

Traumatic Brain Injury in the War Zone

Susan Okie, M.D.

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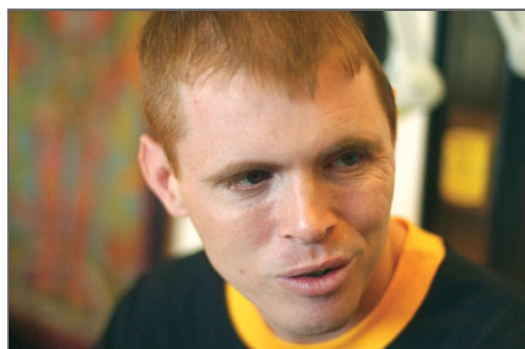
An interview with Dr. Okie can be heard at www.nejm.org.

Sergeant David Emme, a supply officer with a U.S. Army Stryker Brigade, was stationed at a submachine gun on a truck rolling through northern Iraq last November, in a convoy transporting Iraqi volunteers to Mosul for military training. As they entered the town of Talafar, Emme noticed that the streets were unusually quiet: no children were outdoors running toward the vehicles demanding sweets. Emme got on the radio and warned others in the convoy: "Something might happen. They might have some plan for us." Moments later, as they slowed at a traffic circle, an improvised explosive device (IED) went off right next to Emme's truck, knocking him out.

Emme's version of what happened next is patched together, from his own memories and what others told him later. "I remember waking up and wondering who the hell I was, where the hell I was, and why can't I see or hear? My soldier was screaming for me to get out of the truck and I told him no, because it hurt too much. So he literally threw me out of the truck and guided me to a Stryker," a light-weight armored vehicle.

The blast wave and fragments from the explosion had blown out Emme's left eardrum, fractured his skull, injured his left eye, and caused a severe contusion in the left frontotemporal area of his brain. His fellow soldiers rushed him to the nearby military base, where he partially regained his vision and tried to walk before again losing consciousness. He was medically evacuated, first to a combat support hospital in Balad and then to one in Baghdad. There, neurosurgeons performed a craniectomy, removing a large piece of skull from the left temporal region to give Emme's brain room to swell (see diagram). They implanted the bone under the subcutaneous tissue of his abdomen, hoping that it could be replaced later — if Emme survived. He remained unconscious and remembers nothing about his stops in these hospitals.

Dr. Okie is a contributing editor of the *Journal*.



Sergeant David Emme.

