Second Impact Syndrome

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Neuropathology

This Forensic Science Newsletter is devoted to a discussion of **second impact syndrome**, its definition, general information, clinical presentation, treatment, pathophysiology, prevention and epidemiology. Reference through links to recently published articles on concussion and post-concussion syndrome will also be given.

Definition

Second impact syndrome occurs when an athlete who has sustained a mild traumatic brain injury, usually a concussion, with or without loss of consciousness, suffers a second traumatic brain injury before the symptoms associated with the first have cleared. Such patients are at risk for developing intense cerebral vascular congestion followed by diffuse brain swelling, which typically occurs immediately after the second impact to the head or to the trunk, the latter imparting acceleration to the brain. The risk of such brain swelling decreases as the time from the first concussion increases.

To refresh, **concussion** is defined as a trauma-induced alteration in mental status, usually characterized by confusion and amnesia that may or may not involve loss of consciousness, link "Mild Traumatic Brain Injury (Concussion) in Infants, Toddlers, Children and Adolescents."

Most of the athletes experience a lucid interval following the second mild traumatic brain injury or suffer an immediate brief period of loss of consciousness, followed by several minutes of being lucid, which is characteristic of second impact syndrome.

General Information

Typically, the majority of athletes who experience second impact syndrome are under the age of 18, although it can also be seen in college athletes and rarely, professional athletes.

The earliest description of second impact syndrome was by Otto Bollinger in 1891, who described the syndrome as, "Trauma-tische spät-apoplexie." The condition was next described by R. C. Schneider in 1973. The term, "second impact syndrome of

catastrophic head injury," was coined in 1984 by R. L. Saunders and Harbaugh. They described the death of a football player who died after a second, unremarkable concussion and hypothesized the second blow caused a catastrophic rise in intracranial pressure, possibly through the loss of vasomotor tone, because the brain was in a vulnerable state.

From 1980 to 1993, the **National Center for Catastrophic Sports Injury Research in Chapel Hill, NC**, identified 35 probable cases among American football players. Between 1992 and 1998 reports of this entity began to occur more frequently as clinicians became more aware of second impact syndrome. In July 2007 *eMedicine* summarized an article in the **American Journal of Sports Medicine** in which they stated: A study of American high school and college football players demonstrated 84 catastrophic head injuries, which included significant intracranial bleeding or edema over a 13-year period. Seventy-one percent of high school players suffering such injuries had a previous concussion in the same season, with 39% playing with residual symptoms.

There is another term you may occasionally see, "**vascular congestion syndrome**," which was coined by J. P. Kelly *et al* in 1991 following their report of the death of a football player after suffering a reported concussion.

After researching the records of the National Center for Catastrophic Sports Injury Research, Muller and Cantu, reported in an article in 2009, a not uncommon associated injury in second impact syndrome was an **acute subdural hemorrhage**. In subsequent research of American football players, Cantu and Gean found 38% of athletes who had sustained an acute subdural hemorrhage following a previous traumatic brain injury were playing while symptomatic from that head injury. **What is important to keep in mind is acute subdural hemorrhage is the most common cause of death due to head injuries in sports according to the National Center for Catastrophic Sports Injury Research.**

Regarding the **amnesia** that is not uncommonly seen in a **concussion,** there are two types: **anterograde amnesia**, which is the inability to retain new information and **retrograde amnesia**, the inability to remember events preceding a traumatic injury. Typically, the extent of the concussive amnesia correlates with the duration of the loss of consciousness, as well as the severity of the traumatic brain injury.

There are several classifications of concussion. In an article summarizing the **Second International Conference on Concussion in Sports (Prague 2004)**, McCrory *et al* classified concussions as **simple** and **complex**. A **simple** concussion is an athletic head injury that resolves without complications within ten days. A **complex** concussion involves persistent symptoms beyond ten days, or the development of additional symptoms, such as seizures, cognitive impairment, exertional headaches or confusion.

