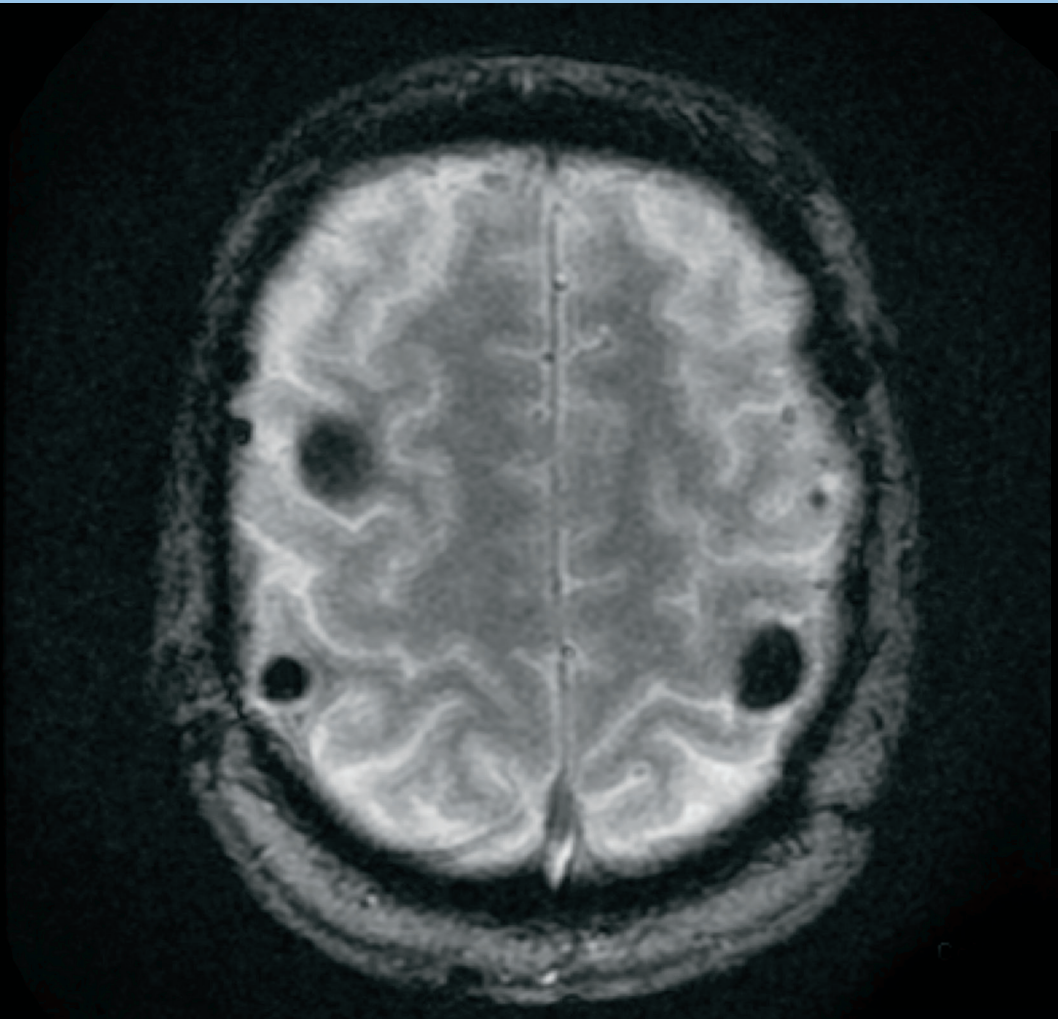
Traumatic Brain Injury

Methods for Clinical and Forensic Neuropsychiatric Assessment

Third Edition



Robert P. Granacher, Jr.

CRC Press
Taylor & Francis Group

Traumatic Brain Injury

Methods for Clinical and Forensic Neuropsychiatric Assessment

Third Edition

Traumatic Brain Injury

Methods for Clinical and Forensic Neuropsychiatric Assessment

Third Edition

Robert P. Granacher, Jr.

Clinical Professor of Psychiatry
University of Kentucky College of Medicine
Lexington, KY, USA

CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

About the cover: The figure depicts "blooming" hemosiderin detected by a T2* GRE MRI following bilateral subdural hematomas due to TBI.

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

Version Date: 20150123

International Standard Book Number-13: 978-1-4665-9481-4 (eBook - PDF)

Contents

Preface to the Third Edition

This edition has been entirely rewritten. The reader will note that the style follows a more traditional neuropsychiatric format. Since the second edition publication, there has been increased awareness and scientific study regarding the effects of blast brain injury as a consequence of the U.S. military experiences in Afghanistan and Iraq. There is increased interest in the phenomenology of mild traumatic brain injury (TBI), and in particular, the forensic complications associated with evaluations of this disorder. Chronic traumatic encephalopathy has received significant scrutiny in the last decade, possibly associated with sports injuries. The science on this entity is currently evolving, and the political economics are highly polarized.

The main purpose of this text is to provide to a physician or a psychologist, a scientifically based schema for the clinical evaluation of TBI to develop a treatment plan for a patient who sustains TBI and to provide assistance to his/her caregivers. A second major thrust of this text is for those physicians and psychologists providing forensic analysis to lawyers, insurance bodies, Workers' Compensation systems, triers-of-fact, and other stakeholders in the adjudication of victims of TBI.

The first eight chapters follow the format of editions one and two, in that these chapters are devoted to clinical assessment following TBI in an effort to provide a comprehensive neuropsychiatric or psychological treatment plan on behalf of a TBI patient. Chapters 9 through 11 are devoted to the forensic aspects of TBI evaluation and analysis. As with the first two editions, if the reader's practice is entirely within the clinical and treatment realm, only the first eight chapters may be relevant, and the remaining three chapters may not be of interest to that clinician. On the other hand, for those providing forensic analysis and evaluation, it will be necessary to first understand Chapters 1 through 8 before applying the forensic principles in Chapters 9 through 11.

The logic and format of the first and second editions have remained in the third edition. The examination techniques follow standard medical concepts within a neuropsychiatric focus. One fifth of this book is devoted to neuropsychological and psychological assessment following TBI. That focus is not at the practice level of most PhD neuropsychologists or psychologists, as Chapters 6 and 7 are primarily designed for physician use, but our psychology colleagues may find some of their content useful in their own practices. New additions to this book include an enlarged focus on military aspects of TBI. Concussion in sports has received expanded attention. There is increased emphasis on the physical syndromes that occur secondary to TBI, which may be a focus for physicians and psychologists performing TBI assessments. The neuroimaging section (Chapter 5) has been modified to include the established guidelines of the American College of Radiology (ACR) as they apply to appropriate use of neuroimaging instruments in the evaluation of TBI, and also, in the forensic section, the inclusion of ACR guidelines within TBI testimony is stressed. The neuropsychological assessment section of Chapter 6 has been greatly expanded to include tests that have been published and updated since the second edition. The important gains in using cognitive behavioral therapy following TBI have led to an increased emphasis of this treatment modality, as described in Chapter 8. Chapter 9 has been significantly enlarged with regard to the multiple medicolegal issues potentially brought to forensic examiners following a TBI. These include criminal issues in those who have sustained a TBI, issues of testamentary capacity and vulnerability to undue influence, healthcare decision making and informed consent, and other diverse challenges of forensic importance that may arise following a TBI. In Chapter 10, emphasis is on the forensics of mild TBI and neuropsychiatric TBI neuroimaging. A substantial expansion of the metrics of symptom validity determination has been included.

The reader is cautioned that this text is not an encyclopedic review of TBI. It is designed for practicing clinicians not only as treaters but also as forensic specialists. Its avowed purpose remains the

same as in prior editions; that is, to provide a physician or psychologist with a practical method for an effective evaluation of TBI based on known scientific principles of brain–behavior relationships and state-of-the-art clinical, neuroimaging, neuropsychological, and psychological techniques. The methods, procedures, and recommendations in this book are grounded in evidence-based science but they also come from more than 5000 cases wherein the author and his contributors have personally examined individuals who have sustained TBI or those claiming to have a sustained TBI.

Preface to the Second Edition

Since the first edition of this text, the number of traumatic head injuries that occur in the United States on a yearly basis has risen to almost three million. These, in turn, produce considerable morbidity and death. This text has two purposes. The first purpose is to provide a physician or a psychologist with a neuropsychiatric schema for the evaluation of a patient who has sustained a traumatic brain injury (TBI) and for whom the clinician wishes to develop a treatment plan. The second purpose is for forensic neuropsychiatric evaluations. As an added benefit, the methods in this book can be used to evaluate and treat any neuropsychiatric disorder, with the addition of appropriate laboratory studies and treatments specific to the pathology. The first eight chapters of this text focus on evaluations for treatment. Chapters 9 through 11 provide a focus for physicians performing forensic TBI examinations. As the medical examination format is not different when examining a patient for treatment than it is when examining a patient for forensic purposes, the first eight chapters can be read by the treatment clinicians, and if they have no interest in forensic issues, Chapters 9 through 11 can be avoided. On the other hand, the physician wishing to perform a competent forensic neuropsychiatric examination will find it necessary to utilize all 11 chapters.

The logic of clinical TBI examination formulated in the first edition remains in the second edition. That is, the examination techniques follow standard medical concepts but with a significant neuropsychiatric focus. in other words, the evaluation techniques are not psychologically based, instead they are brain based. Moreover, there are exciting new clinical findings regarding TBI since the first edition was written. These have been added to improve the quality of the text and enhance the learning experience for the reader. These include the recent reports of blast overpressure brain injury as seen in combat veterans and civilians injured in conflicts in Kosovo, Lebanon, Iraq, Afghanistan, and other world areas. An enlarged review of sports injuries in children, high school students, and college and professional athletes has been added. Inflicted brain injury in children receives more attention. A larger emphasis has been placed on mild traumatic brain injury, particularly from a forensic standpoint, owing to the contribution of litigation to increased symptom expression. Neuroimaging techniques have been considerably expanded so that the neuropsychiatric examiner can provide a better clinical correlation between imaging and the findings from direct medical examination. The literature on outcomes in adults and children following TBI has been expanded to make it of more use for the forensic examiner.

This text is not a comprehensive review of all knowledge of TBI. Moreover, it is not to be used as an encyclopedia. Its purpose is to provide a physician or a psychologist with a practical method for an effective evaluation of TBI using state-of-the-art techniques. The techniques described in this text come from known standards within the world medical and psychological literature as well as from the author's large database of TBI examinations. The procedures and recommendations in this book come from almost 4000 cases wherein the author has personally examined persons with TBI or those claiming to have a TBI.

Preface to the First Edition

Approximately two million traumatic head injuries occur in the United States yearly. These in turn produce more than 50,000 deaths annually. There is a biphasic distribution of brain injury, with the highest incidence found among young people 15 to 24 years of age and a second group of citizens greater than 75 years of age. Almost 25% of head injuries require hospitalization, and nearly 100,000 persons yearly are left with some level of chronic brain impairment.

This text has a specific focus. It provides not only methods for clinical examination but also the forensic evaluation of traumatically brain-injured persons. The reader can be selective in using this book. If he or she is interested only in clinical assessment, treatment planning, and neuropsychiatric treatment, the first eight chapters of the book will suffice. On the other hand, for the physician performing a forensic neuropsychiatric examination, the entire book should be useful. If the clinician is already highly skilled in the clinical evaluation of traumatic brain injury (TBI) but wishes to learn further forensic issues, he or she may focus only on the last four chapters of this text.