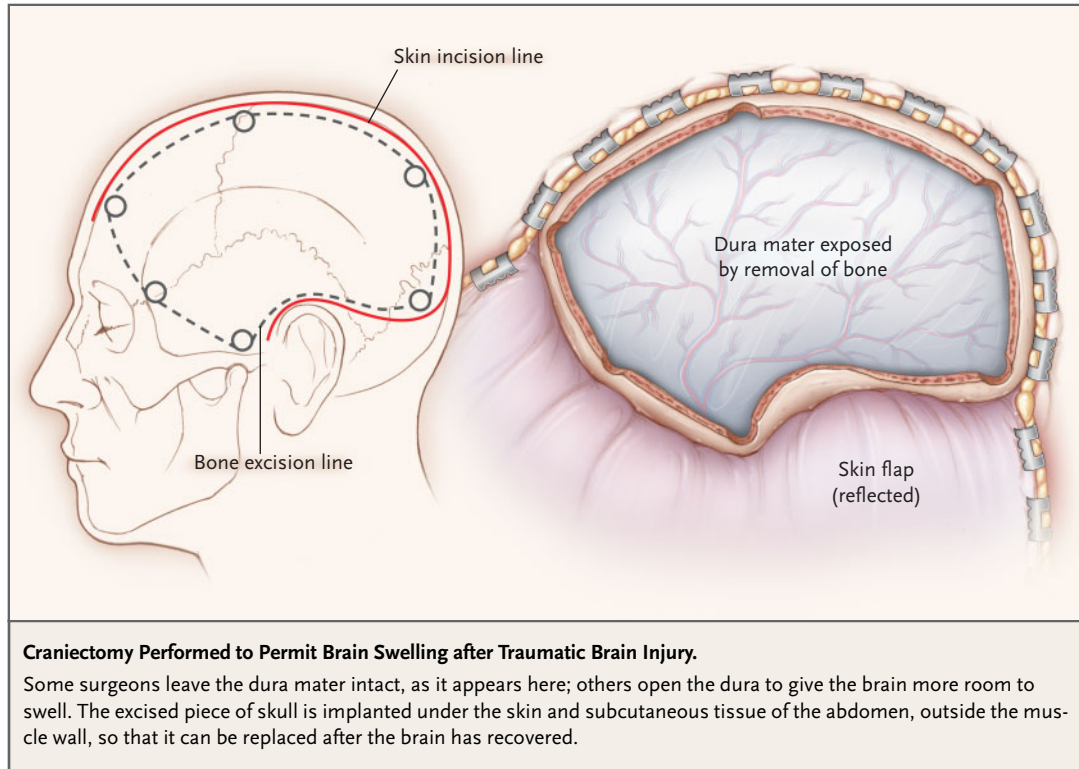
Jonathan Ernst

"The next time I come to, I'm at Walter Reed — like, 10 days later," he recalled.

Emme spent about six days in the intensive care unit, sometimes mistaking nurses for CIA agents or believing he was back in Baghdad. Then he was transferred to a room in ward 58, the neuroscience unit at Walter Reed Army Medical Center in Washington, D.C. At some point, he became alert enough to realize that he was having difficulty speaking.

"I called for the nurse. . . . I kept on just trying to say something, but I couldn't really say anything," Emme recalled. The nurse asked him questions and waited patiently for him to answer. Finally, she left to check on other patients. About a half hour later, she returned, and Emme managed to articulate his message: "My head hurts."

In the five months since then, Emme, 32, has made a remarkable recovery from his severe brain injury. He is a clean-cut young man with expressive brown eyes, a scarred left cheek, and a depression on the left side of his head where the missing piece of skull has yet to be replaced. (That will be done after surgeons finish reconstructing his tympanic membrane.) His vision has returned almost to normal. With time and intensive therapy, his speech and cognitive function have dramatically improved. "Basically, I had to learn what things were again," Emme explained. Then he corrected himself:



“I knew what they were — I just didn’t know what the names of them were.”

Laura W. Battiata, Emme’s speech and language therapist, said that when Emme was first evaluated, 10 days after his injury, his speech was limited and nonsensical, and he could not understand or follow commands. During the ensuing week, this profound receptive and expressive aphasia rapidly resolved as the brain swelling abated. Once his language deficits had improved, Emme’s therapists were able to test his cognitive skills and found that the traumatic brain injury (TBI) had led to defects in reasoning, memory, and problem solving. Emme embarked on daily cognitive-therapy sessions and attended group sessions three times a week.

“Typically, we’ll work on deductive-reasoning tasks, basic problem-solving tasks,” Battiata explained. A patient might be asked to do math exercises, solve puzzles, plan a trip or a meal, or complete a homework assignment. “We know that counseling and giving patients some strategies to use is beneficial,” Battiata added. “Whether it improves their rate of progress, I think, is not well known.”

Emme got better much more rapidly than many of Battiata’s patients with TBIs, some of whom have severely impaired function and show little progress. She said his residual cognitive defects are mild.

Emme’s headaches have abated, and he has begun taking college courses online. Although crowds make him uncomfortable, he has started to socialize, venturing out of his room on the hospital campus: recently, he attended the opening game of the Washington Nationals baseball team with friends. He speaks fluently and eagerly now, occasionally resorting to circumlocution when a word eludes him. During a tour of the Pentagon in December, Emme was excited to meet Paul Wolfowitz, then the deputy secretary of defense. Afterward, he recalled with amusement, “I was telling people about it and I was like, ‘Yeah, I went on that . . . well, I went on . . . I went to the, uh . . . place that had the big bang when they flew planes into it.’”