Robert C. Cantu devised a grading system following extensive review of data concerning concussions, which is as follows:

Grade 1 (mild)
No loss of consciousness;
Post-traumatic amnesia (retrograde and anterograde) or post-concussion signs or symptoms lasting less than 30 minutes

Grade 2 (moderate)
Loss of consciousness lasting less than 1 minute;
Post-traumatic amnesia (retrograde and anterograde) or post-concussion signs or symptoms lasting longer than 30 minutes but less than 24 hours

Grade 3 (severe)
Loss of consciousness lasting more than 1 minute or post-traumatic amnesia (retrograde and anterograde) lasting longer than 24 hours;
Post-concussion signs or symptoms lasting longer than 7 days

Clinical Presentation

The typical clinical scenario of **sudden impact syndrome** is that of an athlete who has suffered a previous concussion (mild traumatic brain injury), but before the symptoms of that injury have cleared they sustain a second head injury, often a concussion, which is associated with a lucid interval without unconsciousness, or a very brief loss of consciousness followed by a lucid interval. The symptoms of the first concussion are those of a headache, tiredness, memory loss, dizziness, irritability, poor attention, depression, difficulty in concentration, sleep problems, personality change, labyrinthine dysfunction (characteristic dysfunction in vision and balance), motor and sensory problems. Before these symptoms clear the athlete resumes a contact sport and sustains a second blow to the head, often very mild with no loss of consciousness. The athlete may appear stunned, typically remaining on their feet for a short time, a few seconds to a minute or so. They may stay on the field of play or walk off the field. The impression the athlete gives to everyone is they are stunned or dazed. After a few seconds to a minute or so they suddenly collapse, lose consciousness, rapidly develop dilating pupils with no eye movement, which rapidly progresses to respiratory failure and death within 2 to 5 minutes.

An immediate CT scan taken at the hospital initially shows a vascular engorged hemisphere with initial preservation of the gray-white junction, which is often followed by rapidly developing cerebral edema with flattening of the gyri and narrowing of the sulci, partial to complete collapse of the ventricles, developing effacement of the gray-white junction, midline shift, collapse of the basal (perimesencephalic) cisterns, distortion of the brainstem due to uncal and diencephalic herniation, and hemispheric asymmetry Fig. 1). Failure of the brainstem frequently occurs between 2 and five minutes after the second impact.

The **mortality rate** is approximately 47-50%. Those who survive have a virtual 100% **morbidity (neurologic disability)**, which is primarily due to **multifocal post-traumatic ischemic infarctions.** The **morbidity** of second impact syndrome is similar to that of

severe traumatic brain injury, which includes persistent muscle spasms, muscle tenseness, emotional instability, hallucinations, post-traumatic epilepsy, mental disability, coma and brain death.

