Army medicine: Untested in battle

New procedures were rushed into theaters of war without rigorous review

By Robert Little Baltimore Sun reporter
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BAGHDAD—
The U.S. Army has quietly altered or abandoned some of its more experimental medical treatments for troops injured in combat, as advances it once hailed as groundbreaking are foundlargely ineffective or perhaps even dangerous.
Advanced battle dressings, a blood-clotting drug, alternative procedures for emergency blood transfusions - each was introduced early in the Iraq war, often with little evidence to support them beyond anecdotes or tests on animals. A few were adopted widely by civilian hospitals, based almost exclusively on accolades from the military.

But an investigation by The Baltimore Sun reveals that military doctors and medics, and in some cases uniformed leaders, have rejected or curtailed use of many of the new devices and techniques as clinical experience and data from the war zone yield disappointing and sometimes troubling results.
Senior Army doctors rushed medical innovations onto the battlefield without the rigorous review common in civilian hospitals, The Sun found, and sometimes changed or disregarded data from their own scientists. In some instances, wounded service members were among the first humans on whom the treatments were used. And while virtually all of the Army's published research supports the treatments, some Army studies concluding that they are ineffective or potentially dangerous haven't been published.

The aggressive push is a point of pride to some Army doctors and officials. Others deride it as reckless, and still others say they felt pressured to defy their own judgments in favor of the military's favored, but unproven, treatments.
"I worry that some soldiers were hurt by the overzealous use of unproven therapies," said Dr. Ian H. Black, head of anesthesia at the Army's main combat hospital in Baghdad in 2006 and 2007 and a former Army researcher. "I look back and I wonder, did I hurt someone?"
]The Army's surgeon general, Lt. Gen. Eric B. Schoomaker, said in an interview that changes in combat medical care show that Army medicine is nimble and responsive to the lessons learned in warfare. "We're not doing experimentation in theater. It's unethical," Schoomaker said.
But he also said, in response to questions by The Sun, that the Army will re-examine its treatment protocols to make sure the service is not "out ahead of the headlights" with novel but unsupported treatments.
"We'll redouble our efforts to make sure that isn't happening," Schoomaker said. "I think we should be concerned about that, and we are."
Among The Sun's findings:

•Roughly 17,000 packages of a blood-clotting substance were shipped to Iraq last year for distribution to Army medics, despite cautions from the service's own scientists against using it on humans. It was quickly recalled when tests on pigs revealed potentially deadly complications.
•An $89 bandage given to every combat soldier and honored by the Army as one of its "greatest inventions" was deployed despite two unpublished studies from the service's research lab showing that it was no more effective than gauze. After mixed reports from the battlefield, it is being recalled and replaced.
•Liberal use of a blood-clotting drug, injected copiously into wounded soldiers in 2005 and 2006, became the Army's "standard operating procedure" more than a year before any clinical studies evaluating the drug's use on trauma patients had been completed. The drug has since proven largely ineffective in three unpublished Army studies and potentially dangerous in at least one, and is now used only in extreme cases.

•Transfusions of fresh whole blood, considered dangerous and unnecessary in civilian medicine, became standard treatments early in the war, based on anecdotes and theoretical arguments. They unwittingly exposed 20 or more patients in Iraq and Afghanistan to hepatitis. Studies of the practice have since found mixed results, and it is now used only in emergency situations.
There is little data or documentation from either the Army or civilian hospitals to prove that the military's aborted new treatments were either helpful or harmful on a broad scale. But a group of current and former military physicians and researchers, many of whom spoke with The Sun, have complained formally to Army investigators that senior medical officials manipulated research and "stressed results at the expense of good science." The complaints have sparked at least two reviews by Army investigators. The Sun's requests under the Freedom of Information Act about the scope or status of the reviews were denied.
Pentagon officials often credit medical innovations in Iraq for a near-doubling of the rate of battlefield survival since the Vietnam War. But it is largely a myth, said Dr. Ronald F. Bellamy, a thoracic surgeon and retired colonel who edited the service's textbooks on combat trauma. Survival rates have declined steadily since the early years of the war, and most improvements are likely attributable to body armor, not medicine, he said. "Unfavorable truth is not something people like to talk about in the Army," Bellamy said.
Doctors and military officials interviewed by The Sun all said the Army had one motivation for taking risks rarely considered in state-side hospitals: saving lives. Each of the new treatments showed, and in some cases still shows, great promise in treating patients with certain injuries.
But critics say that by implementing the new practices broadly, before research made clear which patients were likely to benefit, the military exposed hundreds of soldiers and Marines to the risks of unproven treatments that were unlikely to do much good.