Among surviving soldiers wounded in combat in Iraq and Afghanistan, TBI appears to account for a larger proportion of casualties than it has in other recent U.S. wars. According to the Joint Theater Trauma Registry, compiled by the U.S. Army Institute of Surgical Research, 22 percent of the wounded soldiers from these conflicts who have passed through the military’s Landstuhl Regional Medical Center in Germany had injuries to the head, face, or neck. This percentage can serve as a rough estimate of the fraction who have TBI, according to Deborah L. Warden, a neurologist and psychia-

trist at Walter Reed Army Medical Center who is the national director of the Defense and Veterans Brain Injury Center (DVBIC). Warden said the true proportion is probably higher, since some cases of closed brain injury are not diagnosed promptly.

In the Vietnam War, by contrast, 12 to 14 percent of all combat casualties had a brain injury, and an additional 2 to 4 percent had a brain injury plus a lethal wound to the chest or abdomen, according to Ronald Bellamy, former editor of the *Textbooks of Military Medicine*, published by the Office of the Surgeon General of the U.S. Army. Bellamy said that because mortality from brain injuries among U.S. combatants in Vietnam was 75 percent or greater, soldiers with brain injuries made up only a small fraction of the casualties treated in hospitals.

Kevlar body armor and helmets are one reason for the high proportion of TBIs among soldiers wounded in the current conflicts. By effectively shielding the wearer from bullets and shrapnel, the protective gear has improved overall survival rates, and Kevlar helmets have reduced the frequency of penetrating head injuries. However, the helmets cannot completely protect the face, head, and neck, nor do they prevent the kind of closed brain injuries often produced by blasts. As insurgents continue to attack U.S. troops in Iraq, most brain injuries are being caused by IEDs, and closed brain injuries outnumber penetrating ones among patients seen at Walter Reed, where more than 450 patients with TBI were treated between January 2003 and February 2005. All admitted patients who have been exposed to a blast are routinely evaluated for brain injury; 59 percent of them have been given a diagnosis of TBI, according to Warden. Of these injuries, 56 percent are considered moderate or severe, and 44 percent are mild.

A blast creates a sudden increase in air pressure by heating and accelerating air molecules and, immediately thereafter, a sudden decrease in pressure that produces intense wind. These rapid pressure shifts can injure the brain directly, producing concussion or contusion. Air emboli can also form in blood vessels and travel to the brain, causing cerebral infarcts. In addition, blast waves and wind can propel fragments, bodies, or even vehicles with considerable force, causing head injuries by any of these mechanisms. Approximately 8 to 25 percent of persons with blast-related injuries die.¹

U.S. soldiers in Iraq and Afghanistan who have serious brain injuries receive immediate care on the battlefield and are then transported to military combat support hospitals, where they undergo brain

imaging and are treated by neurosurgeons. Treatment may include the removal of foreign bodies, control of bleeding, or craniectomy to relieve pressure from swelling. Depending on their condition, these soldiers are eventually transferred to one of the DVBIC's eight participating U.S. hospitals for assessment and treatment.

At Walter Reed, the severity of a TBI is assessed according to the duration of loss of consciousness and post-traumatic amnesia, according to Louis M. French, a neuropsychologist who is the DVBIC's clinical director. A mild TBI (which is usually not associated with visible abnormalities on brain imaging) is one that causes loss of consciousness lasting less than 1 hour or amnesia lasting less than 24 hours. A moderate TBI produces loss of consciousness lasting between 1 and 24 hours or post-traumatic amnesia for one to seven days. Injuries causing loss of consciousness for more than 24 hours or post-traumatic amnesia for more than a week are considered severe. In magnetic resonance images from patients with moderate or severe TBIs, punctate hemorrhages may be visible in the corpus callosum or other regions, and there may be other evidence of bleeding or swelling.

Pathological studies in brain-injured animals (and limited postmortem studies in humans) suggest that TBIs typically cause damage to nerve axons in many areas of the brain. Although it is unclear what initiates axonal damage, it begins within minutes after the injury occurs, develops over a period of hours to a few days, and leads to the degeneration of some axons' distal projections and to diffuse loss of synaptic terminals. This loss of neural connections may lead to many of the symptoms associated with brain injuries, and the gradual replacement of lost synapses by the sprouting of nearby, undamaged axons probably underlies the recovery process.² Excitotoxicity and oxidative stress have been suggested as possible mechanisms of cell injury. In addition, in moderate and severe TBIs, hemorrhages, contusion, and pressure caused by swelling may also contribute to tissue damage.