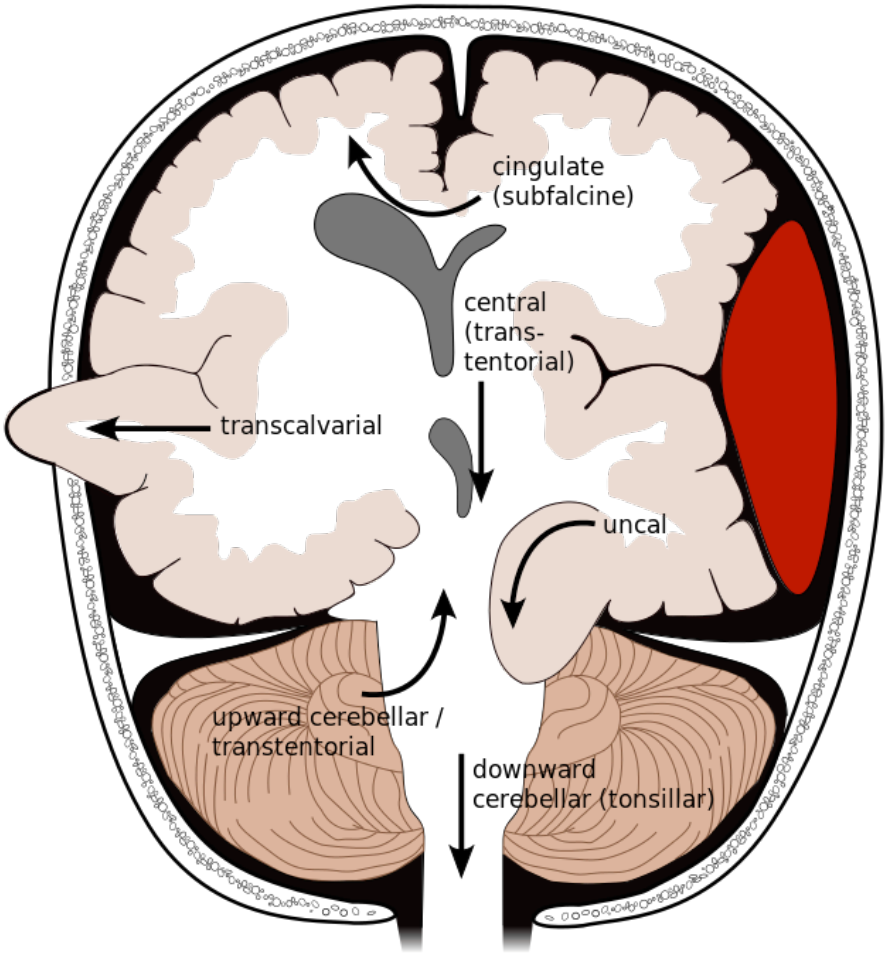

FIg.1. Types of brain herniation: 1) Uncal, 2) Central - The brainstem herniates caudally, 3) Cingulate herniation - The brain squeezes under the falx cerebri, 4) Transcalvarial herniation - through a skull fracture, 5) Upward herniation of the cerebellum, 6) Tonsillar herniation - the cerebellar tonsils herniate through the foramen magnum. (en.wikipedia.org)

There have been a number of second impact cases reported in which the acute hemispheric swelling is associated with a thin subdural hematoma. It is believed the cause of the thin acute subdural hemorrhage in association with the brain swelling of second impact syndrome is due to the acceleration and deceleration forces. The acceleration forces required to produce an acute subdural hemorrhage are greater than those required to produce a concussion or second impact syndrome.

Treatment

Typically, 47-50% of those athletes who develop second impact syndrome are deceased within two to five minutes following the traumatic injury to their head. The traumatic injury is usually a concussion, often mild, may experience a very brief period of loss of consciousness followed by a lucid interval or a lucid interval with no loss of consciousness, before collapsing within seconds to a minute or so. The athlete should immediately be stabilized with intubation. This should be accomplished before transport to the hospital. **The athlete must be transported to the closes hospital and while in route be hyperventilated and receive intravenous (IV) mannitol or hypertonic saline to address the rapidly evolving increase in intracranial pressure due to catastrophic vascular congestion and developing cerebral edema.**

Acute hyperventilation causes immediate cerebral vasoconstriction, which results in an increase in cerebral vascular resistance and a consequent fall in cerebral blood flow. This change is due to the fall in arterial carbon dioxide tension (P_{CO_2}). It is generally accepted that the effect of hyperventilation is mediated by this change in P_{CO_2}, because hyperventilation leads to cerebral vasoconstriction.
If carbon dioxide levels are high, the body assumes our oxygen levels are low, and accordingly, the brain's blood vessels dilate to assure sufficient blood flow and supply of oxygen to the brain. If carbon dioxide levels are low, this causes the brain's blood vessels to constrict, resulting in reduced blood flow to the brain. This is due to the fact hypocapnia (decrease carbon dioxide) cause the blood to become more alkaline, which in turn causes the blood vessels to constrict. The alkalization of the blood also reduces the level of available calcium (hypocalcemia), which also results in the blood vessel constricting.

Mannitol's effectiveness in controlling the patient's rapidly increasing intracranial pressure is believed to be small at best. Recent literature suggest the use of **hypertonic saline** is more effective than mannitol in controlling the patient's increase in intracranial pressure. However, the safety, efficacy, and duration of the intracranial pressure lowering of hypertonic saline is still being evaluated. It is no longer recommended using **steroids** to control the increase in intracranial pressure. In one study, high-dose IV methyprednisolone (Solu-Medrol) was shown to increase mortality, which was presumably due to immunosuppression, hyperglycemia, increased muscle catabolism, and impaired wound healing.

Controlling the rapidly evolving increasing intracranial pressure is very important in preventing the development of brain herniation, which causes compression of the **anterior and or posterior cerebral arteries**. It is the compression of these arteries, which leads to **multiple ischemic infarctions** throughout the brain and catastrophic neurologic morbidity.

Regarding imaging studies, it is recommended the patient undergo an immediate CT scan. CT scans are easier to obtain and are more sensitive than magnetic resonance imaging (MRIs) to detect acute intracranial bleeding and identify surgically reversible injury.