There is a simple logic to the book. It follows traditional medical evaluation concepts with a neuropsychiatric focus. It demarcates differences in the adult evaluation versus the child evaluation. Chapter 8 integrates the clinical section of this text, whereas Chapter 11 integrates the forensic section of the text. The seven preceding chapters in the clinical section of the book proceed logically to a culmination of data analysis and case studies in Chapter 8. The same format applies to the forensic section, Chapters 9 through 12. Chapters 9 through 11 provide the forensic analysis database, and Chapter 12 offers the forensic expert guidance for writing neuropsychiatric TBI reports and providing neuropsychiatric testimony.

This text is not intended to provide complete information regarding the multiple advances within the entire field of TBI. For instance, it provides only a limited focus on the management of acute TBI. This is better left to neurosurgeons and trauma physicians. Its primary intention is to provide the physician, at some time well after the brain injury, with a clinically tested schema for either evaluating and treating a patient or examining a plaintiff or defendant. The genesis for this text comes from the author's database of almost 3000 TBI persons, or those alleging a TBI, examined by extensive historical, physical, imaging, neuropsychological, and laboratory procedures. It is hoped that the reader will find this to be a practical text providing pragmatic information either for evaluation and treatment of one's patient or for providing a state-of-the-art forensic examination of an alleged TBI.

Robert P. Granacher Jr., MD, MBA
University of Kentucky College of Medicine

Acknowledgments

Robert P. Granacher, Jr. acknowledges and thanks the editing and production efforts of Lance Wobus and Jill Jurgensen of Taylor & Francis Group for their professionalism and expertise in producing this book. He also thanks Jasmine Adkins for her tireless efforts in the preparation of the manuscript. He thanks doctors Timothy Allen and John Ranseen for their contributions and assistance, and he acknowledges with gratitude his wife, Linda, and his son, Phillip, who again had to tolerate his incessant dictation for almost a year as he prepared this text.

Author

Robert P. Granacher, Jr., MD, MBA, is a clinical professor of psychiatry in the Department of Psychiatry of the University of Kentucky College of Medicine. He practices privately as a treating neuropsychiatrist and as a forensic neuropsychiatrist and practices as a clinical staff psychiatrist at the Cumberland River Comprehensive Care Center in Mount Vernon, Kentucky.

Dr. Granacher earned his BA in chemistry from the University of Louisville, Kentucky, and his MD from the University of Kentucky, Lexington, and he then served as a resident and chief resident in psychiatric medicine at the University of Kentucky Hospital. He later served as a resident and fellow at Harvard University and the Massachusetts General Hospital and other Harvard University teaching hospitals in Boston. Since the first edition of this book, he has earned an MBA from the University of Tennessee in Knoxville. He has specialized in the neuropsychiatric treatment and evaluation of traumatic brain injury, perinatal birth injury, toxic brain injury, and other complex neurobehavioral disorders for more than 35 years. His forensic neuropsychiatry practice is national in scope.

Dr. Granacher is board certified by the American Board of Psychiatry and Neurology in general psychiatry, with added qualifications in geriatric psychiatry and forensic psychiatry. He is board certified in neuropsychiatry by the United Council of Neurologic Subspecialties. He is also board certified in forensic psychiatry by the American Board of Forensic Psychiatry, Inc., and in sleep medicine by the American Board of Sleep Medicine. He is certified in psychopharmacology by the American Society of Clinical Psychopharmacology. He is a distinguished life fellow of the American Psychiatric Association and a member of the American Neuropsychiatric Association and serves on the Private Practice and Forensic Neuropsychiatry Committees of the American Academy of Psychiatry and Law.

Dr. Granacher is a director of the Kentucky Psychiatric Medical Association. He served for 17 years on the board of directors of St. Joseph Healthcare, Lexington, Kentucky, a corporation managing a number of hospitals and other healthcare facilities in the central Kentucky area. He formerly served as chair of the board of directors of the same corporation. He also is a director and shareholder of C.B.A. Pharma, an oncology and infectious disease research pharmaceutical company based in Lexington. He formerly served at the pleasure of the governor on the board of the Kentucky Traumatic Brain Injury Trust Fund.

Contributors

Timothy Allen, MD, is employed as a part-time associate clinical professor of psychiatry at the University of Kentucky College of Medicine. He is also in the private practice of forensic psychiatry in Lexington, Kentucky, and is owner and operator of Lexington Forensic Psychiatry, LLC. He earned his bachelor's degree from the University of Louisville and then earned a Doctor of Medicine degree from the University of Kentucky College of Medicine in Lexington. Following the completion of his medical degree, he completed a preliminary medicine internship at Tulane University and then served as a resident and chief resident in psychiatric medicine at the University of Kentucky Hospital. Subsequent to his psychiatric residency, he completed a fellowship in forensic psychiatry at Tulane University in New Orleans. He is board certified in psychiatry and forensic psychiatry by the American Board of Psychiatry and Neurology. He currently serves on the Neuropsychiatry Committee of the American Academy of Psychiatry and the Law. He has wide experience in the evaluation and treatment of brain–behavioral disorders, and in particular, in the forensic assessment of traumatic brain injury.

John Ranseen, PhD, is an associate professor in the Department of Psychiatry at the University of Kentucky College of Medicine, and also holds joint appointments in the neurology and psychology departments of that institution. He heads the psychology division of Lexington Forensic Psychiatry. He has extensive experience in neuropsychological and psychological assessment in clinical and forensic settings. He earned his PhD in psychology from Ohio University. He is nationally recognized as an expert concerning the Americans with Disabilities Act (ADA) as it applies to mental disabilities. He is a consultant to numerous state bar examination committees and other professional licensing boards in the United States with regard to students requesting test accommodations for mental disability based on the ADA. He has extensive experience in the psychological and neuropsychological evaluation of toxic brain syndromes, traumatic brain injury, neurodevelopmental brain disorders, and the dementias.

1 Epidemiology and Pathophysiology of Traumatic Brain Injury

INTRODUCTION

Traumatic brain injury (TBI) is not an event, but it is a multifaceted condition that evolves longitudinally after direct head injury (Manley and Maas 2013). Each year in the United States, at least 1.7 million people seek medical attention for TBI (Faul et al. 2010). Moreover, TBI is a contributing factor in a third of all injury-related deaths in the United States (Centers for Disease Control and Prevention 2003b). Direct medical costs and indirect costs, such as lost productivity from TBI, totaled an estimated $76.5 billion in the United States in the year 2000 (Finkelstein et al. 2006).

TBI has been recorded since the dawn of human history as we know it today. Significant anthropological evidence exists demonstrating ancient surgical procedures across suture lines of prehistoric skulls (Thorell and Aarabi 2001). Pott, LeBran, and Heister (Forcht 1997) first correlated an altered mental status following head injury to pressure on the brain rather than damage to the skull itself. Jaboulay (1896) was the first surgeon to emphasize the need for opening the skull to release intracranial pressure, based on his neurosurgical studies in France. The first neuroanatomical evidence of uncal herniation as a result of increased intracranial pressure was published by Jefferson (1938). In the late 1950s and early 1960s, neurosurgical treatment of increased intracranial pressure advanced to the point that intracerebral monitoring was introduced (Lundberg et al. 1968). As noted later, there are two major components to blunt force TBI: primary injury and secondary injury.

As Manley and Maas (2013) recently pointed out, medical understanding of the molecular and cellular mechanisms of TBI has improved. However, even with these advances, research has failed to translate into a single successful clinical trial for non-surgically treating acute TBI. It is suggested that these failures are largely attributable to the overbroad classification of TBI as mild, moderate, or severe, without incorporating the newer insights and findings of diagnostic tools, such as functional imaging and proteomic biomarkers. The original classification scheme of TBI is derived from the *Glasgow Coma Scale* (*GCS*), which is discussed throughout this book (Table 1.1). Outcomes have been measured using the *Glasgow Outcome Scale—Extended* (*GOSE*), which is a global and relatively insensitive tool (see Table 10.5). This symptom-based approach does not permit mechanistic targeting for clinical trials (see Tables 10.5 and 10.6 in Chapter 10). Neurosurgeons are arguing for a more advanced approach, which requires the transition to a much more precise disease classification model for TBI that is based on pathoanatomical and molecular features. The increasing recognition of the complexity of TBI demands a more intensely scientific and focused approach (Manley and Maas 2013).

Our recent military experience in the United States has taught us just how little is known about the basic pathophysiology of TBI. Medical practitioners struggle to answer simple questions such as whether a brain injury has actually occurred, when an athlete can safely return to sports play, or what variables are associated with the development of postconcussion syndrome or posttraumatic stress disorder (PTSD). As noted, the medical science of TBI significantly demands a new classification and taxonomy system, as well as the creation of a scalable and sophisticated infrastructure to promote clinical TBI care and research. In efforts to meet these needs, there is now a global move to improve the research and clinical database of TBI. For instance, the Transforming Research and

TABLE 1.1
GCS Scores

Type of Response		Score	Description
Eye opening	Spontaneous	4	Eyes are open, but this does not imply intact awareness; consistent with active arousal mechanisms in the brain stem.
	To speech	3	Nonspecific response to speech or shout; does not imply patient obeys commands to open eyes; indicates functional cerebral cortex.
	To pain	2	Pain stimulus is applied to chest or limbs; suggests functioning of the lower levels of the brain.
	None	1	No response to speech or pain (not attributable to periorbital swelling).
Motor	Obeys commands	6	Can process instructions and respond by obeying a command.
	Localizes pain	5	Pain stimulus is applied to supraorbital region or fingertip; patient makes an attempt to remove the source of the pain stimulus.
	Withdrawal	4	Normal flexor response; patient withdraws from painful stimulus with abduction of the shoulder.
	Abnormal flexion	3	Abnormal responses to pain stimulus; includes decorticate flexion or extension of upper extremities; indicates more severe brain dysfunction.
	Extension	2	Decerebrate responses to pain stimulus manifested by adduction and hyperpronation of the upper extremities; the legs are extended with plantar flexion of the feet; includes opisthotonos.
	No response	1	Flaccid, fails to respond to a painful stimulus.
Verbal	Oriented	5	Oriented to person (knows identity), place (knows where he or she is), and time (knows the current year, season, and month).
	Confused	4	Responses to questions in a conversational manner, but responses indicate disorientation/confusion.
	Inappropriate	3	Intelligible speech (e.g., shouting or swearing) but no coherent conversation.
	Incomprehensible	2	Moaning and groaning; no recognizable words.
	No response	1	No verbal response.

Source: Institute of Medicine: Gulf War and Health, *Long-term Consequences of Traumatic Brain Injury*, National Academies Press, Washington, DC, 2009; Teasdale, G. and B. Jennett, *Lancet*, 2, 281–284, 1974.

Note: Eye (E) + motor (M) + verbal (V) = total GCS scores.

Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study has determined by magnetic resonance imaging (MRI) that many structural abnormalities occur in mild TBI (mTBI) that cannot be detected by computed tomography (CT) (Yuh et al. 2013). Recently, blood-based glial proteomic biomarkers have been shown to reliably detect the presence and severity of brain injury that can be detected by CT (Okonkwo 2013).

Current international studies are now under way to develop outcome measures to examine patient-oriented domains, including cognitive, psychosocial, physical function, and quality of life. These more refined outcome data will be combined in a *multidimensional scale* that is expected to improve the detection of treatment effects. Large between-center and between-country differences

in outcome may facilitate comparative effectiveness of clinical decisions country by country (Lingsma et al. 2011). The president of the United States has recently unveiled the BRAIN Initiative: Brain Research through Advancing Innovative Neurotechnologies (White House web page 2013).

This chapter reviews the epidemiology of TBI and the pathophysiology of blunt force head trauma, penetrating head injury, blast injury, and sports injury. The various classification systems used to categorize the severity of head and brain injury are reviewed with their strengths and weaknesses. If the reader compares this book with the prior second edition (Granacher 2008), it will be noted that substantial advancements in our knowledge of TBI have occurred regarding military and sports injuries, and the basic bioscience of TBI pathophysiology. A review of various biochemical and genetic markers of acute trauma, and their ability to predict outcome or neurodegeneration, is presented.

