 1.6% saline to lactated Ringer's for hemodynamic instability in pre and in-hospital phase in 34 patients with TBI and GCS \leq 13. | III | Baseline ICP higher and GCS lower in HS group. Despite this, HS effectively lowered ICP; ICP course was not different between groups. Cumulative fluid balance greater in LR group. Daily serum sodium, osmolarity and ICP interventions greater in HS group. GOS was not different between groups. |

III. OVERVIEW

Neuronal injury may result from the initial trauma (primary injury) or as the result of indirect mechanisms (secondary injury), such as hypoxemia, hypotension, and cerebral edema. Injury may also occur as the result of associated conditions that caused the trauma, such as hypoglycemia or drug toxicity. The goal of resuscitation in TBI is to preserve cerebral perfusion and to minimize neuronal injury. As discussed in other sections of these guidelines, hypotension and hypoxemia are associated with poor outcomes in patients with TBI, thus systemic resuscitation is the highest priority in prehospital management.

Management of patients with TBI is directed at maintaining cerebral perfusion. Signs of cerebral herniation include dilated or unreactive pupil(s), asymmetric pupils, extensor posturing, or progressive neurologic deterioration (decrease in the GCS score of more than 2 points from the patient's prior best score in patients with an initial GCS less than 9).³¹

Hyperventilation is beneficial in the immediate management of patients demonstrating signs of cerebral herniation, but it is not recommended as a prophylactic measure.⁶ Mannitol is effective in reducing intracranial pressure (ICP) and is recommended for control of increased ICP. A number of pharmacologic agents have been investigated in an attempt to prevent the secondary injury associated with TBI, but none have proven efficacious.²³

IV. PROCESS

For this topic Medline was searched from 1996 through July 2006 using the search strategy for this question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 69 potentially relevant publications, 6 were used as evidence for this topic. For pediatric studies, of 48 potentially relevant publications, no studies were used as evidence for this topic (see Evidence Table).

V. SCIENTIFIC FOUNDATION

Adult and Pediatrics

- A. Mild or prophylactic hyperventilation (PaCO₂ < 35 mmHg) should be avoided. Hyperventilation therapy titrated to clinical effect may be necessary for brief periods in cases of cerebral herniation or acute neurologic deterioration.

- B. Patients should be assessed frequently for clinical signs of cerebral herniation.

The clinical signs of cerebral herniation include dilated and unreactive pupils, asymmetric pupils, a motor exam that identifies either extensor posturing or no response, or progressive neurologic deterioration (decrease in the Glasgow Coma Scale [GCS] Score of more than 2 points from the patient's prior best score in patients with an initial GCS < 9).

- C. In patients who are normoventilated, well oxygenated, and normotensive – and still have signs of cerebral herniation – hyperventilation should be used as a temporizing measure, and discontinued when clinical signs of herniation resolve.

Hyperventilation is administered as:

- 20 breaths per minute in an adult
- 25 breaths per minute in a child
- 30 breaths per minute in an infant less than 1 year old

The goal of hyperventilation is ETCO₂ of 30–35 mmHg. Capnography is the preferred method for monitoring ventilation.

Foundation. Hyperventilation in the acute setting reduces ICP by causing cerebral vasoconstriction with a subsequent reduction in cerebral blood flow.²⁸ Hyperventilation has been shown to reduce ICP in many patients with cerebral edema.²² There is evidence that hyperventilation also reduces cerebral blood flow, a deleterious effect.²⁸ Class II data indicate that patients chronically hyperventilated in the in-hospital setting

have worse outcomes at 3 and 6 months but equivalent outcomes at one year.²⁴

It appears that in some patients with progressive cerebral edema, hyperventilation can temporize impending herniation. In patients who have objective evidence of herniation, the benefits of hyperventilation in delaying that process outweigh the potential detrimental effects. The key to hyperventilation therapy, therefore, becomes the ability to identify those patients at risk for herniation and to avoid hyperventilation in those not at risk; that is, to carefully avoid the routine hyperventilation of all TBI patients and especially those not at risk for herniation. Unfortunately, unintentional hyperventilation appears to be common in the prehospital environment from a variety of causes.²¹ Even the use of capnography can not assure the avoidance of inadvertent hyperventilation.^{4-7,9,13,17,18,20,29,30,35}

A recent study demonstrated a relationship between field intubation and poor outcomes.¹⁰ The authors investigated the association between hyperventilation and increased morbidity; *post hoc* analysis indicated a relationship between lower PaCO₂ upon arrival in the emergency department and poorer outcomes.^{9,11} These data, however, are retrospective and use emergency department blood gas measurements as a surrogate assessment of field ventilation.

In the hospital setting, intracranial pressure (ICP) is used as a guide for the use of hyperventilation. Since this is not available in the prehospital phase, clinical criteria must substitute to identify those patients at risk. Consequently, hyperventilation is reserved as a temporizing measure for those patients with severe TBI who show signs of cerebral herniation (defined above).