Soldiers with TBI often have symptoms and findings affecting several areas of brain function. Headaches, sleep disturbances, and sensitivity to light and noise are common symptoms. Cognitive changes, diagnosed on mental-status examination or through neuropsychological testing, may include disturbances in attention, memory, or language, as well as delayed reaction time during problem solving. Often, the most troubling symptoms are behavioral ones: mood changes, depression, anxiety,

impulsiveness, emotional outbursts, or inappropriate laughter. Some symptoms of TBI overlap with those of post-traumatic stress disorder, and many of French's patients have both conditions.

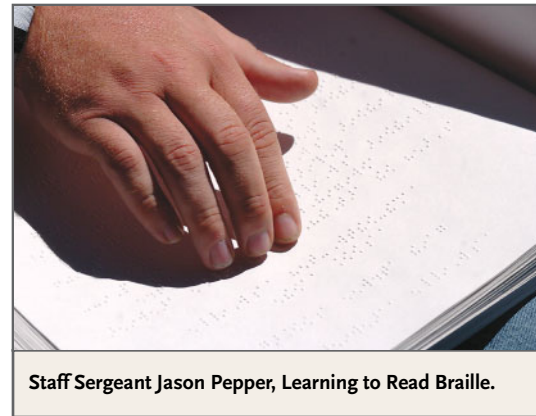
"We are working with a population that tends to be young and healthy going into this, so they're really in a good position to recover," French said. "But complicating things, these people have been hurt in complicated and terrible ways. Certainly, if people get even a mild TBI under circumstances of extreme stress," especially if it is accompanied by other injuries, "that might well affect the outcome."

Last May, Staff Sergeant Jason Pepper experienced the full force of an IED that exploded in a tree next to his armored personnel carrier in Karbala, Iraq. "It kind of detonated in my face," Pepper explained. "The signature of the heat and the shrapnel took out my right eye. The heat and the compression took out my left eye. From the blast itself, I had a small skull fracture on the left side, a subdural hematoma, plus a bruised brain. A right forearm that was completely shattered at the elbow and wrist . . . and then, in my left hand is a mixture of plates, pins, screws, rods, and lacing wire — basically an Erector Set in the making."

Surgeons at a combat support hospital in Baghdad enucleated Pepper's eyes: "There was nothing left for them to save," he said. After undergoing several operations in Iraq, Pepper arrived at Walter Reed a week after he was injured and has been receiving treatment and rehabilitation there for much of the past year. He lost his left index finger, so surgeons have been rebuilding his hand by transplanting the middle finger and releasing tendons to give him a pincer grasp. Between operations, he attended occupational-therapy sessions intended to improve his dexterity, aid his recovery from a moderate TBI, and develop his visualization skills.

Pepper, 28, who was a combat engineer, has close-cropped brown hair and an athletic build, and he finds his way around with the aid of a white cane. His musical name and his wry sense of humor charmed cartoonist Garry Trudeau, who wrote Sergeant Pepper into a "Doonesbury" strip after visiting Walter Reed. Pepper's hobbies used to include video games and softball; "Now," he said, "I sit there listening to XM radio." His wife, Heather, complains that he doesn't want to go out anymore. He has multiday migraines and hates being left alone.

French noted that for soldiers like Pepper who have multiple injuries, recovering from a TBI can complicate the process of rehabilitation because of the brain injury's effects on mood and cognitive



Staff Sergeant Jason Pepper, Learning to Read Braille.

Jonathan Ernst

function. "If you're trying to do blind rehab and you're relying on auditory memory, your attention had better be intact; your auditory memory had better be intact," he said.

Pepper will be transferred soon to the Edward Hines Jr. VA Hospital near Chicago, where he has chosen to undergo an intensive blind-rehabilitation program that is likely to last two months or longer. Participants live in private rooms in a dormitory and receive training for at least seven hours a day on orientation and mobility, manual skills, sensory skills, daily living skills, and computer access.

For Pepper, Emme, and other soldiers with TBIs, overcoming some of the lingering effects of brain injury may take longer than recovering from other wounds. Doctors help them to manage headaches and sleep disorders; therapists work with them to overcome difficulties with memory or concentration. Warden said stimulants such as methylphenidate or dextroamphetamine are commonly used to treat problems with attention or information processing, and selective serotonin-reuptake inhibitor antidepressants are sometimes prescribed for irritability or angry outbursts. Valproate is frequently prescribed because it can be effective both for migraines and for behavioral symptoms.