EPIDEMIOLOGY OF TRAUMATIC BRAIN INJURY

Table 1.2 summarizes some epidemiology features of TBI. These data are compiled by and updated online by the Centers for Disease Control and Prevention in Atlanta (CDC's Injury Center: Traumatic Brain Injury 2013). Not only are national TBI estimates available (http://www.cdc.gov/traumaticbraininjury/statistics), but the reader may also use this website periodically to keep abreast of changes in epidemiology statistics for TBI within the United States, as data are collected nationally on a routine basis with updates at least yearly.

DEFINITIONS OF TRAUMTIC BRAIN INJURY

The definition of TBI continues to evolve. As noted earlier, a number of international initiatives are proposing the interrelation of TBI research among countries to improve the quality of and access to TBI data. One of these groups, Demographics and Clinical Assessment Working Group of the International and Interagency Initiative toward Common Data Elements for Research on Traumatic Brain Injury and Psychological Health, has recently published a working definition and position statement for the defintion of TBI (Menon et al. 2010). The Centers for Disease Control also has a widely used definition of TBI, which is currently adopted by most TBI treatment centers in the United States (Table 1.3). The definition is a bit dated (Thurman et al. 1995).

Since September 11, 2001, increased focus on TBI has come about due to the military forces of the United States becoming engaged in theaters of war. As a result, the Department of Veteran's Affairs (VA) and the Department of Defense (DoD) (Department of Veteran's Affairs, Department of Defense 2009) have promulgated a working definition of TBI. Table 1.4 defines TBI as a traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by the new onset of at least one of the clinical signs listed in the table.

TABLE 1.2
Epidemiology of TBI

- 1.7 Million TBIs occur yearly in the United States, either as an isolated injury or with other injuries.
- TBI is a contributing factor to 30.5% of all injury-related deaths in the United States.
- About 75% of TBIs that occur each year are concussions or other forms of mTBI.
- Those at highest risk for TBI are children of ages 0–4 years, adolescents of ages 15–19 years, and adults of ages 65 years and older.
- Approximately 500,000 ED visits for TBI are made annually by children, ages 0–14 years.
- Adults aged 75 years and older have the highest rates of TBI-related hospitalization and death.
- In every age group, TBI rates are higher for males than for females.
- Males aged 0–4 years have the highest rates of TBI-related ED visits.

Source: CDC's Injury Center: Traumatic Brain Injury, *How Many People Have TBI?*, Centers for Disease Control and Prevention, http://www.cdc.gov/traumaticbraininjury/statistics, 2013.

TABLE 1.3
CDC Case Definition for TBI

A case of TBI (craniocerebral trauma) is defined either as an occurrence of injury to the head that is documented in a medical record, with one or more of the following conditions attributed to head injury:

- Observed or self-reported decreased level of consciousness
- Amnesia
- Skull fracture
- Objective neurological or neuropsychological abnormality
- Diagnosed intracranial lesion

Or as an occurrence of death resulting from trauma, with head injury listed on the death resulting from trauma, with head injury listed on the death certificate, autopsy report, or medical examiner's report, in the sequence of conditions that resulted in death.

The clinical definition of TBI *excludes* the following:

- Lacerations or contusions of the face, eye, ear, or scalp, without other criteria listed above
- Fractures of facial bones, without other criteria listed above
- Birth trauma
- Primary anoxic, inflammatory, infectious, toxic, or metabolic encephalopathies, which are not complications of head trauma
- Neoplasms
- Brain infarction (ischemic stroke) and intracranial hemorrhage (hemorrhagic stroke) without associated trauma

Source: Thurman et al., *Guidelines for Surveillance of Central Nervous System Injury*, Centers for Disease Control and Prevention, Atlanta, Georgia, 1995.

The VA/DoD definition of TBI notes that skull fracture is commonly included in some surveillance definitions as an indicator of possible TBI (CDC definition), but skull fracture by itself is not a TBI. Furthermore, the VA/DoD definition notes that external forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, a foreign body penetrating the brain, forces generated from events such as blast or explosion, or other forces yet to be defined. It should be noted that the VA/DoD criteria define the "events" of a TBI. Most individuals exposed to an external force to the head will not sustain a TBI. Moreover, not all individuals who are exposed to an external force to the head will sustain a TBI, but any person with a history of such an event who manifests any of the signs and symptoms in Table 1.4, occurring immediately or within a short time after the event of external force to the head or surrounding body, can be said to have had a TBI. It goes without saying that meeting the definition of TBI clinically tells us absolutely nothing about the severity of the injury or the outcome of that particular event. Outcome determination must be made based on clinical, laboratory, neuroimaging, and other medical data obtained by examination (see Chapter 10).

CLASSIFICATION OF TRAUMATIC BRAIN INJURY

The current classification of TBI generally follows the simplistic clinical guidelines of "mild, moderate, or severe." As Manley and Maas (2013) have cautioned, the increasingly recognized complexity of TBI demands a more intensely scientific and focused approach, and nowhere is that more obvious than in the attempts to classify such a complex physiological event as TBI using simple groupings of mild, moderate, or severe. It is hoped that the international collaborative currently underway to improve the

TABLE 1.4
VA/DoD Definition of TBI

TBI is defined as a traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by the new onset of at least one of the following clinical signs, immediately following the event:

- Any period of loss of or a decreased level of consciousness
- Any loss of memory of events immediately before or after the injury
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.), also known as an alteration of consciousness
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/paraplegia, sensory loss, aphasia, etc.) that may or may not be transient
- Intracranial lesion

Source: Department of Veteran's Affairs, Department of Defense, V. A./DoD Clinical practice guideline for management of concussion/mild traumatic brain injury (mTBI), http://www.healthquality.va.gov/mtbi/concussion_mtbi_full_1_0.pdf, 2009.

knowledge base and scientific understanding of TBI will aid all persons who either are victims of TBI or work to help victims of TBI, by improving classification accuracy and science.

With these caveats given, the current severity classification is generally based on GCS (Teasdale and Jennett 1974). Although the GCS is internationally accepted as the most common grading system in the field following TBI (Table 1.1), its usefulness in predicting severity is greater for moderate and severe TBI than for mTBI, because the vast majority of mTBI patients have normal to near normal GCS scores within hours after the injury. Moreover, the definition of mild TBI allows the diagnosis of mTBI if there is transient alteration in consciousness without either loss of consciousness or posttraumatic amnesia. Hoge et al. (2009) have especially questioned using the GCS in post-injury screening or surveillance because of these weaknesses. Acute injury severity is best determined at the time of the injury (Department of Veteran's Affairs, Department of Defense 2009); the GCS does not lend itself to predicting outcome accurately. Table 1.1 describes the pattern of signs associated with the various classification scores for GCS (Institute of Medicine: Gulf War and Health 2009). Outcomes are discussed in Chapter 10.

Due to the complexity of definitions for mTBI and the significant overlap with concussion, the continuum of injury from mild to severe has significantly blurred boundaries. As noted, Hoge et al. (2009) have significantly criticized the definition of mTBI, and the reasons for this are because the natural history, risk factors for injury sequelae, expectation of full recovery, and the treatment approaches to TBI differ substantially between mTBI and moderate/severe TBI (mod/sevTBI). Many studies fail to distinguish adequately between these two severity levels, which complicates the interpretation of clinical studies and introduces numerous confounding variables for undertaking TBI surveillance or collecting epidemiological data regarding TBI. When a case definition approach is used to assess mTBI, many weeks or months after the injury on the basis of a self-report from the patient, as is done in many health screening programs, these limitations lead to the subjective attribution of non-mTBI-related symptoms to mTBI. The misattribution of nonspecific symptoms such as headache, which may be due to other causes and not the injury event, can result in inflated estimates of the true numbers of cases of mTBI (Langlois Orman et al. 2011). As discussed later in the forensic aspects of TBI outcome, the importance of misattribution of nonspecific symptoms to a claim of TBI cannot be overstated. Table 1.5 demonstrates a stratification system for classifying the severity of TBI. This is based on the clinical practice guideline of the Department of Defense/Veteran's Administration (2009).

TABLE 1.5
Severity of Brain Injury Stratification

Criteria	Con/mTBI	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of consciousness	0–30 Minutes	>30 Minutes and <24 hours	>24 Hours
Alteration of consciousness/ mental state	A moment up to 24 hours	>24 Hours	Severity based on other criteria
Posttraumatic amnesia	≤1 Day	>1 And <7 days	>7 Days
GCS (best available score in first 24 hours)	13–15	9–12	3–8

Source: Department of Veteran's Affairs, Department of Defense, V. A./DoD Clinical practice guideline for management of concussion/mild traumatic brain injury (mTBI), http://www.healthquality.va.gov/mtbi/concussion_mtbi_full_1_0.pdf, 2009.

CONCUSSION

In this book, to this point the terms "concussion" and "mild traumatic brain injury" have been interchanged because that is the nature of the contemporary literature regarding the subject. Going forward in this book, the term concussion is combined with the term mTBI; however, concussion refers to a specific injury event that may or may not be associated with persisting symptoms or evidence of structural brain injury. Moreover, the term concussion is much more positive in its rehabilitation outlook, whereas the term mTBI conveys permanency, which is generally not justified (Ponsford et al. 2002). As noted in Table 1.6, concussion/mTBI usually leads to a full recovery (Hoge et al. 2009). The diagnosis of concussion does not carry the weight of mTBI, and it should not inadvertently convey to the patient/examinee that the individual is "brain injured." By definition, both concussion and mTBI are "mild" and should be conveyed by the physician to the patient as such. For the remainder of this book, to avoid confusion due to the overlapping scientific literature on concussion and mTBI, the term *con/mTBI* will be used. Table 1.7 lists the elements of concussion defined by the International Symposium on Concussion in Sport held in Prague, Czech Republic, 2004 (McCrory et al. 2005).

The American Medical Society for Sports Medicine recently published a position statement on concussion and sport (Harmon et al. 2013). Although the statement is somewhat of an advocacy position for sports medicine physicians, it does at least publish the competency guidelines expected for those physicians who wish to work with injured athletes. The statement notes that sports medicine physicians are specifically trained to provide care along the continuum of sports concussion from the acute injury to return-to-play decisions. The care of athletes with sports concussion is ideally performed by healthcare professionals who have specific training and experience in the assessment and management of concussion. Their competence should be determined by training and experience, not dictated by specialty. This position statement points out that a history of concussion is associated with a higher risk of sustaining another concussion. Moreover, a greater number, severity, and duration of symptoms after a concussion are predictors that the athlete will have a prolonged recovery. They also cite a gender difference that in sports with similar playing rules the reported incidence of concussion is higher in female athletes than in male athletes. Preinjury mood disorders, learning disorders, attention deficit disorders, and migraine headaches complicate the diagnosis and management of a concussion. The reader is referred to the literature for further details of this important position statement (Harmon et al. 2013).