Although not specifically supported by TBI outcome data, current best practice would appear to be to assure adequate oxygenation as described elsewhere in this document, and per American Heart Association Cardiopulmonary Resuscitation ventilation protocols. For patients who demonstrate or develop signs of cerebral herniation, hyperventilation should be instituted, as determined by ventilatory rate; that is 20 bpm in an adult, 25 bpm in a child, and 30 bpm in an infant less than one year old.²

Hyperosmolar Therapies. Mannitol has long been accepted as an effective tool for reducing intracranial pressure.^{3,15,19,33,36} Numerous mechanistic laboratory studies support this conclusion. However, there is no evidence to support its use in the prehospital setting. In addition, its impact on outcome has not been demonstrated in a Class I trial that tests mannitol against placebo. Schwartz *et al.* conducted a study comparing mannitol to pentobarbital which failed to demonstrate the superiority of pentobarbital and which demonstrated better outcomes and maintenance of CPP in the mannitol group.³³

Hypertonic saline offers an attractive alternative to mannitol as a brain targeted hyperosmotic therapy.

Its ability to reduce elevated ICP has been demonstrated with studies in the ICU and in the operating room.^{12,16,25,26} Hypertonic saline is a low volume resuscitation fluid. While the qualities that make it useful as a low volume resuscitation fluid and as a brain targeted therapy are related, this discussion will be limited to its role as a brain targeted therapy.

There is no consensus on what is meant by "hypertonic saline". Concentrations of 3%, 7.2%, 7.5%, 10% and 23.4% have all been used. There is no consensus on the optimum concentration for reduction of ICP.^{12,16,25,37} Hypertonic saline is dosed in different ways. In some studies, it is given as an infusion, the goal of which is to elevate serum sodium to 155- 160 mEq/L, although some investigators have gone as high as 180 mEq/L. This elevated serum sodium is thought to help stabilize ICP and reduce the therapeutic intensity required to prevent elevated ICP.^{26,27} This modality would not be used in the prehospital environment.

Multiple animal studies and several human studies have demonstrated that hypertonic saline, as a bolus, can reduce ICP in a monitored environment such as the operating room or ICU where ICP monitoring is present.^{14,35,37} Comparison of these studies is difficult since they do not use the same concentrations or protocols. Unlike mannitol, no study has demonstrated an effect of hypertonic saline on clinical indicators of herniation, such as pupillary widening or posturing.

One Class II study evaluated the impact of prehospital hypertonic saline on neurological outcome.⁸ Hypertonic saline did not demonstrate any advantage over normal saline on neurological outcome when given as a prehospital resuscitation fluid. Similarly, a Class III study comparing 1.6% saline to lactated Ringer's found no difference in outcomes between groups, but baseline differences and other flaws limit the findings of this study.³⁶ The current literature therefore does not support the use of hypertonic saline as a brain-targeted therapy in the prehospital environment. This conclusion, however, does not extend to its use as a resuscitation fluid, a topic covered elsewhere in these guidelines.

Pediatrics – Additional Considerations

As stated in the Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents,¹ the effect of hyperventilation on long-term outcome has not been addressed in pediatric TBI. We used their recommendations relevant to prehospital care, which were based upon indirect evidence from adult studies.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

Further data on the impact of the prehospital use of hypertonic saline on TBI outcome is needed. Cognitive

recovery as a separate endpoint from blood pressure resuscitation needs to be investigated.

The use of capnography in managing prehospital hyperventilation needs to be better defined. Current extrapolations from in-hospital and operating room settings are inaccurate and misleading. Independent prehospital data on the use and limitations of capnography is needed. Evidence-based capnography thresholds need to be developed.

Better prehospital methods are needed for assessing which patients are at risk for herniation or in need of high level TBI interventions.

The role of mannitol in herniation should be investigated.

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DECISION MAKING

VII. DECISION MAKING WITHIN THE EMS SYSTEM: DISPATCH, SCENE, TRANSPORTATION, AND DESTINATION

I. RECOMMENDATIONS

Strength of Recommendations: Weak
 Quality of Evidence: Low, from Class III studies, contradictory findings, and indirect evidence.

Adult

- A. All regions should have an organized trauma care system.
- B. Protocols are recommended to direct Emergency Medical Service (EMS) personnel regarding destination decisions for patients with severe traumatic brain injury (TBI).
- C. Patients with severe TBI should be transported directly to a facility with immediately available CT scanning, prompt neurosurgical care, and the ability to monitor intracranial pressure (ICP) and treat intracranial hypertension.

- D. The mode of transport should be selected so as to minimize total prehospital time for the patient with TBI.