Pathophysiology

To have a complete understanding of the pathophysiology of second impact syndrome we need to understand what occurs to an athlete when they experience the initial concussion.

The athlete who suffers a concussion may develop cerebral edema, which accounts for memory impairment, disorientation, headaches with or without loss of consciousness and amnesia, anterograde and or retrograde (see above discussion on page 2). Typically, the symptoms do not progress due to the brain's autoregulatory mechanisms, which compensate for the blunt force traumatic injury and the subsequent neurophysiologic stress, protecting the patient from massive hyperemia and brain swelling. This occurs through the brain's autoregulatory mechanism, which acutely limits cerebral blood flow, which in turn leads to an accumulation of lactate and intracellular acidosis.

What is of interest is researchers have shown lactic acid protects the white matter in the brain through its beneficial effect on the myelin forming oligodendrocytes. The brain's white matter is mainly composed of nerve tracts, which connect the various parts of the brain together and carry the nerve signals up and down the spinal cord. The electric signals travel rapidly through the myelin. Lactic acid is also known to benefit neurons.

This initial phase is then followed by a state of altered cerebral metabolism, which may last 7 to 10 days or in some cases several weeks. It is during this phase there is a decrease in protein synthesis and a reduction in oxidative capacity. Research has suggested the symptoms of concussion, such as a loss of consciousness after the mild traumatic brain injury, the subsequent development of secondary brain damage, and the enhanced vulnerability of the brain after the initial concussion is largely due to ionic fluxes, acute metabolic changes, and cerebral blood flow alterations that occur immediately after the concussion. For example, extracellular potassium concentration can increase substantially in the brain after a concussion, followed by a state of hypermetabolism lasting 7 to 10 days or several weeks. This makes the brain very vulnerable and susceptible to death after often either mild traumatic injury to the athlete's head, typically with no loss of consciousness, or a blow to the chest, which indirectly injures the athlete's brain through subjecting the brain to acceleration forces.

Secondary brain damage refers to the indirect result of a traumatic brain injury. It results from processes initiated by the trauma. It occurs in the hours and days following the primary injury and plays a large role in the brain damage and death that results from traumatic brain injury. Examples of secondary brain damage are ischemia (insufficient blood flow), cerebral hypoxia (insufficient oxygen in the brain), hypotension (low blood

pressure), cerebral edema (swelling of the brain), and an increase in intracranial pressure (the pressure within the skull).

Other secondary injuries include hypercapnia (excess carbon dioxide levels in the blood), acidosis (insufficient blood flow), alterations in the release of neurotransmitters, imbalances in some neurotransmitters, which can lead to excitotoxicity and damage to brain cells that result from overactivation of biochemical receptors, damage to cells by free radicals potentially leading to neurodegeneration ("Postconcussive-Syndrome-Adults").

The pathophysiology of the second impact syndrome is still somewhat controversial, but it is generally believed to be caused by a loss of autoregulation of the cerebral vasculature. This dysautoregulation leads to a loss of the brain to autoregulate cerebral perfusion pressure and intracranial pressure. Such loss of autoregulation causes intense vascular congestion, hyperemia, which in turn causes pronounced brain swelling due to cerebral edema, which leads to a marked increase in intracranial pressure. The intense vascular congestion of the brain is immediate. This is rapidly followed by cerebral edema, which is primarily vasogenic but also has a cytotoxic component. The intense vascular congestion and cerebral edema cause an increase in intracranial pressure, which leads to inferomedial herniation of the temporal lobes, herniation of the cerebellar tonsils through the foramen magnum, which distorts and compresses the brainstem. Once brainstem distortion and compression occurs, occular involvement and respiratory failure rapidly follow. The usual time from the second impact to brainstem failure is between 2 to 5 minutes. Research has shown the vascular engorgement of the brain after the second impact can be very difficult, if not impossible to control. To further emphasize the rapidity at which the clinical deterioration occurs in second impact syndrome, it occurs far more rapidly than that seen with an epidural hemorrhage.

Some cases of second impact syndrome also have an **acute subdural hemorrhage**. Typically, in these cases the forces are usually greater than those causing second impact syndrome. Usually, these forces cause instantaneous unconsciousness and prolonged coma due to direct injury to the **reticular activating system**. The instantaneous unconsciousness and prolonged coma in these cases is not due to brain herniation as it is in second impact syndrome. Additionally, the lucid interval, or brief period of lose of consciousness followed by several minutes of being lucid, which is characteristic of second impact syndrome, is not seen in these cases.