TABLE 1.6
Comparison of mTBI with Moderate and Severe TBI

Variable	Con/mTBI	Moderate and Severe TBI
Clinical definition	<30 Minutes loss of consciousness, any alteration in consciousness, or posttraumatic amnesia lasting <24 hours. GCS score of 13–15.	Loss of consciousness ≥30 minutes up to prolonged coma. Posttraumatic amnesia ≥24 hours up to permanent memory loss. GCS score of 3–12.
Epidemiological evidence of causation between injury and sequelae	Inconsistent. Debated	Not debated.
Neurocognitive testing	Often inconclusive beyond acute injury period. Often reveals response bias to testing.	Essential and valuable component of ongoing clinical care and assessment.
Neuronal cell damage	Metabolic and ionic processes caused by axonal twisting or stretching can lead to secondary disconnection.	Combination of cellular disruption cascade directly related to injury and subsequent alteration of metabolic and ionic processes.
Focal neurological signs	Generally none or transient.	Frequently present.
CT or MRI	Usually negative or very minor.	Lesions usually diagnostic.
Natural history	Usually leads to full recovery. There is lack of consensus on the natural history of postconcussive symptoms or syndrome; some evidence of possible prolonged sequelae in the minority of cases.	Natural history and recovery are directly related to severity of injury and functional neuroanatomical injury.
Case definitions and specificity of injury sequelae	Case definitions of postconcussion syndrome have low reliability and validity and show poor correlation with each other. There are high rates of these symptoms in healthy populations, and high rates of "postconcussive syndrome" after nonhead injuries.	Injury sequelae are not debated.
Predictors of persistent symptoms of disability	Risk factors that have most consistently been shown to be associated with persistent symptoms include psychological factors (e.g., depression, anxiety, or PTSD), compensation and litigation, and negative expectations and beliefs toward injury.	Directly related to injury characteristics.

Source: Hoge et al., *N. Engl. J. Med.*, 360, 1588–91, 2009.

BLUNT FORCE HEAD INJURY

Blunt head trauma may or may not result in TBI. Another term of art used with respect to blunt head trauma is *closed head injury*. This implies that the cranial vault was not violated by penetration or any other means. The outcome of blunt head trauma is twofold: injury may only occur to the scalp and skull without any injury to the brain contents or, as a result of energy transmitted into the brain by a skull contact with a force, the tissue is injured either primarily or secondarily.

TABLE 1.7
International Symposia on Concussion in Sport, Definition of Concussion

Concussion is defined as a complex pathophysiological process affecting the brain, induced by traumatic biomechanical forces. Several common features that incorporate clinical, pathological, and biomechanical injury constructs that may be utilized in defining the nature of a concussive head injury include the following:

- Concussion may be caused either by a direct blow to the head, face, neck, or elsewhere on the body or by an "impulsive" force transmitted to the head.
- Concussion typically results in the rapid onset of short-lived impairment of neurologic function that resolves spontaneously.
- Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury.
- Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. In a small percentage of cases, postconcussive symptoms may be prolonged.
- No abnormality on standard structural neuroimaging studies is seen in concussion.

Source: McCrory et al., *Brit. J. Sports Med*., 39, 196–204, 2005.

Table 1.8 lists the types of brain injuries and lesions generally seen pathologically with blunt force head injury. The lesions are focal, diffuse, or mixed. Since World War II, modern medical practice has had a dramatic impact on reducing the mortality of TBI. There has been a steady decline in mortality rates associated with severe TBI at approximately 10% reduction per decade (Bullock et al. 1996). However, for moderate or severe TBI the figures of mortality and morbidity still remain quite extreme with 31% dead, 3% left in a vegetative state, 16% severely disabled, 20% moderately disabled, and only 31% reasonably recovered 6 months after mod/sev TBI (Murray et al. 1999).

To emphasize again, the GCS is essentially a measure of functional impairment of the neurological mechanisms subserving eye movement, motor function, and verbal ability shortly after injury. It gives to the examiner no indication of the underlying pathological or structural basis for the acute impairment. Thus, it is extremely important to remember that patients with the same GCS score may have different underlying pathological lesions producing the impairment and function, and delayed progression of these processes may cause death, even in patients with a GCS score above 9 (Blumbergs et al. 2008). Shortcomings of the GCS (Table 1.1) include the inability to test the verbal component in intubated patients and the omission in GCS of abnormal brain stem reflexes and breathing patterns. Neuropsychiatrists generally do not need this information, but if the reader wishes the lower GCS scores can be distinguished further using the Mayo Clinic FOUR (Full Outline of Unresponsiveness) score, in which brain stem and respiratory patterns are graded from 0 to 4. This may be important for forensic analysis of neurointensive care records, as noted later in this book (Wijdicks et al. 2005) (see Chapter 11).

Primary traumatic brain damage is a result of mechanical forces to the head producing tissue deformation at the moment of injury and resulting brain lesions (see Table 1.9). In turn, these deformations may directly damage blood vessels, axons, neurons, and glia in a focal, multifocal, or diffuse pattern, in one hemisphere or both hemispheres, and thus initiate a dynamic and evolving process. Recall from earlier that TBI is not an event but a multifaceted condition that evolves along a time line after direct injury (Manley and Maas 2013).

When CT became available, neurosurgeons were able to determine and develop the concept of focal versus diffuse brain injuries (Gennarelli et al. 1982). The focal injuries were determined to present as a mass lesion on CT oftentimes (Zimmerman et al. 1979). In 56% of severely head-injured persons with a GCS score less than 8 focal mass lesions were found, and 44% without focal lesions were classified as having suffered a diffuse brain injury (Marshall et al. 1991). The mortality

TABLE 1.8
Lesions of Blunt Force Head Injury

Primary injuries
- A. External to the brain
  - Scalp bruising and laceration
  - Skull fractures
- B. Parenchymal injury
  - Contusion
  - Lacerations
- C. Intracranial hemorrhage
  - Extradural (epidural) hematoma
  - SDH
  - SAH
  - Intracerebral hemorrhage
  - IVH

Secondary brain injury
- A. Injuries secondary to raised intracranial pressure.
- B. Ischemic brain injury
- C. Diffuse traumatic axonal injury
- D. Brain swelling
  - Diffuse swelling of one cerebral hemisphere
  - Diffuse swelling of both cerebral hemispheres

TABLE 1.9
Biomechanical Mechanisms to the Head Causing TBI

Mechanism	Features
Static loading:	≥200 ms to develop
Skull bending	
Skull volume change	
Dynamic loading:	≤20 ms to develop impulsive or impact
Impact	
Impulsive	
Acceleration	
Translational	All brain particles move simultaneously in same direction, linear.
Rotational-angular	Particles of brain tissue move angular to others, shear forces common, causes DAI.
Coup lesions	Predominate if head is accelerated
Contrecoup lesions	Predominate if head is decelerated
Strain	Compression, tension, or shear to tissue

rate of patients with diffuse injury was 23.9% compared with 40.4% of patients with focal injuries (Marshall et al. 1991). The patients who had CT evidence of diffuse injury and were in coma showed widespread white matter axonal damage. As a result, Adams and colleagues (Adams et al. 1982) coined the term "diffuse axonal injury" (DAI). Over time, this led to the general medical acceptance of DAI as the pathological substrate of posttraumatic coma in the absence of mass lesions (Marshall et al. 1991). From a forensic standpoint, DAI may very rarely occur in the absence of impact (head contact) forces, but most fatal human head injuries are the result of direct head impacts (McLean

1995). From a forensic standpoint, non-impact rotational acceleration of the head during a car crash may be followed by single or multiple head impacts against the interior of the vehicle or, in the case of those who are ejected, an object outside the vehicle. In the absence of contact injuries to the head, in a living person the level of rotational acceleration may not be known, as the brain may be normal by neuroimaging and macroscopic examination. Axonal injury may be apparent only on microscopic examination (Blumbergs et al. 2008).

In blunt force head injury, a mechanical loading to the head is necessary to produce brain injury. Head loading occurs generally by either static loading or various forms of dynamic loading (Graham et al. 2002). Table 1.9 displays the various biomechanical mechanisms thought to underlie the tissue strain and loading that occurs to cause TBI. Static loading commonly occurs in earthquakes and mining accidents where large amounts of dirt or weight press on a person's head. This is generally a gradual and slow process relative to dynamic loading. As noted in Table 1.9, the time sequence usually requires more than 200 milliseconds for the brain injury to develop, whereas dynamic loading occurs in less than 20 milliseconds. In static injuries, commonly eggshell comminuted fractures occur at the base of the skull and coma or severe neurological signs are generally not prominent unless cranial nerves are damaged. If deformation of the skull is severe, the brain becomes compressed and distorted, and death occurs due to fatal lacerations of parenchyma.

Dynamic loading occurs in two categories: impulsive and impact. Impulsive loading is uncommon and occurs when the head is set in motion and then the moving head is stopped abruptly without it being either directly struck or impacted (inflicted child TBI/child abuse by shaking). Conceivably, this occurs in very high-speed collisions where the body is fixed, such as in airplane crashes. The resulting brain injury is due to the inertia produced by acceleration/deceleration forces. Impact loading is the commonest cause of TBI in the world and occurs when a blunt object or blast air pressure column strikes the head. It is the commonest cause of death and/or injury in motor vehicle accidents, falls, and inflicted head trauma.

The commonest cause of tissue injury to the brain is due to parenchymal deformation causing tissue strain. Parenchymal tissue is elastic and subject to deformation, whether this is induced by inertia or by contact to the head. There are three kinds of strain: compression, tension, and shear (Table 1.9). Compression strain is the amount of deformation that a tissue undergoes as a result of a mechanical force being applied, whereas tensile strain is the amount of elongation that occurs when a material is stretched, like a rubber band. Characteristically, brain tissue withstands strain better if it is deformed slowly rather than quickly. As the rate of strain increases, the brain tissue exponentially becomes more brittle and then begins to act as a solid rather than a plastic substance. Thus, it will tear at lower strain levels under rapidly applied loads. Within the skull, three principal tissues are affected by blunt force head injury: bone, blood vessels, and brain parenchyma. As these tissues have wide variance in density and tolerance to deformation, patterns of injury are extremely variable depending on the locus and vector of forces into the cranial vault. Bone commonly breaks at a strain of 1%–2%, whereas brain and vascular tissue may not tear until a 10%–20% strain is applied. On the other hand, it takes considerably more force to cause a 1%–2% strain in bone than it does to produce a 10%–20% strain in brain tissue, as the brain is virtually incompressible in the living state. Because brain substance has a very low tolerance to tensile or shear strain, these two types of strain are the usual causes of physical brain tissue damage. The same description holds for vascular tissue as well, but it fails under more rapidly applied loads than does brain tissue (Graham et al. 2002).

PENETRATING BRAIN INJURY

Penetrating brain injury is much less frequent than blunt force brain trauma. However, in most large cities of the world penetrating brain injury is not an infrequent occurrence. The objects used to penetrate the skull, and thus the brain, include the following: missiles due to firearms, knives, crossbow bolts, shrapnel, nails, and so on. The focus of this section is on injury due to firearms.

The main pathological difference between firearm missile injuries to brain and injuries as a result of knives, ice picks, and other similar penetrating objects is that firearm injuries produce massive tissue concussion as a result of the velocity of the missile, which is directed at the brain with great force as a result of the explosion generated in the gun cartridge. There is a direct relationship between the velocity of the gunshot and the resulting brain tissue destruction and/or death. Missile velocities greater than 1000 m/s have a severe tissue damaging effect on the brain; this damage usually is incompatible with survival. There has been an evolution of gunshot wounds to the head causing great tissue damage and/or death in recent years due to the availability of military firearms to civilian populations (Blumbergs et al. 2008). In civilian gunshot wounds, only 7%–27% of patients survive the initial brain insult (Kordestani et al. 1995). For those who survive their initial injury, 30%–68% eventually die later, but the majority die at the scene of the shooting (Benzel et al. 1991). In most instances of cerebral gunshot, the bullet enters the skull and produces a penetrating (71%) or perforating (29%) injury (Freytag 1963). By definition, in penetrating injuries there is no exit wound, whereas in perforating injuries entering and exit wounds are present. Secondary laceration of the brain may occur as a result of bone fragments lacerating the parenchyma.