Pediatrics

- A. In a metropolitan area, pediatric patients with severe TBI should be transported directly to a pediatric trauma center if available.
- B. Pediatric patients with severe TBI should be treated in a pediatric trauma center or in an adult trauma center with added qualifications to treat children in preference to a Level I or II adult trauma center without added qualifications for pediatric treatment.

II. EVIDENCE TABLES

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|-----------------------------|--|------------|--|
| Guss, 1989 ¹⁰ | Compared non-CNS and CNS preventable deaths before and after a trauma system was implemented. | III | Preventable deaths for both non-CNS and CNS patients decreased after placement of a trauma system. |
| Norwood, 1995 ²¹ | Compared outcome of injured patients in a rural hospital before and after becoming a level II trauma center. | III | For TBI patients, survival was 15.4% before and 32% after meeting the criteria |
| New Studies | | | |
| Baxt, 1987 ³ | Analysis of 232 TBI patients to compare survival for those transported by ground ambulance vs. helicopter. The helicopter was staffed by a physician and a nurse. | III | 9% reduction in mortality for patients transported by helicopter. |
| Cornwell, 2003 ⁵ | Examined a trauma registry: used a before-after design to determine the effect of systematic changes to achieve a Level I trauma center designation. | III | Among severe TBI patients there was a 7% decrease in mortality rates that was not statistically significant. |
| Davis, 2005 ⁷ | Reviewed data from a trauma registry on 10,314 patients with a head Abbreviated Injury Score of 3 or more and compared those transported by ground ambulance to those transported by helicopter. | III | Patients transported by helicopter had a better odds of survival (1.90; 95% confidence interval 1.6 to 2.25) compared to ground transport after controlling for potential confounding variables. |

EVIDENCE TABLE 1. Adult

| Reference | Study Description | Data Class | Conclusion |
|----------------------------------|--|------------|--|
| Di Bartolomeo, 2001 ⁸ | Analysis of a trauma registry in Italy to compare outcome of severe TBI patients transported by a ground ambulance with nurse level providers to helicopter transport with a physician level provider. | III | No significant difference between groups. |
| Hannan, 2005 ¹¹ | Used the New York state trauma registry to compare outcomes between regional trauma centers and other receiving facilities for trauma patients. | III | Patients with TBI had a lower odds of death when treated at a regional trauma center compared to other treatment facilities. |
| Hunt, 1995 ¹³ | Before-after comparison of survival rates among TBI patients after a regionalized trauma system was established. | III | A decrease in mortality from 42% to 26% was observed, that was not statistically significant. |
| Lee, 2002 ¹⁵ | Analysis of a trauma registry in Sydney, Australia to compare outcomes for patients treated by Basic Life Support (BLS) providers vs. physician/paramedic providers. Stratified by TBI. | III | There was no increased benefit for either level of provider among patients admitted to the ICU. There was an increased risk of death among those treated by physicians or paramedics if they did not go to the ICU (possibly due to selection bias at dispatch). |
| Lokkeberg, 1984 ¹⁷ | Analysis of a trauma registry for 3 major trauma hospitals in Texas to determine factors related to outcome from TBI. | III | Time to emergency department arrival was not a significant predictor of outcome. Transport by ambulance vs. helicopter did not affect outcome. |
| McConnell, 2005 ¹⁹ | Retrospective analysis of mortality at 30-day post hospital discharge for TBI patients transferred to Level I vs. Level II trauma centers. Used bivariate probit, instrumental variables model. | III | Significantly lower mortality for patients transferred to Level I vs. Level II centers (p = 0.017). Mean absolute mortality benefit of transfer to Level I center = 10.1% (95% CI: 0.3%, 22.1%). |
| Wilberger, 1991 ²⁷ | Examined the effect of time to surgery for patients with acute subdural hematoma. | III | No statistically significant difference in outcome for early operative treatment. 10% absolute decrease in mortality for those treated within 4 hours. |

EVIDENCE TABLE 2. Pediatrics

| Reference | Study Description | Data Class | Conclusion |
|------------------------------------|--|------------|---|
| Potoka et al., 2001 ²³ | Retrospective medical record review of children treated for TBI in Pennsylvania. Independent variable was Level of pediatric accommodation in trauma center (Pediatric Trauma Center - PTC, Adult Trauma Center -ATC, Additional Qualifications- AQ, Adult Trauma Center Level I -ATC I, Adult Trauma Center Level II - ATC II). Dependent variables were mortality, neurosurgical procedures, mortality for patients receiving neurosurgical procedures. | III | Survival higher in PTC or ATC AQ than Level I or II ATCs for severe TBI. Equal chance of survival for severe TBI requiring neurosurgery in PTC, ATC AQ, or Level I ATC, but not Level II ATC. Equal chance of survival for moderate TBI regardless of facility. For moderate TBI, more likely to have neurosurgery in PTC or Level I ATC, and if they do, less likely to die; less likely to have neurosurgery in ATC AQ or Level II ATC, and if they do, more likely to die. |
| Johnson et al., 1997 ¹⁴ | Prospective non-randomized comparison of mortality for direct (n = 135) vs. indirect (n = 90) transports to Level I PTC. | III | For severe TBI, survival higher for Direct Transport patients than Indirect Transport patients. Equal chance of survival for moderate TBI regardless of transport method. |