Most adults with a mild TBI recover completely within a year, but moderate and severe TBIs are more likely to cause lingering effects. An estimated 5.3 million Americans are living with disabilities that resulted from TBIs, according to the Centers for Disease Control and Prevention. Warden said many patients with such injuries who are treated at Walter Reed are able to return to active duty; others retire from the military and receive medical disability payments. The Department of Veterans Affairs is now planning for the large influx of veterans with TBIs from the current conflicts who will need continuing care during the coming years. "These

are people who are going back into our communities all across the country, who are potentially going to be struggling,” said Warden. “Keep in mind, these patients, because of the nature of their brain injuries, can be the ones at highest risk of falling through the cracks.”

French said that Pepper and Emme have had better-than-average recoveries so far, in part because they are highly motivated and are working hard at their rehabilitation programs.

“Not all of them recover,” noted Colonel Jean Dailey, a nursing supervisor on the neuroscience

unit. “It can wear on you.” Dailey added that nurses on her unit have higher turnover rates than those on the hospital’s orthopedic ward, which chiefly treats soldiers with limb injuries. Unlike the young amputees, she said, “these guys’ personalities are not the same” as before they were injured. In fact, she says, “they may never be the same.”

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2. Povlishock JT, Erb DE, Astruc J. Axonal response to traumatic brain injury: reactive axonal change, deafferentation, and neuroplasticity. *J Neurotrauma* 1992;9:Suppl 1:S189-S200.

Perinatal Mortality in Developing Countries

Jelka Zupan, M.D.

Each year, 10.7 million children under the age of five years die — 4 million during the first four weeks of life. Another 3.3 million are stillborn. And these are only the official reports. In the less developed countries, which account for 98 percent of reported neonatal deaths and 97 percent of reported stillbirths, these births and deaths are not always registered.

Since 2000, when the United Nations Millennium Declaration was signed, efforts to reduce mortality among children younger than five years of age have been accelerating. It will be difficult to reach the stated goal — cutting the rate by two thirds by 2015 — without reducing the number of neonatal deaths. Many useful interventions can be implemented in resource-poor settings, but weak health care delivery systems remain an important barrier. Research is ongoing on alternative approaches, including the training and deployment of traditional birth attendants, as reported by Jokhio et al. in this issue of the *Journal* (pages 2091–2099). But the problems involved are so many, and the resources so limited, that the task remains daunting.

The highest neonatal mortality rates and rates of stillbirth occur in sub-Saharan Africa, followed by Asia and Latin America (see graph). In countries where the mortality is highest, almost 10 percent of babies do not survive more than one month.

Neonatal deaths generally result from complications of preterm birth, asphyxia or trauma dur-

ing birth, infections, severe malformations, or other specifically perinatal causes. The proportion attributable to each cause varies: in areas where neonatal mortality is lower, preterm birth and malformations play a larger role; where mortality is higher, the contributions of asphyxia, tetanus, and infections are greater. Maternal health and nutrition are important for neonatal health, and maternal infections contribute to adverse outcomes.

But the real causes of adverse outcomes are untreated or poorly treated maternal complications, inadequate neonatal care, and harmful home care practices, such as the discarding of colostrum, the application of unclean substances to the umbilical-cord stump, and the failure to keep babies warm. The risk of death for a pregnant woman with severe preeclampsia, for example, is 0.5 percent, and the risk of perinatal death for her child is 13 percent. If the condition remains untreated and eclampsia develops, the risk of death increases to 5 percent for the mother and 28 percent for the baby.

In addition, infections, which cause many infant deaths, have diverse origins; many are community-acquired bacterial infections in previously healthy infants. It is estimated that in about 25 percent of the stillbirths in less developed countries, death occurs shortly before birth and most likely results from complications of delivery.¹

Targeting new interventions for neonatal survival should be easy in one sense: we know when pregnant women and newborns will need care, since we estimate in advance the date of birth and most complications arise during late pregnancy and

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