There is severe tissue deformation from the average gunshot wound to the head and the released kinetic energy of the bullet produces a penetrating and crushing injury, destroying all the cellular elements in its path. It also produces a stretching injury of the tissue adjacent to the bullet path due to the rapid radial acceleration of the tissues away from the path of the bullet. A temporary cavity forms, and the maximum radial extent of that temporary cavity is a function of the amount of energy transferred to the tissue by the traveling bullet (Blumbergs et al. 2008). The radial movement of this tissue away from the missile path may oscillate several times, creating pressure waves that exceed atmospheric pressure by a factor of 20–30 in magnitude and last several milliseconds. This also causes damage to brain tissue remotely from the permanent cavity made by the missile (Carey 1996).

It is possible to survive a gunshot wound to the head and, because 50% are suicide cases, oftentimes low-velocity, small-caliber weapons are used. Survival is more likely if the individual shoots himself with a submental or transoral gunshot using a low-velocity handgun. The calibers generally range from .22- to .25- or .32-caliber weapons. The resulting neuropsychiatric syndromes generally present with executive dysfunction and frontal lobe syndromes due to the nature of the shot that allowed survival (Kriet et al. 2005). Most physicians who examine survivors of self-inflicted gunshot wounds are more likely to see an individual who has produced an anteroposterior (A-P) gunshot wound rather than a lateral penetrating gunshot wound. This is because the mortality rate is 25% for A-P wounds, versus 83% for the lateral injury group (Izci et al. 2005). There are no good data delineating a common neuropsychiatric syndrome following gunshot wounds to the head. The gunshot wound to the head causes not only extensive damage to parenchymal tissue but also significant damage to blood vessels and other non-parenchymal tissue elements of the intracranial cavity and produces a biologically dirty wound, and thus prediction of neurobehavioral syndromes from gunshot wounds is difficult to impossible to offer. Table 1.10 delineates the essential elements of penetrating head trauma.

TABLE 1.10
Characteristics of Penetrating Head Trauma

- Survivors usually sustain low-velocity missile injuries.
- Intracranial infection rate is very high.
- Tissue damage is proportional to missile size and velocity.
- Seizures, blood vessel damage, and false aneurysm rates are high.

Source: Salazar et al., *Missile Wounds of the Head and Neck, Volume 2*, Rolling Meadows, IL, AANS Publications Committee, 1999; Haddad et al., *Neurosurgery*, 28, 1–7, 1991.

As noted, gunshot wounds to the brain are usually fatal, with reported survival rates that vary from 7% to 15%. In 2008, a level-1 trauma center in Arizona instituted a new aggressive resuscitation policy for persons who sustain gunshot wounds to the head. This involved treating all patients with one or more blood products, red blood cells to fresh frozen plasma, hyperosmolar therapy and vasopressors, prothrombin complex concentrate to correct coagulopathy. These researchers retrospectively reviewed 132 records for 132 patients between 2007 and 2011. The overall survival rate was 30%, with rates increasing yearly from 10% in 2008 to 46% in 2011. Survivors had higher initial systolic blood pressures (mean of 110 vs. 79 mmHg), higher *GCS* scores (median of 8 vs. 3), and more single hemispheric injuries (60% vs. 17%). Survivors had lower injury severity scores (median of 16 vs. 23), *Head Abbreviated Injury Scale* scores (median of 4 vs. 5), and international normalized ratios (mean of 1.4 vs. 1.6). Of the non-survivors, the number of organs procured per donor increased from 1.3 to 2.8 (Joseph et al. 2013). Obviously, this is a single-center study and multicenter studies for confirmation of these promising results remain to be completed, but it does forewarn those performing neuropsychiatric examinations of TBI survivors that if these procedures are adopted universally at level 1 trauma centers there will be far more persons alive with impairment as a result of gunshot wounds to the brain.

MILITARY OR BLAST BRAIN TRAUMA

Blast injury and overpressure brain trauma is more likely during military operations than in civilian populations. With respect to military populations, the data are primarily from U.S. military service personnel. Since the terrorist attacks against the United States on September 11, 2001, America has deployed 1,348,405 service members in Iraq and Afghanistan at the time of the writing of this chapter. Those conflicts have produced 17,363 military member deaths and 50,632 military members wounded in action. Since 2000, a total of 266,810 Department of Defense service members worldwide have been diagnosed with TBI. Of these, 155,282 (58%) were U.S. Army soldiers, whereas 38,809 were members of the U.S. Marines; 36,370 were members of the U.S. Navy; and 36,349 were members of the U.S. Air Force. It is important to note that 84% of all TBIs reported by the Department of Defense from 2000 to 2011 are non-deployment related and include training accidents, self-defense training injuries, motor vehicle accidents, sports-related concussions, accidental falls, and other trauma to the head, meaning only 16% were combat related (Logan et al. 2013).

Chen et al. (2013) have noted that after exposure of the human body to blast kinetic energy, the blast shock waves might be transferred into hydraulic energy in the cardiovascular system to cause a rapid physical movement or displacement of blood (a volumetric blood surge). This volumetric blood surge moves through blood vessels from the high-pressure body cavity to the low-pressure cranial cavity, causing damage to tiny cerebral blood vessels in the blood–brain barrier (BBB). It is suggested that large-scale cerebrovascular insults and BBB damage occur globally throughout the brain and may be the main causes of non-impact blast-induced brain injuries, including the spectrum of TBI and PTSD. Much of the work of Chen et al. (2013) is under way and remains to be completed.

The consequences of blast or explosion overpressure trauma are significant and are outlined in Table 1.11. Many believe that explosive blast TBI is unique from other forms of TBI, because the physical forces responsible for explosive blast causing TBI are different from those for closed head TBI and penetrating TBI. There is a unique force associated with an explosive blast, causing a shock pressure wave, which moves like an advancing wall against the body at the speed of sound (approximately 750 mph/1200 kph). It has a specific profile, which has been described as the "Freidlander curve." This pressure–time curve is characterized by an initial, very rapid up-rise, followed by a longer decay in the shock wave that reaches a negative inflection point before returning to baseline. The diffuse interaction of the pressure wave with the brain leads to a complex cascade of events that affects neurons, axons, glial cells, and blood vessels (Duckworth et al. 2013).

There are four basic mechanisms of blast injury: primary, secondary, tertiary, and quaternary. Primary injuries result from the intense overpressurization impulse created by a detonated high

TABLE 1.11
Mechanisms of Blast Injury

Category	Characteristics	Body Part Affected	Types of Injuries
Primary	Unique to HE, results from the impact of the overpressurization wave with body surfaces.	Gas-filled structures are most susceptible: lungs, gastrointestinal tract and middle ear	• Blast lung (pulmonary barotrauma) • Tympanic membrane rupture and middle ear damage • Abdominal hemorrhage and perforation • Globe (eye) rupture • Concussion (TBI without physical signs of head injury)
Secondary	Results from flying debris and bomb fragments.	Any body part may be affected	• Penetrating ballistic (fragmentation) or blunt injuries • Eye penetration (can be occult)
Tertiary	Results from individuals being thrown by the blast wind.	Any body part may be affected	• Fracture and traumatic amputation • Closed and open brain injury
Quaternary	All explosion-related injuries or diseases not due to primary, secondary, or tertiary mechanisms. Includes exacerbation or complications of existing conditions.	Any body part may be affected	• Burns (flash, partial, and full thickness) • Crush injuries • Closed and open brain injury • Asthma, COPD, or other breathing problems from dust, smoke, or toxic fumes. • Angina • Hyperglycemia, hypertension

Source: Centers for Disease Control and Prevention, Explosions in blast injuries: A primer for clinicians, http://www.emergency.cdc.gov/masscasualties/pdf/explosions-blast-injuries.pdf, 2003.

explosive, as explained earlier. The blast injuries to tissue come from the direct, or reflective, overpressurization force that impacts the body's surface (Centers for Disease Control and Prevention 2003a). Explosives are categorized as high-order explosives (HEs) or low-order explosives (LEs). HEs produce an over-pressurization shock wave, as previously discussed. Examples of these types of explosives include substances such as TNT, C-4, Semtex, nitroglycerin, dynamite, and ammonium nitrate/fuel oil. The fertilizer–diesel fuel mixture was used in the Oklahoma City bombing in the United States (Sample et al. 2012). LEs tend to cause shrapnel-type injuries to humans, as they lack the significant over-pressurization wave of HEs, such as was demonstrated in the Boston Marathon explosions. Any of the aforementioned substances can be made to produce improvised explosive devices (IEDs).

When performing a neuropsychiatric examination of a person who has been subjected to blast, it is important to review the organ systems other than the brain with the patient. Blast injury to organs outside the brain may have a very negative impact on an individual who has TBI due to blast. The primary blast injury can affect the auditory complex, producing hearing loss, tinnitus, vertigo, and other similar otological conditions. The patient may have sustained significant abdominal injury, because the blast wave can lead to perforation of any gas-containing organ such as bowel, and it may also produce mesenteric shear injuries, solid organ lacerations of the liver or spleen, or testicular rupture. The examiner does not need to understand all of the tissue injuries possible in blast trauma, but a neuropsychiatric examination requires attention to other organ systems that may have a negative impact on behavioral function. Table 1.11 gives the mechanisms of blast injury and the four categories that may result from blast.

The Naval Health Research Center in San Diego, California, conducted a descriptive analysis of 4,623 combat explosion episodes in Iraq between March 2004 and December 2007. The Barell matrix was used to describe the nature and body regions of injuries due to a combat explosion. A total of 17,637 ICD-9 codes were assigned to these episodes, with an average of 3.8 ICD-9 codes per episode. The three most frequent injures were mTBI (10.8%), lower extremity wounds (8.8%), and open wound to the face (8.2%), which included tympanic membrane ruptures. The extremities were the body regions most often injured (41.3%), followed by head and neck (37.4%), and torso (8.8%). This study supported previous observations that TBI was the preeminent injury of the wars in Iraq and Afghanistan, with mTBI being the most common single injury in this large cohort of explosion episodes (Eskridge et al. 2012).

There are some unusual findings detected from blast injury as our military physicians and researchers continue to gather more data. Sams et al. (2012) reported on two cases of concussion without loss of consciousness as a result of military injuries, as this has rarely been reported in the literature previously. Their studies concluded that syncope following an IED blast may be related to centrally mediated autonomic dysregulation at the brain stem level and syncope should be added to the list of possible symptoms that occur follow a concussion, in particular concussions following blast injuries.

MacDonald's group (MacDonald et al. 2011) at Washington University in St. Louis, Missouri, reported on diffusion tensor imaging (DTI) studies of blast-related injury. They studied 63 U.S. military personnel who had a clinical diagnosis of mild uncomplicated TBI and who were evacuated from the field to the Landstuhl Regional Medical Center in Landstuhl, Germany. They underwent DTI scanning within 90 days after injury. All subjects had primary blast exposure plus blast-related secondary injures, such as being struck by a blunt object or falling from a vehicle. Abnormalities revealed on DTI were consistent with traumatic axonal injury. These were compared against controls, and the research subjects showed marked abnormalities in the middle cerebral peduncles ($p < .001$). Follow-up DTI scans were performed in 47 subjects with TBI 6–12 months post-enrollment, and they revealed persistent abnormalities that were consistent with evolving injuries.

The Veteran's Brain Injury Center in Maryland recently reported on neuropsychological outcome following mTBI associated with blast injury. The subjects were 56 U.S. military service members who sustained con/mTBI, and they were divided into two groups based on mechanism of injury: (1) non-blast-related injury (21 subjects) and (2) blast plus secondary blunt trauma (35 subjects). Neurocognitive measures were performed and controlled for the influence of psychological distress such as depression or PTSD. There were no differences between the non-blast and blast group on all measures. These findings provided little evidence to suggest that blast exposure plus secondary blunt trauma results in worse cognitive or psychological recovery than blunt trauma alone (Lange et al. 2012).