III. OVERVIEW

Prehospital recognition of TBI and the subsequent response are paramount to the patients' recovery. Decisions made in the prehospital setting by EMS dispatchers and care providers in the field occur in a stepwise fashion, and include:

1. Information gathered by EMS call-takers and dispatchers to determine if a patient potentially has a significant brain injury.
2. Dispatcher decisions about the type of personnel to be dispatched, resources to be deployed, and assignment of priority for a response.
3. Prehospital care provider assessment of the overall neurologic situation through evaluation of the mechanism of the injury (i.e., vehicular deformation, windshield violation, the use or nonuse of seat belts or other safety devices), the scene, and the patient examination.
4. Based on the overall assessment, prehospital interventions are initiated to prevent or correct hypotension or hypoxemia and to address other potential threats to life or limb. At this step, the decision regarding the level of responder dispatched to the scene impacts patient care.

5. Prehospital care providers select a transport mode (e.g., ground ambulance versus helicopter, red lights and siren versus neither).
6. Prehospital care providers select the appropriate destination facility.

IV. PROCESS

For this update Medline was searched from 1996 through July 2006 using the search strategy for this question (see Appendix B), and results were supplemented with literature recommended by peers or identified from reference lists. For adult studies, of 39 potentially relevant publications, 10 were added to the existing table and used as evidence for this question. For pediatric studies, of 14 potentially relevant publications, 2 were included as evidence for this topic (see Evidence Tables).

V. SCIENTIFIC FOUNDATION

Adult

- A. All regions should have an organized trauma care system.
- B. Protocols are recommended to direct Emergency Medical Service (EMS) personnel regarding destination decisions for patients with severe traumatic brain injury (TBI).
- C. Patients with severe TBI should be transported directly to a facility with immediately available CT scanning, prompt neurosurgical care, and the ability to monitor intracranial pressure (ICP) and treat intracranial hypertension.
- D. The mode of transport should be selected so as to minimize total prehospital time for the patient with TBI.

Foundation

Dispatch

While there is no definitive evidence that formal interrogation of callers requesting emergency aid (i.e., calls to 9-1-1 or the local emergency access number) can assist dispatchers in accurately identifying TBI patients, evidence for other disease processes supports its potential for TBI patients.¹² It is critical for a well functioning EMS system to consistently match the right providers to the patient. Formalized interrogation of callers by specially trained dispatchers is capable of sorting patients based on need.^{2,6,25} However, other researchers have found that the accuracy is not as high compared to the findings of providers who evaluate the patient for need in person.^{20,22} This discrepancy indicates that the ideal interrogation system may not yet have been developed.

A secondary roll of emergency medical dispatchers is their ability to provide pre-arrival instructions. At

this time it is unknown what instructions, if any, dispatchers could provide to callers that might improve outcomes for patients with TBI. However, it has been shown that callers expect to receive instructions from the dispatchers.⁴

Level of Care at the Scene

Determining the necessary resources to send to the scene depends on the effect those resources will have on patient outcome. The primary choice is the level of care that is needed. This has traditionally been stated as basic life support (BLS) or advanced life support (ALS). However, since the skills taught to BLS and ALS providers can vary by state and even by region it is difficult to provide a universal definition for these provider types.

In a study by Di Bartolomeo and colleagues in Italy, outcome of TBI patients cared for by nurses who transported by ground ambulance was compared to physicians treatment in helicopter transport.⁸ The authors found no significant difference in patient outcome between the transport protocols. Lee *et al.* looked at mortality from TBI among those treated and transported by BLS providers compared to those treated and transported by paramedic or physician level providers.¹⁵ This group found no significant difference in outcome among patients admitted to the intensive care unit. Those who died in the first 24-hours were more likely to have been treated and transported by physicians or paramedics, but this finding may have been due to selection bias since the dispatch process selected the more severely injured for their response. Therefore, the most appropriate level of provider to care for a patient with TBI is unknown.

Identification of Traumatic Brain Injury

Recognition of patients who have a high potential for TBI involves consideration of physiologic (e.g., GCS score) and anatomic (e.g. depressed skull) signs and symptoms as well as mechanisms of injury (e.g., falls of greater than 20 feet) that result in sufficient force to increase the potential for injury.