There appears to be similarities between the clinical presentation and imaging studies in blunt force trauma injuries to the head of children, non-accidental trauma (child abuse) and sudden impact syndrome involving adolescent football players. Although, the mechanism of brain injury in both entities is still being developed, they have several things in common. In both the patients have sustained several head injuries over a finite period. Secondly, it has been shown there is an increased incidence of hypoxic-ischemic injury in infants and children who are victims of non-accidental trauma (child abuse) in comparison to accidental trauma. There is also evidence which shows a

predilection for hypoxic-ischemic injury in those who survive second impact syndrome. Such patients will show on imaging studies evidence of multifocal bilateral ischemic injury without white matter shearing lesions and intracerebral hemorrhage. Thirdly, not uncommonly victims of non-accidental trauma (child abuse), like some of the second impact syndrome victims, may show a small acute subdural hemorrhage, which although present is not the underlying cause of the massive increase in intracranial pressure. Fourth, the unusual vulnerability to dysautoregulation seen in second impact syndrome, especially in adolescent football players, is also seen in the victims of child abuse who sustained head trauma. Lastly, the outcome of the victims of sudden impact syndrome is poor as is true of some of the survivors of child abuse victims who have sustained repetitive head trauma. Often both the survivors of sudden impact syndrome and child abuse victims with repetitive head trauma suffer permanent neurologic morbidity.

In an article published in the August 2016 issue of the **Journal of Neuropathology and Experimental Neurology, "Delayed Hypoxemia Following Traumatic Brain Injury Exacerbates White Matter Injury,"** it was shown following the primary direct mechanical injury to the brain, important secondary injuries develop over hours to days from multiple mechanisms including hypoxemia, ischemia, and immunoexcitotoxicity. An in depth discussion of immunoexcitotoxicity is given in the following, "Postconcussive-Syndrome-Adults," pages 4-11. The clinical observations in this article pointed to the strong association between early hypoxemia (pre-hospital, such as on the football field or in the emergency room setting) following a traumatic brain injury and poor clinical outcome. Experimentally induced traumatic brain injury have shown hypoxemia immediately after such an injury exacerbates brain edema and ischemia, hippocampal neuronal cell death, neuroinflammation (immunoexcitotoxicity), axonal injury and behavioral deficits.

Epidemiology

The Centers for Disease Control and Prevention estimates about 1.1 million patients with nonfatal traumatic brain injury are treated and released from U.S. hospital emergency departments annually. Approximately 300,000 traumatic brain injuries are mild to moderate and some 235,000 require hospitalization.

Concussion is not uncommon, affecting 128 people per 100,000 in the United States yearly. Young children have the highest rate of concussion, with sports and bicycle accidents accounting for the majority of cases in the 5-14 age group. Falls and vehicular accidents are the most common cause of concussion in adults.

There is little epidemiological data concerning sudden impact syndrome. The overall incidence of secondary concussion and sudden impact syndrome is unknown. Most of the information comes from case reports and series. One study analyzed the 30-year US National Registry of Sudden Death in Young Athletes (1980-2009). Of the 1827 deaths of athletes aged 21 years or younger, 261 (14%) were caused by trauma related injuries, usually involving the head and or neck (mean: 16 ± 2 years; 90% male) in 22

sports. The highest number of events in a single year was 16 (1986), with an average of 9 per year throughout 30 years. The mortality rate was 0.11 in 100,000 participations. The largest number of deaths was in football (148 [57%]), including 17 high school athletes who sustained concussions shortly before fatal head trauma (second impact syndrome).

The relationship between football position and trauma related death risk was analyzed in 123 of the 148 deaths. Overall, defensive positions were associated with greater numbers of deaths (n = 69) than were offensive positions (n = 54). Among the 69 deaths in defensive players, 24 (35%) were in backs, 24 (35%) were in linebackers, 12 (17%) were linemen, and 9 (13%) were special-team players. However, the player position in which fatal trauma related injury was sustained most commonly was offensive running back, accounting for 33 (61%) of deaths among offensive players.

Track and field was associated with 27 deaths (10%); predominantly pole vaulting (n = 22); baseball was associated with 18 deaths (7%); boxing, 12 deaths (5%); and soccer 11 deaths (4%).