Prior research literature on mood disorders associated with TBI suggest that major depressive disorder that develops after blast-related con/mTBI is associated with higher rates of loss of consciousness in afflicted individuals. Matthews et al. (2012) at the Veteran's Affairs San Diego Health Care System examined 46 individuals who underwent blast-related con/mTBI. They were examined by DTI. Their studies compared individuals who had loss of consciousness versus individuals who had a brief alteration of consciousness. Their preliminary results indicated that loss of consciousness is associated with detectable alterations in brain microstructure. MacDonald's group, using DTI, has also found evidence of white matter abnormalities in the cerebellum following blast injury in U.S. military personnel (MacDonald et al. 2013).

Little is known about the long-term outcome following blast injury. A recent follow-up examination of survivors of the Oklahoma City bombing in 1995 (which was a fertilizer–diesel fuel air blast explosion) was conducted on a phenomenological basis using in-person interviews, videotaped reviews, Internet communication, and research of journals as the primary data set. It is noted that 20 of the 46 bombing survivors who sustained TBI (44%) participated in the study. A common

thread running through the interviews of survivors with TBI was a recitation of life-long medical, emotional, vocational, and residential needs after the bombing. What the victims experienced in the months extending into years after the bombing was beyond their own anticipation or that of their families and healthcare professionals (Sample et al. 2012).

SPORTS INJURIES

For the period 2001–2009 in the United States, 2,651,000 young persons visited emergency departments (EDs) as a result of a sports injury (Nonfatal traumatic brain injuries related to sports 2011). Of these, 6.5%, or 173,000 persons, sustained a TBI. This sports-related TBI study gives rank ordering of sports injuries from the National Electronic Injury Surveillance System—All Injury Program, United States, 2001–2009. Interestingly, bicycling, for this time period, is the most likely sports activity to result in a TBI, and it exceeds other causes, including football, basketball, soccer, baseball, and hockey (Nonfatal traumatic brain injuries related to sports 2011). These statistics are only for children and teenagers less than or equal to 19 years and do not include the large population of adults who are injured while playing sports as well (see Table 1.12).

CONCUSSION IN SPORTS

Concussion in sports has been of international note since at least 2001. A number of international symposia on concussion in sports have been held. *The British Journal of Sports Medicine* published a definition of concussion in 2005, which is still widely used today (McCrory et al. 2005). Table 1.7 provides an adaptation summary of this definition. Refer to Chapter 10 for forensic issues in concussion analysis.

Concussion in athletes is typically produced by acceleration/deceleration forces. These include both linear (translational) and rotational (angular) components to the head trauma (Elson and Ward 1994). The University of Pittsburgh Medical Center widely published online a sideline concussion card to enable coaches to recognize the signs and symptoms of a concussion in an athlete who may have been stunned during play. Table 1.13 lists these signs and behaviors that may be observed by athletic staff or symptoms that may be reported by the athlete.

CHRONIC TRAUMATIC ENCEPHALOPATHY

There is a concern that athletes who sustain more than one concussion are at increased risk for long-term changes to brain structure and/or function, slower recovery, and increased risk of future seizures (Collins et al. 2013). The National Football League (NFL) is under legal attack by numerous plaintiff lawyers, claiming that repeated concussions in professional football players have caused brain injury consistent with chronic traumatic encephalopathy (CTE). This concern and subsequent litigation was markedly aggravated by the media report of Junior Seau, the release of his autopsy pathology report and a statement from the National Institutes of Health (NIH) (Fairnarv-Wada et al. 2013).

The NIH received tissue samples from the brain of Junior Seau after a completed autopsy. The pathological diagnosis was multi-focal tauopathy, consistent with a diagnosis of CTE. The autopsy demonstrated clusters of tau immunoreactive neurofibrillary tangles and neuropil threads in the neocortex, as well as occasional tangles in the subcortical gray matter and brain stem. On January 10, 2013, the NIH released a statement that his brain had been donated by his family, and the NIH National Institute of Neurological Disorders and Stroke invited several nationally recognized neuropathologists to consult in the analysis of Seau's brain tissue. The family requested that the NIH release the results of the analysis.

The NIH stated that on initial examination his brain looked normal, but under the microscope, with the use of special staining techniques, abnormalities were found that were consistent with a

TABLE 1.12
Rank Order of ED Visits for all Nonfatal TBIs Related to Sports and Recreation Activities among Persons Aged ≤19 Years, by Type of Activity—United States, 2001–2009

Activity	Rank Order by Number of TBIs
Bicycling	1
Football	2
Playground	3
Basketball	4
Soccer	5
Baseball	6
Other specified	7
All-terrain vehicle riding	8
Skateboarding	9
Swimming	10
Hockey	11
Miscellaneous ball games	12
Horseback riding	13
Moped/dirt bike riding	14
Scooter riding	15
Gymnastics	16
Combative sports	17
Softball	18
Exercising	19
Tobogganing/sledding	20
Trampolining	21
Golf	22
Ice skating	23
Volleyball	24
Amusement attractions	25
Roller skating/unspecified skating	26
Go-cart riding	27
In-line skating	28
Track and field	29
Racquet sports	30
Bowling	31

Source: Centers for Disease Control and Prevention, *JAMA*, 306, 2318–20, 2011.

form of CTE. The unanimous diagnosis was a "multi-focal tauopathy" consistent with a diagnosis of CTE. The following caveat from the NIH was included in the press release:

> CTE research is in a very early stage. Currently, physicians are unable to diagnose the multi-focal tauopathy form of CTE in a living person; CTE can only be confirmed by examining the brains from individuals upon autopsy. No data are available to indicate the frequency of CTE. Similarly, we do not understand which individuals with multiple impacts to the head or exposures to blast injury are at risk for CTE. Investigators at N.I.H. are now attempting to correlate brain tissue pathology with detailed images taken with the N.I.H.'s high-resolution 7 Tesla MRI scanner. Only research will reveal answers to the vexing problems that this condition presents.

TABLE 1.13
University of Pittsburgh Medical Center's Sideline Concussion Card: Signs and Symptoms of Concussion

Signs/Behaviors Observed by Staff	Symptoms Reported by Athletes
Loss of consciousness	Feeling "foggy" or groggy
Forgets events prior to play (retrograde)	Change in sleep pattern (appears later)
Forgets events after hit (posttraumatic)	Feeling fatigued
Appears to be dazed or stunned	Headache
Is confused about assignment	Nausea
Forgets plays	Balance problems or dizziness
Is unsure of game, score, or opponent	Double or fuzzy/blurry vision
Moves clumsily	Sensitivity to light or noise
Answers questions slowly	Feeling sluggish or slowed down
Shows behavior or personality change	Concentration or memory problems

Source: http://www.neurologyminutia.blogspot.com/2010/03/concussion-university-of-pittsburgh-medicalcenter-sideline-mental-status-exmaination, published March 3, 2010.

Thus, the reader is warned that the emerging legal arena of *neurolaw* (see Chapter 10) has put litigation well ahead of the science on this matter and, currently, there is an insufficient research base to link CTE to the sports life of an individual person or athlete, or the military life of an individual veteran. Moreover, the increasingly popular "second impact syndrome" is conceptualized as an extraordinarily rare cascade of events, in which an athlete experiences a catastrophic brain injury following a seemingly mild concussion. The second impact syndrome, as a true clinical entity, has been questioned. McCrory and colleagues (McCrory et al. 2012) have stated, "The scientific evidence to support this concept is nonexistent." It has been reported that relatively few athletes, approximately 35 or more in the years between 1981 and 1993, have succumbed to this alleged syndrome. When it occurs, morbidity is 100% and mortality is reported to occur in up to 50% of cases, while most cases have been reported in children (Collins et al. 2013). However, Osborn (2013) gives detailed radiographic analysis of the putative disorder.

On August 29, 2013, the NFL agreed to pay $765 million to settle a lawsuit brought against it by more than 4500 NFL players and their families. This settlement occurred 1 week before the opening of the 2013–2014 season for the NFL. A court-appointed mediator helped the two sides reach the settlement. At the time of the writing of this chapter, the approval was forthcoming by Judge Anita B. Brody of the U.S. District Court at Philadelphia. The settlement agreement states that the funds will be used for medical examinations, concussion-related compensation, and a program of medical research for retired players and their families. The money, which may not be distributed for many months, will be available to all retired players with neurological problems, not just the plaintiffs. The NFL also agreed to pay legal fees for the plaintiff's lawyers, a sum that could exceed tens of millions of dollars (Belson 2013).

The concept of CTE harks back to the lesions described at autopsy in boxers. Martland (1928) first described the syndrome known as "punch drunk." Parker (1934) is credited with coining the term "traumatic encephalopathy." Where the controversy exists presently is the failure to acknowledge the significant differences from the historical reports of CTE in boxers to the more recent cases that have been "autopsy confirmed." Most of these modern athletes were not boxers but elite athletes from the NFL, professional ice hockey, and professional wrestling venues. Some scientists have reported a connection or causal relationship between CTE and the death of these

athletes (Cantu 2007). The creation of a causal link between athletic concussions and CTE has been highly criticized by the scientific community. The primary criticisms have been that the neuropathological findings in modern athletes are not consistent with the prior CTE literature on boxers, and adequate clinical case histories have not been provided. Moreover, the case reports published to date attribute the entirety of the gross and microscopic pathology to neurotrauma and do not properly consider other possible contributing factors (Casson et al. 2006). Later, the primary research group in the United States studying CTE at Boston University acknowledged these causation problems and the need for further discussion and research (Stern et al. 2011).

Most CTE researchers have not given proper consideration to the high rates of steroid use in athletes who may suffer concussions. Moreover, chronic anabolic steroid use can result in psychiatric problems resembling those attributed to CTE in football, hockey, and wrestling. The use of these substances can also skew the behavioral profile of the athlete, as anabolic–androgenic steroid abuse has been reported to result in aggressiveness, anxiety, and depression linked to functional changes in monoamine and peptidergic systems (Halberg 2011). Another confounding factor to the behavioral profile of athletes is chronic pain. Chronic pain is associated with depression, drug and alcohol abuse, and even suicide in some persons (Cheatle 2011). There are no detailed autopsy cases in the medical literature presently of sports subjects with chronic pain, drug and alcohol abuse, psychiatric illness, and/or steroid abuse without any significant neurotrauma. Therefore, the statement that "CTE is the only known neurodegenerative dementia with a specific identifiable cause; in this case, head trauma" (Gavett et al. 2011) is not scientifically supportable at this time (Collins et al. 2013).

PEDIATRIC TRAUMATIC BRAIN INJURY

Unlike adults, TBI is the most common cause of morbidity and mortality in children. During 2002–2006, in the United States there was an annual rate of 474,000 ED visits for children of ages 0–14 years. Of these total ED visits, 35,000 required hospitalization and a bit more than 2,000 died. As noted earlier, the rate of TBI is highest in children of ages 0–4 years (1,256 per 100,000) and older adolescents, ages 15–19 years (757 per 100,000). In the young child 0–4 years of age, 50% of TBIs are caused by falls, 25% are caused by being struck against an object, and 7% are caused by motor vehicle accidents. In the year 2006, $2.5 billion was spent for medical care due to TBI in children (Faul et al. 2010; Shi et al. 2009).

There is a significant pathophysiological difference in the reaction of the child brain to trauma compared to the adult brain, as noted later. Children have increased brain water content relative to adults, less myelination in very young ages, increased cerebral metabolic rate, increased blood flow, a greater number of synapses, and different skull elasticity (Kurowski et al. 2013). The primary injury factors of contusions and shear injury are very similar to that seen in adults, and the secondary injury factors of hypertension, hypoxia, seizure activity, and infarction are also similar to those in adults. The major difference is in the healing pattern of the immature brain. Moreover, over the decades it has become clear that our previous thoughts about recovery from brain injury during childhood were wrong, because recent research finds that insults to the very young child brain are associated with poorer outcomes compared to similar lesions that occur later in childhood or in adulthood (Anderson et al. 2010).