In general, the American College of Surgeons Committee on Trauma Field Triage Decision Scheme is used by most states to identify patients that require transport to a trauma center.^{24,26}

Transport Mode

Determining the most appropriate mode of transport requires providers to determine whether to transport the patient by ground ambulance or helicopter and if the patient is transported by ground ambulance whether or not to use lights and siren. The primary advantage of one transport mode over another is a reduction in transport time. However, the entire prehospital time interval must be considered and not just the

time interval from departure from the scene to arrival at the hospital.

The effect of delayed prehospital time on outcome from TBI is unknown. Prehospital providers are typically trained that all patients must be transported so that they are able to receive surgery within the first hour after injury. This concept, referred to as the golden hour, is an excellent teaching tool for prehospital providers but the exact effect of time on patient outcome is unknown.¹⁶

It has been shown that acute subdural hematomas in severe TBI patients are associated with a 90% mortality if the patient undergoes surgery more than 4 hours after injury, and 30% mortality if evaluated earlier.²⁸ One study reported a 70% decrease in mortality if subdural evaluation is performed within two hours of injury.²⁹ Wilberger *et al.* evaluated the effect of time from injury to operative care among patients with subdural hematoma.²⁷ They found no statistically significant difference. However, for those patients who were treated within 4 hours there was a 10% absolute reduction in mortality compared to those treated greater than 4 hours. Further, this study only looked at time to operative treatment and did not look at the potential positive effects of other hospital interventions that were being provided earlier. In the study conducted by Di Bartolomeo, described above, there was an almost 60 minute difference in time to arrival at the receiving facility, yet the authors did not identify a difference in patient outcome.⁸ Lokkeberg and Grimes, while controlling for confounding variables like injury severity score, found that among patients with severe blunt TBI time to definitive care was not a significant predictor of patient outcome.¹⁷

Alternatively, Baxt and Moody found a 9% reduction in mortality for TBI patients transported by helicopter compared to ground ambulance.³ In the Baxt study, helicopters were staffed by a physician and a nurse, while the ground ambulance was staffed by a paramedic. Davis *et al.* assessed 10,314 patients with a head Abbreviated Injury Score of 3 or more and found that those who were transported by helicopter had a better odds of survival (1.90; 95% confidence interval 1.6 to 2.25) compared to ground transport, after controlling for a number of potential confounding variables.⁷

Transport Destination

Evidence suggests that mortality for TBI patients decreases when patients are transferred directly to a Level I trauma center.¹⁹ In most regions the treatment destination decision is made in the context of a formalized trauma system. In comparisons between organized and nonorganized EMS and trauma systems, patient outcome was worse without organization.^{4,20} Although the need for the immediate attention of a neurosurgeon

has been questioned,⁹ recent literature about general trauma patients suggests that the outcomes for trauma patients improve when they are treated at a Level I trauma center.¹⁸

A retrospective study that compared TBI outcome before and after the implementation of a trauma system in Oregon reported an odds ratio of 0.80 for mortality after system implementation.³⁰ A report of preventable deaths in San Diego County compared non-TBI and TBI deaths before and after instituting a regional trauma care system.¹⁰ Reviewers were blinded to the facility where care was rendered. Preventable deaths for non-TBI cases decreased from 16/83 (20%) to 2/211 (1%) ($p < 0.005$), and for TBI cases, preventable deaths decreased from 4/94 (5%) to 1/149 (0.7%) ($p < 0.10$), respectively, before and after the trauma system was put in place. Another before-and-after study compared outcome of injured patients in a rural hospital before it met American College of Surgeons Committee on Trauma guidelines for a level II trauma center with outcome after it received that designation.²¹ Survival for all patients who had a calculated probability of survival of 25% was 13% before and 30% after meeting Level II trauma center criteria. For patients with TBI, the survival was 15.4% before and 32% after meeting the criteria. In New York State, Hannan found that patients with TBI had lower odds of death (0.67, 95% confidence interval 0.53–0.85) when treated at a regional trauma center compared to other hospitals.¹¹ Cornwell *et al.*, evaluated the change in trauma patient mortality using a before-and-after design to determine the effect of having made systematic changes to achieve a Level I trauma center designation.⁵ Among severe TBI patients they found a 7% decrease in mortality rates that was not statistically significant. Finally, Hunt *et al.*, compared survival rates among TBI patients before and after a regionalized trauma system was put into place. They found that mortality fell from 42% to 26%, but this difference was not statistically significant.¹³

Pediatrics

1. In a metropolitan area, pediatric patients with severe TBI should be transported directly to a pediatric trauma center if available.
2. Pediatric patients with severe TBI should be treated in a pediatric trauma center or in an adult trauma center with added qualifications to treat children in preference to a Level I or II adult trauma center without added qualifications for pediatric treatment.

Foundation. There is no new information specific to prehospital care of pediatric patients since the publication of the Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents.¹ The recommendations

for this publication are duplicated from the pediatric guidelines.