"I am proud of the care we gave. I know to a man we did, and would have done, anything to help those soldiers," said Black, who left the service last year, partly, he said, over frustration with the military's promotion of untested treatments. "Maybe that was the problem; that eagerness to help."
Before the war in Afghanistan started in 2001, battlefield medical care had evolved little since Vietnam, and few Army surgeons had experience in combat trauma.

And so Army leaders, eager for innovative treatments to manage mounting casualties

from Afghanistan and Iraq, enlisted a team of medical researchers in San Antonio, Texas, to recommend and implement new ideas. Headed by veteran trauma surgeon Col. John Holcomb, head of the Army's Institute for Surgical Research, the group was given almost complete authority to issue treatment guidelines throughout the war zones and analyze combat data to determine whether the treatments were working, according to Army documents obtained through the Freedom of Information Act and from published accounts in medical journals.
Holcomb and the others challenged long-held assumptions by advocating practices like frequent application of tourniquets or limited use of intravenous fluids. Today both practices are hailed as lifesaving.
They also bypassed checks and balances common in civilian medicine. For instance, implementing a new treatment in Iraq required just four steps: writing it, submitting it to Holcomb and a handful of senior physicians, circulating it "for informational purpose only," and publishing it

The same process at the Department of Veterans Affairs involves up to 19 steps, including multiple reviews by independent committees.
According to interviews with dozens of Army physicians and scientists, many of whom spoke to The Sun on the condition of anonymity because they said publicity would imperil their careers, the group sometimes moved so aggressively to implement unproven medicines and techniques that some doctors felt pressured to defy their own judgment.

Doctors who challenged the use of a blood-clotting drug said they were berated by senior physicians from the San Antonio laboratory.
At one point in 2006 military leaders proposed to measure a physician's use of the Army's guidelines as a measurement of the quality of treatment - meeting with a backlash from clinicians in the combat zone, three doctors told The Sun.

Dr. Arthur Caplan, a professor of bioethics at the University of Pennsylvania, said a system that allows medical researchers to establish treatment protocols should have concerned the Pentagon.
"Certainly there is a need for the military to try to learn from the tragic opportunity that war presents," said Caplan. "But if you're going to try novel things, you owe it to the people who are your subjects to have as many eyeballs on it as you can. The potential for someone to pursue and promote their own biases is too great."

A report issued in December 2007 cleared Holcomb and his institute of complaints about his command style and alleged inattention to research, but the stress of the investigation pushed him to retire from the military last July, according to a transcript of his interview with investigators.
Holcomb declined to comment for this article. But in numerous interviews with The Sun the past four years he has defended the Army's aggressive push for new treatments as necessary. Greater risks are acceptable, he said, given the devastating nature of today's combat injuries.
"These guys don't have the luxury of waiting," for more scientific data, he said in one interview in Baghdad in 2006.
He is still revered by many Army doctors - and decried by others.
In interviews with investigators, transcribed in a 453-page report obtained by The Sun, an Army officer who worked at the Institute for Surgical Research referred to Holcomb,

in the same sentence, as "arrogant, obnoxious, overbearing" and "exactly the type of leader the ISR needed."
Much of the Army's system of testing and implementing medical treatments in combat has been restructured over the last year. Practice guidelines must be reviewed by an advisory panel before being implemented, for instance.
"I won't argue with you that early on it may have appeared unsophisticated and less than optimal in its alignment with direct data being derived from theater, because we lacked some of the fidelity of data that we needed," Schoomaker said. "But we now have evolved. We've evolved while in the fight."
Here are The Sun's findings:
Finding: An $89 bandage distributed to combat soldiers and honored as one of the service's greatest inventions was deployed despite two unpublished studies from the Army's research lab showing that the dressing was no more effective than plain gauze. After mixed reports from the battlefield, it was recalled and replaced.