When attempting to grade the severity of child brain injury or coma immediately following injury, it is recommended that the *Pediatric Glasgow Coma Scale* (*PGCS*) be used rather than the adult form (Simpson et al. 1991). Table 1.14 characterizes PGCS, which is widely published in numerous sources and is available online by a Google search. The scoring for this table is exactly the same as the adult. In other words, eye opening = 4 verbal response = 5, and motor response = 6 for the maximum score and the lowest score possible is 1 + 1 + 1 = 3.

Duration of unconsciousness is used to rate the initial effects of brain injury severity in adults and children. However, in children less than 15–30 minutes of unconsciousness is commonly categorized as mTBI, 15 minutes to 24 hours of unconsciousness is categorized as moderate TBI, 1–90

TABLE 1.14
PGCS

	>1 Year		<1 Year	Score
Eye opening	Spontaneously		Spontaneously	4
	To verbal command		To shout	3
	To pain		To pain	2
	No response		No response	1
Motor response	Obeys		Spontaneous	6
	Localizes pain		Localizes pain	5
	Flexion withdrawal		Flexion—withdrawal	4
	Flexion abnormal (decorticate rigidity)		Flexion—abnormal (decorticate rigidity)	3
	Extension (decerebrate rigidity)		Extension (decerebrate rigidity)	2
	No response		No response	1
	>5 Years	**2–5 Years**	**0–23 Months**	
Verbal response	Oriented	Appropriate words/ phrases	Smiles/coos appropriately	5
	Disoriented/ confused	Inappropriate words	Cries and is consolable	4
	Inappropriate words	Persistent cries and screams	Persistent inappropriate crying and/or screaming	3
	Incomprehensible sounds	Grunts	Grunts, agitated and restless	2
	No response	No response	No response	1

Total Pediatric Glasgow Coma score (3–15)

Source: Simpson, D. and P. Reilly, *Lancet*, 2(8295), 450, 1982.

days of unconsciousness is severe TBI, and greater than 90 days of unconsciousness is categorized as profound TBI (Krach et al. 2010). In instances where the child is intubated, researchers found that a *Grimace Score* has good intra-observer reliability and could replace the verbal component of PGCS in intubated children (Kurowski et al. 2013). Outcomes for pediatric TBI are discussed more fully in Chapter 10.

The vast majority of TBI in the pediatric population is of the mild severity and should cause little clinical concern, as most children go on to develop normally. Inflicted pediatric TBI is discussed more thoroughly in the forensic sections of Chapters 9 through 11, as most neuropsychiatric examinations of children who have sustained inflicted TBI come to forensic assessment. However, whether the injury is accidental or inflicted the age at which the head injury is sustained is important in determining the vulnerability to injury and the recovery pattern of the child. Unlike adult head injury patients, the severity of the injury and outcome in a pediatric brain injury is modified by the maturation of the developing skull and nervous system at the point in time when the injury is received. Pediatric brain injury, even though it shares some similarities, differs significantly from adult brain injury due to the immaturity of many of the components of the developing child nervous system. The younger the child, generally, the worse the outcome for comparable injuries compared

to a child of more advanced years or compared to an adult. Since myelination in the human brain begins in utero and continues into early adulthood, approximately to ages 25–27 years, the young child's brain responds very differently to traumatic insult than an adult brain for a given force (Smith 2011).

There are some distinct differences in inflicted brain injury to very young children that are not seen in older children or adults. For instance, Geddes et al. (2001a,b) reviewed data from 53 cases of inflicted brain injury in 37 infants less than 1 year of age and 13 children greater than 1 year of age. These studies demonstrated that the injury sustained by the child was influenced by the age of the child. Infants were susceptible to localized axonal injury at the cervicomedullary junction. This is a feature that is not seen in any older children. Unlike adults with similar injuries, global cerebral ischemia with associated cerebral swelling and raised intracranial pressure was a common finding. Acute subdural bleeding associated with retinal hemorrhages was also common and seen in 72% of the cases, and they were very similar regardless of age. In infants younger than 3 months, they presented with sudden systemic collapse and apnea associated with skull fracture, thin film subdural hemorrhages, and axonal injury at the cervicomedullary junction. Extracranial injuries to the head and skull generally were not a feature in these children. On the other hand, the older children tended to have more significant extracranial injuries and larger subdural hematomas (SDHs) when axonal injury was present. The pattern was more consistent with that seen in traumatic axonal injury of adults.

GERIATRIC TRAUMATIC BRAIN INJURY

Because the geriatric population in the United States (persons 65 years of age or older) is increasing on a yearly basis, the number of brain injuries as a percentage of the population will increase as well. This is because in 2005 nearly 13% of the U.S. population was in this age group, and it will increase to 20% by the year 2040 (U.S. Bureau of the Census: population projections of the United States by age, sex, race and Hispanic origin: 1995: 2050 2008). Falls cause 70% of accidental deaths in persons over the age of 75 years and are the fifth largest cause of death in the elderly. In fact, it is well known among neuroscience clinicians that impaired balance may be a harbinger of early cognitive decline and increased risk of fall in this age group.

Following head injury, intracranial hematomas are three times more frequent in persons over 65 years than a younger population (Pentland et al. 1986). The negative aspects of age are seen frequently in the neurotrauma intensive care unit, as severe TBI in elderly patients has been reported to produce a mortality of 79% compared to younger patients with a mortality of 36% (Pennings et al. 1993). Moreover, younger patients following TBI, in one study, became responsive to commands in less than 24 hours, whereas patients over 60 years took longer than 7 days on average (Rothweiler et al. 1998).

More recent geriatric studies have shown that the overall mortality rate is approximately 40% for all elderly brain injuries in a review of 24 studies by meta-analysis (McIntyre et al. 2013). Invariably, among all research studies the most frequent mechanism of TBI in the elderly was falls, and most studies show that approximately 70% of TBIs in the elderly are due to falls (Labib et al. 2011). Chapter 10 covers forensic aspects of TBI outcome more extensively, but the neuropsychiatric examiner should remember that elder abuse is also a common contributor to TBI in the elderly population (Murphy et al. 2013).

The normal neurobiology of aging is an adverse factor in the elderly person who sustains TBI. Reduced vascular versatility is thought to contribute to this phenomenon (Depreitere et al. 2012). Age-related cerebrovascular changes lead to a progressive reduction in cerebral perfusion and associated reductions in regional cerebral metabolism (Tumeh et al. 2007). Overall, brain shrinkage associated with aging and cerebral atrophy increases the space between the brain surface and the inner table of the skull. This exposes dural vessels to greater shearing forces in TBI and leads to the accumulation of hematomas in the elderly (Cummings and Benson 1992).

MOLECULAR BIOLOGY AND PATHOPHYSIOLOGY OF TRAUMATIC BRAIN INJURY

Blunt force TBI is generally divided first into primary and secondary injury, and then primary injury is further subdivided into focal and diffuse injury. The reader should be aware that focal or diffuse classification is a very simplistic analysis of blunt force TBI and does not do justice to the complexity of TBI. In fact, Povlishock and Katz (2005) have argued that too much emphasis is placed on the focal versus diffuse injury dichotomy and, thus, it is not a satisfactory explanation for the levels of severity of injury. It certainly does not adequately take into account the significant complications due to secondary brain damage. The reader should recall that Manley and Maas (2013) have argued for a more advanced approach to TBI evaluation and treatment. It must be remembered that there is significant overlap, particularly for moderate and severe brain injuries, of focal and diffuse brain pathology. The division into focal, diffuse, primary, and secondary categories is somewhat artificial, but it is the best that can be done currently within the state of the art of TBI research.

PRIMARY DIFFUSE BRAIN INJURY

Diffuse Axonal Injury

DAI was described more than 60 years ago by Stritch (1956). The patients in the original study were unconscious immediately after blunt force trauma, and later they were described by Gennarelli (1993) to have microscopic traumatic axonal damage involving the whole brain without significant intraparenchymal lesions. More recently, blast-related TBI was also shown to cause DAI (MacDonald et al. 2011). Povlishock's group in Virginia has produced remarkable research on the pathobiology of DAI within the last two decades. DAI is a process rather than an event, and it is a progressive response involving a traumatic disruption of the axonal membrane over 24–48 hours in humans, which is caused by calcium influx at ion channels near the nodes of Ranvier along the axonal membrane (Pettus et al. 1994). Other reviews have confirmed this probable mechanism as well (Povlishock and Christman 1995).

Immediately after the initial traumatic shock to the neuron, the cytoskeleton of the cell comes under attack. Calcium substances activate the calpain system, which causes a partial dissolution of the cytoskeletal structure by proteolysis (Kampfl et al. 1997). Microscopically, within minutes of the neuronal trauma, the cytoskeleton becomes distorted, which in turn leads to a loss of microtubules. The neurofilaments become increased in space, especially at the node of Ranvier along the axis of the axon (Maxwell et al. 1997).

The ultimate outcome of the destructive impact to the cytoskeleton of the axonal structures is a disconnection of the axon from its distal attachment to the neuron over a 24- to 48-hour period. Neuropathologists have called this "axotomy by secondary biochemical processes." Students of neuropathology are familiar with the outcome of this phenomenon, which produces a "retraction ball." This is the characteristic signature of DAI seen under the microscope of the neuropathologist (Povlishock and Katz 2005). At the molecular genetics level of pathology, the calcium influx generated due to the biomechanics of neuronal injury initiates activation of the calpain system. This, in turn, produces injury to the mitochondria and causes cytochrome *c* release and activation of the caspase system. These microchemical actions, in turn, aggravate the axonal injury and may trigger apoptosis (programmed cell death) (Yokobori and Bullock 2013). The final outcome of the disruption of axonal flow is Wallerian degeneration, which causes the distal axon to degenerate and produces a disconnection of the neuronal–axonal system from the distal neuronal fields previously serviced by the trauma affected and degenerated axons.

PRIMARY FOCAL BRAIN INJURY

It is the rule rather than the exception that focal brain injury very frequently occurs in combination with diffuse brain injury. Focal brain injury is usually related to brain and vascular tissue strains at sites of contact of the brain against the cranial coverings of skull bones. The most likely locations for focal brain injury to occur in TBI are the anterior and inferior surfaces of the frontal lobes (frontal poles and infraorbital areas) and the temporal lobes (temporal poles and lateral temporal lobe surfaces). Focal brain injury can also occur at points of intracranial impact, with or without a skull fracture, although a depressed–comminuted cranial bone fracture increases the probability of an underlying contusion or even laceration of the brain surface.

The neuropsychiatric examiner should be aware that a focal brain injury usually occurs as a result of the victim's head being struck by an object of small surface area with high velocity. This includes sticks, fists, golf clubs, baseball bats, and so on, or even during falls when the curved cranial surface (occiput and lateral frontal areas) strikes a hard surface, such as concrete or ice. In these cases, the impact of focal brain injury generally does not cause prolonged coma or stupor, but it is likely to cause focal neurological deficits, which are correlated with the particular brain area containing the focal lesion. Focal head injuries, causing focal brain injury, are often found to cause an epidural hematoma (EDH), which produces a rapidly enlarging focal mass effect (see Chapter 5).

Contusion of the Cerebral Cortex

Shearing forces tend to cause focal cortical contusions by injuring arteries, veins, and large capillaries, but this also includes neurons and glial cells. The contusions are usually on the surface of the left or right hemisphere, but they can also occur in the cerebellum, brain stem, striatum, and deeper areas of the cerebral hemispheres. Contusions on the surface of the brain injure gray matter gyri and are usually associated with superimposed subarachnoid hemorrhages (SAHs). These may be either focal or diffuse.