Johnson *et al.* conducted a prospective, non-randomized comparison of mortality among admitted patients, some of whom were transported directly to Children's Hospital in Washington, D.C. (CHOW), a Level I PTC, and some of whom were first transported to other hospitals and then transferred to CHOW.¹⁴ Patients included children from 1 to 12 years of age treated in neurosurgical services between 1985 and 1988.

Fifty-six severe TBI patients received direct transport and 42 received indirect transport. However, statistical significance was only reported for the overall group, which included patients with mild and moderate TBI. Mortality rate for *all* patients was significantly greater in the Indirect Transport group (4.7%) than the Direct Transport group (1.9%).

The trauma score was significantly higher in the Direct Transport group (9) than the Indirect Transport group (7), indicating that the patients in the latter group were less stable physiologically, and constituting a baseline difference between groups. Authors suggest, however, that this is better viewed as an outcome than a baseline difference; that the physiological deterioration occurred as a function of delays in appropriate treatment due to the transfer.

This Class III study suggests that in this metropolitan area, pediatric patients with severe TBI are more likely to survive if transported immediately to a PTC than if transported first to another type of center and then transferred to a PTC.

Potoka *et al.*²³ conducted a retrospective review of medical records of patients 0 to 16 years old treated at pediatric or adult trauma centers in the state of Pennsylvania between 1993 and 1997. Four patient groups were specified, according to the type of trauma center in which they were treated:

PTC – Pediatric Trauma Center (n = 1,077)

ATC AQ – Adult Trauma Center with added qualifications to treat children (n = 909)

ATC I – Level I Adult Trauma Center (n = 344)

ATC II – Level II Adult Trauma Center (n = 726)

While the study included patients with mild and moderate TBI, this evaluation is based upon the patients with severe TBI (GCS from 3 to 8). Dependent variables were mortality, number of neurosurgical procedures, and mortality for patients who received neurosurgical procedures.

Method of and criteria for referral and transfer within the statewide system were not discussed in this study. Distributions for injury severity based upon injury severity score (ISS) were presented for the parent group of all traumas, but not for the subgroup of TBI. This Class III study suggests the following:

1. Pediatric patients with severe TBI are more likely to survive if treated in PTCs, or ATC AOs, than in Level I or Level II ATCs.
2. The pediatric patient with severe TBI who requires neurosurgical procedures has a lower chance of survival in Level II ATCs vs. the other centers.

VI. KEY ISSUES FOR FUTURE INVESTIGATION

Prospective, controlled Class I and II studies are needed to answer the following questions:

1. Can dispatchers accurately identify patients with TBI by interrogating callers? What questions are critical in determining the best resources to send to the scene? How do dispatch decisions affect patient outcome?
2. What pre-arrival instructions for callers who request emergency aid can improve patient outcome?
3. What effect do prehospital assessment, treatment, transport, and destination decisions have on the outcome of the patient with severe TBI?
4. How is outcome affected when patients are treated by organized EMS systems within a trauma system vs. EMS systems without a trauma system? These studies should evaluate the various levels of EMS provider training and hospital preparation, and include patients with different degrees of severity of injury.
5. What is the impact of transport time on the outcome of patients with TBI, and under what conditions should a closer hospital be bypassed in order to bring a patient to a trauma center?
6. What are the minimum requirements for a facility that treats patients with severe TBI?
7. What is the optimum destination for patients with mild-to-moderate TBI based on patient outcome?
8. What specifically should prehospital TBI transportation destination guidelines include, and how can they be kept current, as new safety devices are introduced and engineering changes are made in vehicles and other places where injuries occur?

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APPENDICES

APPENDIX A: CHANGES IN QUALITY RATINGS OF PUBLICATIONS FROM THE 1ST EDITION TO THE 2ND EDITION

| Topic & Reference | 1st Ed. 2000 | 2nd Ed. 2006 | Reason for Change |
|--------------------------------|--------------|--------------|--|
| Oxygenation and Blood Pressure | | | |
| Chesnut 93 | II | III | Descriptive Epidemiological |
| Fearnside 93 | II | III | Descriptive Epidemiological |
| Kokoska 98 | II | III | Descriptive Epidemiological |
| Marmarou 91 | II | III | Descriptive Epidemiological |
| GCS | | | |
| No changes | | | |
| Pupils | | | |
| No changes | | | |
| Airway | | | |
| Chesnut 93 | II | III | Descriptive Epidemiological |
| Stocchetti 96 | II | III | Descriptive Epidemiological |
| Winchell 97 | II | III | No control for confounding factors and differences between groups on prognostic factors. |
| Fluids | | | |
| Vassar 93 | I | II | Inadequate sample size; no intention-to-treat analysis; also 37 patients were excluded after randomization because they did not meet inclusion criteria. |
| Wade 97 | I | III | Not clear on how many of the requested records were received. No power calculation. |
| Cerebral Herination | | | |
| New Topic | | | |
| Hospital Transport | | | |
| Shackford 87 | II | III | Case Series |
| Smith 90 | II | III | Excluded one center for protocol violation, but report results with and without this center; unclear if statistical analysis was appropriate. |
| Smith 90 | II | III | Differences at baseline in age and patients with multiple fractures; not adjusted in analysis. |