Most athletes were engaged in organized high school (178 [68%]), middle school (26 [10%]), and youth and other organized sports programs (21 [8%]). The remaining athletes had advanced beyond the high school level into college (28 [11%]) and professional sports (8 [3%]).

Prevention

Any athlete who shows signs of a concussion, such as tiredness, headache, memory loss, dizziness, irritability, poor attention, depression, difficulty in concentration, sleep problems, personality changes, disorientation, labyrinthine dysfunction (dysfunction in vision and balance), nausea or vomiting should not be allowed to return to the game or any future games until these symptoms have cleared. **Coaches, teachers and parents must closely observe the athlete.**

A guideline which has been used in the management of sport related concussions developed by the American Academy of Neurology, is as follows:

Symptoms	**First Concussion**	**Second Concussion**
Grade1: No loss of consciousness, transient confusion, resolution of symptoms and mental abnormalities in <15 min.	Remove from play. Examine at 5-min intervals. May return to play if symptoms disappear and results of mental function exam return to normal within 15 min.	Allow return to play after 1 week if there are no symptoms at rest or with exertion.

Grade 2: As above, but with mental symptoms for >15 min.	Remove from play and disallow play for rest of day. Examine for signs of intracranial lesion at sidelines and obtain further exam by a trained person the same day. Allow return to play after 1 week if neurological exam is normal.	Allow return to play after 2-week period of no symptoms at rest or with exertion. Remove from play for season if image shows abnormality.
Grade 3: Any loss of consciousness.	Perform thorough neurological exam in hospital and obtain imaging studies when indicated. Assess neurologic status daily until post-concussive symptoms resolve or stabilize. Remove from play for 1 week if loss of consciousness lasts seconds; for 2 weeks if it lasts minutes; must be asymptomatic at rest and with exertion to return to play.	Withhold from play until symptoms have been absent for at least 1 month.

The best prevention for sudden impact syndrome is to prevent the first concussion. In contact sports it is highly recommended for the player to wear headgear that not only extends around the head, but also covers the ears. **Experts advise wearing a helmet during high-impact contact sports and above all, preventing or mitigating especially head-to-head contact and unnecessary violent impacts to the torso, which will induce sudden acceleration of the brain.**

Summary

Reviewing the scientific information concerning sudden impact syndrome, prevention of high impacts, whether that be head-to-head or to the torso, which imparts sudden acceleration of the brain, is an absolute priority in contact sports. What is essential is the prevention of the first concussion. **Should the athlete sustain a concussion, with or without loss of consciousness, under no circumstances are they to return to play until all concussive symptoms have cleared as outline above in the American Academy of Neurology's Guidelines in the management of sport related concussions.** The American Academy of Neurology has further enhanced the above guideline.

Second Impact syndrome refers to a rapid and catastrophic swelling of the brain that occurs when an athlete experiences a second concussion before symptoms of an earlier concussion have resolved. The global form of edema, which rapidly develops is both vasogenic and cytogenic, although predominantly the former. This global edema is due to the immediate development of an intense neurogenic vascular engorgement due to autoregulatory failure and dysfunction of the vasomotor center in the brainstem.

If the athlete has any hope for survival with minimal neurological morbidity, they must be immediately stabilized with emphasis on airway management with rapid intubation and hyperventilation to decrease cerebral blood flow and control intracranial pressure. At this point it appears hypertonic saline is far more effective than mannitol in abating an increase in intracranial pressure. Prevention of brain swelling leading to herniation, which in turn leads to compression of the anterior and or posterior cerebral arteries, is the primary goal. It is the compression of these arteries, which cause multifocal cerebral infarction and catastrophic neurologic morbidity.

There are now several books available for your review on the website, http://www.forensicjournals.com/books/. These books are entitled, “Traumatic Injuries to the Head, Vertebrae, Spinal Cord and Peripheral Nerves of the Newborn During Birth,” which is under the heading of Neuropathology. Under the heading of Forensic Pathology are two books entitled, “Nonsexual and Sexual Traumatic Injuries of the Perineum, External Genital Organs and the Breasts: Adult, Elderly and Pediatric,” and “Traumatic Injuries of the Organs of the Pelvis: Adult and Pediatric.” A fourth book, “Traumatic Injuries of the Organs of the Retroperitoneal Space,” will be available shortly.