There is a recognized progression of the neuropathological process associated with contusions. The contusion usually covaries with ischemia (reduction of blood flow), which generally occurs with vasogenic edema and localized hemorrhage. A predominant intravascular inflammatory response occurs, and at the margins of the contusion significant levels of polymorphonuclear leukocytes congregate. These white blood cells turn up almost immediately after the injury, and then over the next 3–5 days the inflammation progresses to a complex consisting of reactive microglia monocytes/macrophages, polymorphonuclear white blood cells, and CD4 T-cells (Clausen et al. 2007).

Over time, the contusion generally undergoes necrosis and may actually transform to a cystic structure within parenchyma. However, the tissue destruction associated with contusions is complex and can be caused by apoptosis, necrosis, or autophagy, or a combination of all three (Kochanek et al. 2013). If the cerebral contusion does not meet a certain threshold to induce necrosis, it may progress to apoptosis (Bonfoco et al. 1995). Kochanek et al. (2013) has suggested that future therapies for TBI might be directed toward blocking apoptosis in mild to moderate ischemic damage and toward using other strategies to block necrosis for more severe and prolonged ischemic insults. They suggest that apoptosis presents a window of opportunity to possibly reverse the harmful effects to the brain tissue around the lesion of contusion.

Deep Intracerebral Hemorrhage

Brain hemorrhage with a diameter greater than 2 cm and not in contact with the brain surface parenchyma is defined as an intracerebral hemorrhage. As the reader will note in Chapter 5, this is categorized for radiological purposes as an intra-axial lesion. Deep intracerebral hemorrhages are present at autopsy and in 15% of severe head injury cases (Kochanek et al. 2013). The deep intracerebral hemorrhages are caused at impact by the rupture of intraparenchymal arterial or venous blood

vessels. Smaller deep intracerebral hemorrhages can present as petechial in nature. Neurological deterioration after TBI is often related to delayed traumatic intracerebral hemorrhage. This has been reported in up to 51% of patients following a repeat CT scan in the first 24 hours (Yokota et al. 2002). This is why neurosurgeons and neurointensive care specialists perform serial CT examinations for the first few days after a moderate to severe TBI to perform monitoring of changes in hemorrhage. Sometimes, the intensive care unit physician will order computed tomographic arteriography or magnetic resonance arteriography (CTA or MRA, respectively), due to concern of a possible rupture of an arterial venous malformation (AVM) or unrecognized aneurysm or pseudoaneurysm.

Traumatic Intraventricular Hemorrhage

Intraventricular hemorrhage (IVH) is a common occurrence at autopsy in patients who sustain severe head injury and do not survive long enough to reach the hospital. It is thought that the bleeding comes from small tears in the veins of the cerebral ventricular walls, and due to tears in corpus callosum, septum pellucidum, and the fornices. Some tears even occur in the choroid plexus. In the era of neuroimaging, by using CT it has been found that 1½%–3% of patients with blunt force head trauma, and 10% of patients with severe brain injury due to blunt force brain trauma, have IVH (LeRoux et al. 1992).

It is generally accepted that the presence of IVH in a living person after TBI is consistent with the presence of DAI. Many patients with IVH also have bleeding in the frontal and temporal lobes, and within basal ganglia and into the ventricular system, often following a sagittal-plane head impact (Fujitsu et al. 1988). At least half or more of cases with neuroimaging evidence of DAI in the corpus callosum and dorsolateral brain stem also show IVH (Wilberger et al. 1990). Prior experimental studies of lateral head acceleration in primates, other than humans, have shown rapid bleeding into the ventricles almost immediately after impact where IVH occurs (Blumbergs et al. 2008).

Focal Vascular Injury

Cerebrovascular tissue generally has greater tensile strength than parenchyma and is more resistant to shear damage as a result than axons. With serious head injuries, focal injury is almost always superimposed on diffuse injury (Kuijpers et al. 1995). Penetrating brain injuries, as noted earlier, may cause significant vascular injury, whether by gunshot, knife, or other missile form. With penetrating injuries, often traumatic aneurysms form in the larger cerebral vessels affected by the penetration. If one of these pseudo-aneurysms ruptures, the prognosis dramatically worsens (Risdal and Menon 2011). The reader should review Chapter 5 to gain more knowledge from a neuroradiological standpoint regarding extra- and intra-axial structural injuries and mass lesions.

Extracerebral Hemorrhage

Epidural Hematoma

Extracerebral hemorrhage is categorized by radiologists as being extra-axial. EDH is one of the extra-axial lesions detectable by structural neuroimaging (see Chapter 5). EDH occurs in almost 2% of TBIs and in up to 15% of severe TBIs (Yokobori and Bullock 2013). The usual origin of EDH is a tear of a middle meningeal artery, often associated with a skull fracture or severe inward skull bending. The size and potential lethality of the EDH depends on the diameter of the injured vessel, and the degree of its adhesion between the dura and the skull. The blood-filled lesion classically appears as a "lens-shaped" mass on neuroimaging. Moreover, EDHs are not very common in infants and toddlers, because the dura of infants strongly adheres to the developing skull and it will not peel away under arterial pressure, as it happens in the adult or adolescent. In the geriatric population, the meningeal vessels over time become embedded in bone and are therefore at greater risk of tearing

and bleeding with skull fracture or deformation. EDH often presents after head injury with a "lucid interval," wherein the person talks and maybe even walks and suddenly develops an altered level of consciousness and rapidly becomes neurologically obtunded. Without rapid neurosurgical care, death or high morbidity often occurs.

Subdural Hematoma

SDH is a common outcome of TBI. However, the reader must be aware that nontraumatic causes are common and are often associated with persons who are anticoagulated, for instance. With respect to head injury, SDH occurs in about 5% of cases. The frequency of SDH directly varies with the severity of the head injury. Adams et al. (1980) originally published that at autopsy acute SDH is seen in 20%–63% of cases. The commonest cause of acute SDH is rupture of bridging veins (cortical veins passing from the cortical surface to a dural sinus). This has been described in the literature as a "pure" SDH. SDH can also occur in association with a contusion due to damage to cortical veins or arteries, or the underlying leptomeninges. Most SDHs occur in the frontal, parietal, and temporal parts of the cranial fossa. They are rarely found in the posterior fossa, and when present their occurrence is usually due to damage to the vein of Galen or from a tear to the straight sinus.

Unlike the lens-shaped EDH, the blood products of SDH follow the gyral brain pattern on the affected side. If they become large enough to become a space-occupying lesion, they compress the gyri on the opposite side of the cerebrum to become flattened against the cranial vault. In some persons, SDH may become chronic. Even trivial head injuries can produce these lesions, as in 25%–50% of cases the physician cannot find a history of trauma. In chronic SDH cases, alcohol abuse, homelessness, and limited functional capacity of the individual are not unusual comorbid issues. As noted, anticoagulants may increase the likelihood of SDH, but it also occurs in coagulopathies associated with chronic liver disease or blood dyscrasias such as thrombocytopenia.

Subarachnoid Hemorrhage

Unlike EDH or SDH, SAH by itself is rarely significant. There is one exception to this statement: rupture of the vertebral or basilar artery due to trauma can produce a highly morbid or fatal SAH. Primary traumatic SAH of this type has a very high mortality, and the blood distribution is predominately around the base of the brain (Blumbergs et al. 2008).

SECONDARY TRAUMATIC BRAIN INJURY

Secondary brain injury has two major components. The first component is due to four major mechanisms, as outlined in Table 1.15. These include the following: (1) ischemia, excitotoxicity, and energy failure, which results in cell death cascades; (2) secondary cerebral swelling or increased intracranial pressure; (3) axonal injury; and (4) inflammation and regeneration. Numerous neurochemicals and genetic alterations of cell receptor systems are involved as mediators of secondary brain damage. At present, there is no silver bullet that accounts for all the resultant damage from TBI.

TABLE 1.15
Major Mechanisms of Secondary TBI

- Ischemia, excitotoxicity, and energy failure
- Secondary cerebral swelling and increased cerebral pressure
- Axonal injury
- Inflammation and regeneration

Ischemia, Excitotoxicity, Energy Failure, and Cell Death Cascades

Ischemia/hypoperfusion after severe TBI often presents very early. It is now recognized as an important secondary brain injury factor in the pathotrajectory of TBI (Betrus and Kreipke 2013). Trauma studies have shown that a hypoperfused brain is at high risk and thus may be incapable of mounting an appropriate response to the added insults by failure to vasodilate vessels appropriately (Chestnut et al. 1993). Maintaining blood perfusion is one of the most daunting challenges within the neurocritical care unit following TBI. Physicians caring for persons with severe TBI must struggle with balancing the systemic causes of cerebral ischemia, such as hypotension or refractory intracranial hypertension. Numerous mechanisms probably underlie early posttraumatic hypoperfusion, but they are too extensive to explore in this book and the reader is referred to more extensive textbooks on the subject.

Associated with the ischemia is excitotoxicity. This describes the process by which glutamate and other excitatory amino acids cause neuronal damage. Glutamate is the most abundant excitatory neurotransmitter found within the brain. Unfortunately, exposure to toxic levels of this substance produces neuronal death (Choi et al. 1987). When glutamate is activated in response to brain tissue injury, minutes after exposure, sodium-dependent neuronal swelling occurs, and this is followed by delayed calcium-dependent degeneration. These effects are mediated by multiple agonists through ionophore-linked receptors. When these receptors are activated, there is a dramatic influx of calcium through either receptor-gated or voltage-gated channels and the increased intracellular calcium concentration then triggers several processes that lead to cellular injury or death (Choi 1987). Studies of anti-excitotoxic substances have been very disappointing in clinical efforts to reduce excitotoxic neuronal damage.

Following a TBI, when neuronal cells die they do so as a continuum; on the low end simple necrosis occurs, and on the upper end apoptosis (programmed cell death) occurs (Clark et al. 1999; Rink et al. 1995). Apoptosis is defined as a combination of cell shrinkage and nuclear condensation with DNA fragmentation in nucleosomes, causing the formation of apoptotic bodies. This is in contrast to cells that die of simple necrosis, as they display cellular and nuclear swelling and dissolution of membranes (Kerr et al. 1972). Cells dying of necrosis do so in a much simpler fashion than that required for apoptosis. Apoptosis occurs as a cascade of intracellular events before cell death is completed. This led to the term "programmed cell death" (Steller 1995). The reader is referred to more extensive reviews of cell death cascades following TBI, such as the one by Kochanek et al. (2013).

Necrosis and apoptosis make up two of the triad of cell death pathways following TBI. The third is autophagy, and it is one of the mechanisms within the evolution of secondary injury after TBI. It is a highly regulated process that involves a series of proteins related to autophagy that orchestrate the formation of an autophagosomal vesicle around brain material and other organelles, such as mitochondria, which are later digested to amino acids by lysosomes. The reader is referred to Lai et al. (2008) for a more comprehensive review of this topic.

Secondary Cerebral Swelling

While axonal damage and neuronal death through cascade mechanisms have been progressively elucidated over the last three decades, it is now also well understood that brain swelling is often a hallmark of severe TBI. It is less likely to occur in moderate TBI and almost nonexistent in mTBI. Swelling (edema) causes the development of intracranial hypertension, which may lead to death or other devastating neurological consequences. There are two major ways that increased intracerebral pressure (ICP) can contribute to or cause secondary damage following the original traumatic insult to parenchyma. The first major way is interference with cerebral blood perfusion, which then causes ischemia (reduction of blood flow). In addition, cerebral swelling can produce a mass effect and cause a displacement of brain tissue, resulting in herniation syndromes, as the intracerebral volume increases with the swelling process. Table 1.15 outlines the