The bandage, called HemCon, made from a substance derived from shrimp shells, was approved by the Pentagon's advisory committee on combat medicine in 2003 as the preferred dressing for combat. The committee based its recommendation on animal tests conducted by San Antonio researchers showing HemCon to be significantly more effective than plain gauze, according to committee members. The Army named the bandage one of its "greatest inventions" in 2005, eventually distributing it to every soldier in the combat zones.
But in two animal studies in San Antonio before the war in Iraq began in 2003, the results of which were shown to The Sun by a retired Army researcher, HemCon was found to be no more effective than gauze, and in one case perhaps less effective.

According to Army documents, after the second study was completed and eight pigs treated with HemCon fared roughly the same as eight pigs treated with gauze, Army scientists who had helped develop the dressing removed results from a pig that was treated with HemCon but quickly died. They determined it was an "outlier," or a fluke. Without it, HemCon came out statistically superior.
Statisticians interviewed by The Sun said that removing subjects from such a small study is questionable and should be disclosed prominently in the research's conclusions. Schoomaker and people involved in the advisory committee's deliberations told The Sun they never knew of the failed tests.
Once HemCon was in the combat zone, the Army published a series of anecdotal reports suggesting that it was effective, but the dressing was not universally embraced. Medics in Iraq told The Sun that the dressings were too small and rigid for battlefield injuries, and a supply officer said troops were discarding them unused. The Navy's top trauma surgeon publicly challenged HemCon's effectiveness. Then, early last year, in a new San Antonio study, just one of 10 bleeding pigs treated with the dressing survived. The Army ordered the dressing removed from the field last summer in favor of a newer dressing.

Schoomaker said HemCon was never ideal but was the best product available at the time. An Army researcher in San Antonio told The Sun, however, that the service's enthusiasm seemed driven more by hope than science. "It just never lived up to the hype, even in our own laboratories," he said.
Finding: A blood-clotting dressing sent to Iraq late last year as a possible replacement for HemCon was distributed even as Army scientists cautioned against using it to treat

soldiers. It was quickly recalled by Army leaders when tests on pigs revealed potentially deadly complications.

That dressing, called WoundStat, was touted as "significantly more effective" than other dressings in the same San Antonio study that questioned HemCon's effectiveness and led to its recall.
The authors of the study, however, cautioned that WoundStat posed "a potential safety risk that must be investigated in survival studies before this product can be recommended for use by the military." They feared that because it is a loose clay material rather than a bandage, WoundStat could drift into veins and arteries and cause potentially deadly clots.
But those findings, which were shared with The Sun, did not appear in the scientists' final report and were never published. Schoomaker decided in June to send WoundStat to Iraq - unaware, he says, of the scientists' complete assessment.
After WoundStat was already in Iraq, the same San Antonio scientists tested the product last December on eight pigs with bleeding neck wounds. Within several hours, according to Army officials and other accounts relayed to The Sun, seven of the animals developed a complete blockage of the blood vessels at the site of their wounds. On Dec. 18, the Army ordered WoundStat removed from the field.
The Army is still trying to determine whether the product was used on wounded troops in Iraq or Afghanistan, and whether any complications arose, said Col. Paul R. Cordts, a vascular surgeon and the Army's director of health policy and services.

Finding: Liberal use of a blood-clotting drug, injected copiously into wounded soldiers in 2005 and 2006, was the Army's "standard operating procedure" more than a year before a study into the use of the drug in trauma patients had been completed. The drug has since proven largely ineffective in three unpublished Army studies and potentially dangerous in at least one, and it is no longer routinely used.
Army officials said in interviews two years ago that Recombinant Activated Factor VII, a drug approved by the FDA only for treating hemophilia, arrived in the trauma hospitals in Iraq in early 2004, soon after they got an early look at data from what was then the only clinical trial conducted with trauma patients without hemophilia.

According to Army documents provided by doctors deployed to Baghdad, however, the first guideline from San Antonio on using Factor VII was issued a year earlier, before the war began. It cited only laboratory studies, a handful of anecdotal treatments in Israel and clinical tests on pigs as references.
The guideline recommended giving the drug to almost any casualty with a traumatic injury, even when the extent of bleeding was unclear. The Army didn't begin formal research into Factor VII until more than 2,000 doses had been shipped to hospitals in Iraq, according to documents from the Army's Medical Research and Materiel Command.