APPENDIX B. ELECTRONIC LITERATURE SEARCHES

Oxygenation and Blood Pressure

Database: Ovid MEDLINE(R) <1996 to April Week 4 2005>

Search Strategy:

- 1 exp Craniocerebral Trauma/(23620)
- 2 Emergencies/(7417)
- 3 exp Emergency Medical Services/(23541)
- 4 exp Emergency Medical Technicians/(1559)
- 5 exp Emergency Treatment/(22567)
- 6 prehospital\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1888)
- 7 2 or 3 or 4 or 5 or 6 (49371)
- 8 1 and 7 (1217)
- 9 exp Blood Pressure/(46819)
- 10 exp HYPOTENSION/(4630)
- 11 9 or 10 (50003)
- 12 8 and 11 (75)
- 13 hypotens\$.mp. (14485)
- 14 8 and 13 (78)
- 15 12 or 14 (111)
- 16 limit 15 to (humans and english language) (76)
- 17 exp Ischemia/(108044)
- 18 exp Hypoxia-Ischemia, Brain/(16340)
- 19 17 or 18 (113401)
- 20 8 and 19 (45)
- 21 limit 20 to (humans and english language) (32)
- 22 16 or 21 (104)
- 23 from 22 keep 1-104 (104)

GCS

Database: Ovid MEDLINE(R) <1996 to April Week 4 2005>

Search Strategy:

- 1 exp Craniocerebral Trauma/(23620)
- 2 Emergencies/(7417)
- 3 exp Emergency Medical Services/(23541)
- 4 exp Emergency Medical Technicians/(1559)
- 5 exp Emergency Treatment/(22567)
- 6 prehospital\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1888)
- 7 2 or 3 or 4 or 5 or 6 (49371)
- 8 1 and 7 (1217)
- 9 exp trauma severity indices/(7322)
- 10 8 and 9 (302)
- 11 exp "sensitivity and specificity"/(138031)
- 12 10 and 11 (36)

13 exp "OUTCOME AND PROCESS ASSESSMENT (HEALTH CARE)"/(214175)

14 10 and 13 (102)

15 glasgow.mp. (4406)

16 8 and 15 (250)

17 12 or 14 or 16 (277)

18 limit 17 to (humans and english language) (236)

19 from 18 keep 1-236 (236)

Pupils

Database: Ovid MEDLINE(R) <1966 to May Week 1 2005>

Search Strategy:

1 exp PUPIL DISORDERS/or pupil\$.mp. or exp PUPIL/(16201)

2 exp Diagnostic Techniques, Ophthalmological/(71826)

3 exp Observer Variation/(15225)

4 "reproducibility of results"/ or exp "sensitivity and specificity"/(254752)

5 Reference Values/(104424)

6 1 and 2 and (3 or 4 or 5) (204)

7 limit 6 to (humans and english language) (171)

8 exp Craniocerebral Trauma/(74984)

9 1 and 8 and (3 or 4 or 5) (40)

10 limit 9 to (humans and english language) (39)

11 7 or 10 (208)

12 from 11 keep 1-208 (208)

Airway

Database: Ovid MEDLINE(R) <1996 to April Week 4 2005>

Search Strategy:

1 exp Craniocerebral Trauma/(23620)

2 Emergencies/(7417)

3 exp Emergency Medical Services/(23541)

4 exp Emergency Medical Technicians/(1559)

5 exp Emergency Treatment/(22567)

6 prehospital\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1888)

7 2 or 3 or 4 or 5 or 6 (49371)

8 1 and 7 (1217)

9 exp INTUBATION, INTRATRACHEAL/(8509)

10 exp PULMONARY VENTILATION/(9375)

11 exp Oximetry/(2715)

12 exp Capnography/(394)

13 hypoxia, brain/(1585)

- 14 exp Monitoring, Physiologic/(33448)
- 15 exp OXYGEN/(28380)
- 16 exp Carbon Dioxide/(12207)
- 17 14 and (15 or 16) (1436)
- 18 9 or 10 or 11 or 12 or 13 or 14 or 17 (53965)
- 19 8 and 18 (168)
- 20 limit 19 to humans (163)
- 21 limit 20 to english language (139)
- 22 from 21 keep 1-139 (139)

Fluids

Database: Ovid MEDLINE(R) <1996 to April Week 4 2005>

Search Strategy:

