

## New clue to sepsis as more aggressive care urged

October 4 2010, By LAURAN NEERGAARD, AP Medical Writer

(AP) -- It's one of the most intractable killers you've probably never heard of: Sepsis, an out-of-control reaction to infection that can start shutting down organs in mere hours.

A new push is beginning for hospitals to be more aggressive in rolling out care at the first hint of trouble - even as scientists discover an intriguing clue to what may fuel the deadly cascade estimated to kill more than 200,000 people a year in the U.S. alone.

There's no simple <u>diagnostic test</u> for sepsis, but there are warning signs if health providers pay close attention, says Dr. James O'Brien, a critical care specialist at Ohio State University Medical Center.

"Minutes matter," he adds, saying delays too often are "just an issue of not treating this like a medical emergency."

Once misleadingly called blood poisoning, sepsis is the body's overreaction in fighting an infection that in turn injures its own tissues, leading to shock and <u>organ failure</u>.

That doesn't mean the infection has spread throughout the body - it doesn't always, stresses sepsis specialist Dr. Kevin Tracey of the Feinstein Institute for Medical Research in New York, part of the North Shore-Long Island Jewish Health System. Instead, complex interactions between the microbe and the immune system make the latter run amok.



"At that point even if you eradicate the bacteria - we can do that most of the time - the damage continues to spread because of the <u>toxic reaction</u> that's unleashed," says Tracey, who helped lead a meeting of international sepsis experts last week who formed a "Global Sepsis Alliance" to urge more aggressive care.

Even people who've survived sepsis may not have heard the term, because it's such a hard-to-explain concept that many doctors instead just say they battled a tough infection, Tracey says.

And the earliest symptoms that someone with an infection is sliding into sepsis are vague: Confusion, shortness of breath, an increase in <a href="heart rate">heart rate</a>, dropping blood pressure, weakness.

But the alliance's goal: Start antibiotics and intravenous fluids, to counter the shock or low blood pressure, within an hour of suspicion of sepsis. Every hour of delay lowers survival by nearly 8 percent, yet many hospitals don't get appropriate care started for four or even six hours, O'Brien told the meeting.

Still, with millions dying worldwide and death rates near 30 percent in the U.S., new treatments are needed. Now scientists from Portugal have uncovered a new culprit that may help determine which sepsis patients are at highest risk of death - and points to a possible new treatment approach.

During sepsis, red blood cells can become injured and leak an iron-based substance called heme that's normally part of the hemoglobin that carries oxygen. But when it leaks into the bloodstream at the same time the body is experiencing lots of inflammation - a given during sepsis - the heme becomes toxic to organs, explains lead researcher Miguel Soares of Portugal's Instituto Gulbenkian de Ciencia.



In a series of experiments with infected mice, Soares' team first showed extra heme led to more deaths.

Next, the body makes a molecule to clean up leaky heme - but in the mice, as heme levels rose, levels of that molecule, known as hemopexin, dropped.

So they injected sick mice with extra hemopexin and more survived, they reported last week in the journal *Science Translational Medicine*.

Finally, Soares tested blood samples from 56 sepsis patients in a Brazilian hospital - and found those who survived had significantly higher natural hemopexin levels than those who died.

More research is needed to confirm the findings, but the work raises the prospect of a way to monitor sepsis risk in hospitalized patients, and possibly of creating a medication. In New York, Tracey says the study makes sense - adding that it might help explain why people who require blood transfusions seem at higher risk for developing sepsis.

Meanwhile, no one knows what triggers <u>sepsis</u> in some people with garden-variety infections. It's more common in the elderly, the very young and people who've just undergone surgery, but can strike anyone, as Linda Haltman, 49, of Woodbury, N.Y., learned last summer.

She awoke from a nap suddenly feeling bad after a day of tennis and swimming. Her husband pulled out his blood pressure monitor thinking to prove she was fine - only to race her to the hospital when it read a super-low 70 over 50.

"I said to my 20-year-old daughter, 'We're going to the emergency room, we'll be back in an hour.' That's all I remember for 13 days," recalls Haltman.



ER doctors first suspected a different illness but, importantly, started antibiotics anyway because her level of infection-fighting white blood cells was abnormally high. Still, delirium set in within hours. By morning, her lungs were filled with fluid. She needed a ventilator. Doctors eventually diagnosed strep bacteria, but never discovered where her infection started.

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