In 2006 doctors at the main combat hospital in Baghdad proposed greatly curtailing Factor VII's use, noting safety concerns and their own review of unpublished data that found "no mortality benefit" when the drug was used. They proposed giving it only to patients with "blunt" injuries, and withholding it from the other 90 percent of casualties with "penetrating" injuries.

The doctors say they transmitted their proposal up the medical chain of command at

about the same time The Sun reported on Factor VII's possible link to deadly blood clots, but never heard back. Schoomaker and other Army officials said they don't recall seeing it.

Sometime around January 2007, according to documents and electronic messages shown to The Sun, one of the service's top transfusion researchers, using data collected from several hundred patients in Iraq, concluded that Factor VII was "associated with increased mortality" and at best had no measurable effect when variations in injuries and treatments were considered. Two other Army researchers separately reached similar conclusions last year, according to summaries and internal messages shown to The Sun.

None of the research was peer-reviewed or vetted by statisticians, a process that can often lead to different conclusions. And Army officials said the research critical of Factor VII did not look at enough patients to be statistically relevant. Yet the Army's most recent published research related to Factor VII - one study in mid-2007 based on 61 patients, and one in early 2008 based on 124 patients - analyzed smaller groups of patients. Both concluded that the drug is beneficial.

A large clinical trial testing Factor VII in trauma patients was canceled last June by the drug's manufacturer when it became clear halfway through the study that it wouldn't show that the drug was working.
Today the military's use of Factor VII has been significantly scaled back. Physicians at the Baghdad hospital said last summer that they recalled using it about a dozen times in the first six months of 2008. During a trip to the same hospital two years previously, The Sun twice saw a dozen doses given in a single day.

Finding: Transfusions of fresh whole blood, a rarity in civilian medicine, became a standard treatment early in the war, based mostly on anecdotes and theoretical arguments. But the practice unwittingly exposed 20 or more patients to hepatitis, studies of its effectiveness have found mixed results, and it is now used only in emergencies.

The first guideline for Factor VII called for giving two units of fresh whole blood along with the drug.
The concept goes against standard practice in the United States, which is to break down blood into components - platelets, plasma, red blood cells - and give only the components a doctor thinks are required. Components broken down in a laboratory are rigorously tested for diseases such as hepatitis and HIV, whereas whole blood can only get cursory testing, if that.
During the run into Baghdad in 2003, fresh blood was often the only thing available, particularly as a source of platelets, which don't travel well but are important for stopping blood loss. In interviews, Army doctors recounted success stories of the "walking blood banks" early in the war.
But even as medical facilities in Iraq improved and the emergency need for whole blood diminished, many military doctors kept using it, based solely on their observations that fresh whole blood worked better than frozen components. According to one Army study, more than 6,000 units of whole blood were transfused by military doctors in the first four years of the war - much of it because no other blood was available but also because some doctors preferred it.
For months a debate raged between doctors in the United States and their counterparts in Iraq, according to e-mail traffic shown to The Sun. The Navy's top trauma adviser

called whole blood "like nothing I have ever seen" and said he orders it for every massive transfusion patient. The chief of transfusion research at Walter Reed Army Medical Center called its routine use "indefensible" and said: "You are risking death, malignancy or lifelong infection with hepatitis."

Schoomaker said in December that 20 units of whole blood contaminated with hepatitis made it through the military's screening procedures in the war zones. At least one soldier contracted Hepatitis C from a transfusion and is now in treatment. While the odds of infection are still low, given the thousands of units of blood transfused during the war, the military issued a guideline in early 2007 limiting the use of fresh blood to times when nothing else is available.

But the debate continued. Last summer, Army surgeons in Iraq fought to save a 32-year-old Army captain who kept bleeding from multiple gunshot wounds even after numerous surgeries, 50 units of transfused components and a dose of Factor VII. Desperate, they called Capt. Victoria McCarthy, officer in charge of the blood bank, and asked about activating a whole blood drive.