- 1 exp Craniocerebral Trauma/(23620)
- 2 Emergencies/(7417)
- 3 exp Emergency Medical Services/(23541)
- 4 exp Emergency Medical Technicians/(1559)
- 5 exp Emergency Treatment/(22567)
- 6 prehospit\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1888)
- 7 2 or 3 or 4 or 5 or 6 (49371)
- 8 1 and 7 (1217)
- 9 (fluid\$ adj2 resuscitat\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (997)
- 10 Fluid Therapy/(3275)
- 11 exp Rehydration Solutions/(458)
- 12 (hypertonic\$ or isotonic\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (7273)
- 13 9 or 10 or 11 or 12 (10972)
- 14 8 and 13 (63)
- 15 limit 14 to (humans and english language) (40)
- 16 from 15 keep 1-40 (40)

Brain Targeted Therapy

Database: Ovid MEDLINE(R) <1966 to May Week 1 2005>

Search Strategy:

- 1 exp Craniocerebral Trauma/(75013)
- 2 Emergencies/(26280)
- 3 exp Emergency Medical Services/(50843)
- 4 exp Emergency Medical Technicians/(3049)

- 5 exp Emergency Treatment/(59030)
- 6 prehospit\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (3739)
- 7 2 or 3 or 4 or 5 or 6 (123681)
- 8 1 and 7 (3383)
- 9 glucose.mp. or exp GLUCOSE/(256326)
- 10 mannitol.mp. or exp MANNITOL/(13565)
- 11 exp "Hypnotics and Sedatives"/or exp CONSCIOUS SEDATION/(80142)
- 12 (sedative\$ or sedation\$ or sedate\$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (31289)
- 13 analgesi\$.mp. (75207)
- 14 exp ANALGESICS/(318665)
- 15 lidocaine.mp. or exp LIDOCAINE/(19360)
- 16 exp Neuromuscular Blocking Agents/(17798)
- 17 exp Neuromuscular Blockade/(734)
- 18 exp Neuromuscular Junction/de [Drug Effects] (7015)
- 19 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (707058)
- 20 8 and 19 (256)
- 21 limit 20 to (humans and english language) (172)
- 22 from 21 keep 1-172 (172)

Decision Making Within the EMS System: Dispatch, Scene, Transportation, and Destination

Database: Ovid MEDLINE(R) <1996 to August Week 4 2005>

Search Strategy:

- 1 (trauma\$ adj3 (system\$ or center\$)).mp. (4420)
- 2 prehospital\$.mp. (1974)
- 3 exp AMBULANCES/ or ambulance\$.mp. (2708)
- 4 exp "Transportation of Patients"/(3021)
- 5 triage.mp. or exp TRIAGE/(3501)
- 6 2 or 3 or 4 or 5 (8536)
- 7 exp Craniocerebral Trauma/(24689)
- 8 ((head or skull or brain or cereb\$) adj3 (wound\$ or injur\$ or trauma\$ or damag\$)).mp. (29021)
- 9 7 or 8 (39874)
- 10 1 and 6 (485)
- 11 limit 10 to english language (455)
- 12 9 and 10 (63)
- 13 limit 12 to english language (59)
- 14 from 13 keep 1-59 (59)

APPENDIX C. MIXED PATIENT SAMPLES

Criteria for Including a Study that Mixes TBI Patients with Other Pathologies

If:

- the sample for a study has patients with TBI as well as patients with other pathologies,
- and the data are not reported separately for TBI,
- and there is an effect of the study,

it cannot be known if the effect existed for the TBI group, or if it was large in the non-TBI group and non-existent in the TBI group. Therefore there is limited confidence that the intervention had an effect for TBI.

The following is required to include a study as evidence for a guideline topic:

1. Sample size > 25 patients.
2. 85% or more of the patients are TBI.
3. Such a study could never be used to support a standard.
4. Such a study can only support a Level II or III recommendation. It cannot be used to support a Level II recommendation if it is the only Class II study available.
5. If the study does not report the percent of patients with TBI, it cannot be used as evidence at any level.

When a publication mixed the results of pediatric patients with those of adults, the mean and standard deviation (when provided) were used to calculate the proportion of pediatric patients.

APPENDIX D. LITERATURE SEARCH YIELD

| Topic | Full Text Publications | | |
|--|------------------------|-------|------------|
| | Abstracts | Adult | Pediatrics |
| Oxygenation and Blood Pressure | 103 | 28 | 53 |
| Glasgow Coma Scale Score | 265 | 105 | 42 |
| Pupils | 107 | 24 | 9 |
| Airway, Ventilation, Oxygenation | 139 | 55 | 62 |
| Fluid Resuscitation | 36 | 15 | 23 |
| Cerebral Herniation | 151 | 69 | 48 |
| Decision Making Within the EMS System: Dispatch, Scene, Transportation, and Destination | 190 | 39 | 14 |