"I said no," McCarthy said. "I had components available, and told them they couldn't use soldiers as guinea pigs."

The captain bled to death well before any whole blood would have been available.

"There's no science to suggest that fresh whole blood leads to better outcomes, just some idiosyncratic views about health and disease that are based on anecdotes," said Dr. David Walker, chairman of the Defense Health Board's subcommittee on emergency transfusions, which issued a report last year calling whole blood "undesirable." "If data comes out that it's better, that's different."

Controversy over the experimental nature of Army medical care continues in Iraq over a procedure that Army leaders consider "the single most important advance in trauma care for hospitalized civilian and military casualties from this war."

The standard procedure for an emergency blood transfusion before the war started was to give a patient red blood cells, the basic oxygen-carrying component in real blood, and then order other components after diagnosis.

But beginning in 2002 in Afghanistan, and continuing in 2003 in Iraq, reports from battlefield surgeons suggested that patients were bleeding to death because their blood had become too diluted with red cells or fluids to clot, not simply because of their injuries. In 2004, doctors in Iraq recommended thawing frozen plasma - a vital component in the clotting process - and using it at the beginning of the transfusion process. Each time a casualty got a unit of red cells, the guideline stated, he should also get a unit of plasma.

The concept behind the 1:1 ratio was simple: It's the same ratio found in whole blood. The new procedure was institutionalized by an Army-wide memo issued in January 2007 and became known as "damage control resuscitation."

But plasma has been implicated in lung infections and other complications, and the new ratio quadrupled the standard dose of plasma. Like some other guidelines, the 1:1 ratio was initially based solely on anecdotes, theories and computer modeling performed in San Antonio.

In 2007, in a scientific paper based on the treatment of patients in Iraq, Army researchers concluded that increased use of plasma improved survival by as much as 60 percent. At the time, the Army said it was the only published research based on the treatment of human patients.

Damage control resuscitation has since been widely adopted by civilian trauma centers. "It's a paradigm shift," said Dr. Stephen Smith, who implemented the practice at the Via Christi Regional Medical Center in Wichita, Kan., before moving last year to the new Virginia Tech medical school.
Said Dr. Juan C. Duchesne, a trauma surgeon and researcher at Tulane University Hospital in New Orleans: "It turns out we've been doing it wrong for the last 50 years."

Yet the Army's evidence has also been condemned by some civilian specialists - and by some of the scientists within the Army's lab.
Dr. Jeannie Callum, director of transfusion medicine at the University of Toronto, urged transfusion specialists to speak out against the Army's "dangerous conclusion" in reviewing the service's research last April in the journal Transfusion Medicine Reviews. The Army's research, she wrote, is statistically unsound and shows "survival bias" - meaning it assumes, incorrectly, that patients who lived long enough to be treated benefited from the treatment.
"Based on the quality of this report, it would be unwise and potentially quite harmful to prematurely apply the U.S. Military's transfusion policy to civilian trauma patients," she wrote.

In private e-mails shared with The Sun by sources within the Army, some of the service's senior researchers and trauma experts in San Antonio applauded Callum's opposition and offered her discreet assistance in challenging the Army.

Several civilian hospitals have studied the Army's plasma ratio, with varying results. Studies in Houston and Louisiana concluded that the practice saves lives. In Denver, researchers found a higher death rate. Doctors in Alabama suggested that the ratio isn't what matters - that patients don't survive because they got more plasma, but get more plasma because they survive.
At the R Adams Cowley Shock Trauma Center in Baltimore, doctors initially endorsed the Army's transfusion practice and collected data from 806 of their patients over two years in hopes of verifying it. They concluded that the 1:1 ratio had no effect.

Dr. Thomas M. Scalea, physician in chief at Shock Trauma, presented his findings last summer at a gathering of the American Surgical Association, minutes after Holcomb presented data championing the concept. He acknowledged the military's different conclusion and said that perhaps combat injuries are too different from civilian injuries for comparison. But for whatever reason, Scalea said, in his hospital the practice didn't work.

"This was an attempt to get some traction on our own practice and to analyze what it is that we're doing - were we saving lives?" Scalea said. "Frankly, we expected the answer to be other than what we found out."