

The Destruction of the
Memphis Lung Research Program

The Global Human &
Economic Repercussions

Dr. G. Umberto Meduri

THE WHISTLEBLOWER



- Dr. G. Umberto Meduri is a former tenured Professor in the Department of Medicine at the University of Tennessee Health Science Center (UTHSC) in Memphis.
- **He was also the Director of the Memphis Lung Research Program at UTHSC.**
- He is recognized as the global expert on the study and use of corticosteroids in Acute Respiratory Distress Syndrome (ARDS).

WHAT HAPPENED

The Destruction of the
Memphis Lung Research
Program

- * In 2001-2002, there was a coordinated scheme to shut down Dr. Meduri's MLRP—which was conducting research on the use of corticosteroids for Acute Respiratory Distress Syndrome (ARDS).
- * This scheme was carried out by several members of the staff and administration of **UTHSC**— aided by an investigator for pharmaceutical giant **Eli Lilly**; and later **official regulatory and public health agencies.**

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A L L I A N C E

WHAT HAPPENED

May 17, 2002—The Wall Street Journal published a front page story on Dr. Meduri's research

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Why Cheap Drugs That Appear To Halt Fatal Sepsis Go Unused

THE WALL STREET JOURNAL

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FRIDAY, MAY 17, 2002 • VOL. CCXXXIX NO. 97 • \$1.00

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Why Cheap Drugs That Appear To Halt Fatal Sepsis Go Unused

Steroids Need Big Human Trial, But Pharmaceutical Makers Lack Incentive to Fund One

Dr. Meduri's 15-Year Quest

By THOMAS M. BURTON

It was strictly happenstance that sent the doctor off on his quest. A young mother hovering near death in a Connecticut hospital was misdiagnosed, and given a drug she would otherwise have gotten. She recovered.

Then the doctor, G. Umberto Meduri, learned that what the woman actually had was sepsis, a devastating condition that has long been as baffling as it is deadly. Often beginning as a blood infection after surgery, sepsis can quickly turn lethal. It kills an estimated 215,000 people in the U.S. annually—more than the combined toll of the worst cancers, of the lung and colon.

The puzzling thing was that the drug, this woman got was a steroid, supposedly worthless for sepsis. Researcher coming to show this family was common at the time. "In the late 1980s, anyone in our field would have said you're an idiot if you use steroids" for sepsis, says Dr. Meduri, who is now at the University of Tennessee Health Science Center in Memphis.

What followed was 15 years of tantalizing but tiny studies that seemed to jibe with what happened in the Connecticut hospital. Now, Dr. Meduri and colleagues in the U.S. and Europe have accumulated a modest body of evidence that the deadliest forms of sepsis often yield to cheap, common steroids such as cortisone. A researcher at the University of Paris recently found that steroids led to nearly a 30% drop in deaths from septic shock, a severe form of sepsis in which blood pressure plummets. If the approach is indeed effective, it would be big economic news: It typically costs less than \$10. The only drug specifically approved for sepsis is about \$7,000 a dose.

That drug, Eli Lilly & Co.'s newly approved Xigrist, was the fruit of huge studies costing hundreds of millions of dollars, and Lilly is spending lavishly to promote it. The Meduri approach languishes, because no one has ever done the large-scale studies that most doctors need to be convinced.

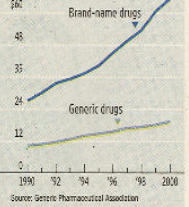
The steroids saga illustrates one reason research remains in low prices: generic drugs. There is little incentive for big pharmaceutical companies—the main financiers of drug research—to pay for studies of using steroids against sepsis, because the steroid's patents have expired. The National Institutes of Health also turned Dr. Meduri down. It primarily funds basic scientific research, not human trials of drugs.

Dr. Meduri, who finally got modest funding from a church-affiliated healthcare foundation in Tennessee, has recently had to slash the size of what he hoped would be a major study, as his funding ran low. He has laid off some researchers and he lost one of his labs when the University of Tennessee reassigned it. Still, in France, are thousands of blood-pharma samples that might reveal which patients' genetics make them likeliest to benefit—samples there is no money to analyze.

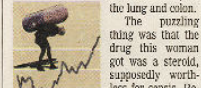
"Meduri has been a voice crying in the wilderness," says John J. Marrin, a University of Tennessee professor. "He has been a voice crying in the wilderness." He has laid off some researchers and he lost one of his labs when the University of Tennessee reassigned it. Still, in France, are thousands of blood-pharma samples that might reveal which patients' genetics make them likeliest to benefit—samples there is no money to analyze.

Widening Gap

Average retail prescription price of brand-name and generic drugs



Source: Generic Pharmaceutical Association



DRUG PRICES

Why They Keep Soaring Fourth in a Series

Why they've soared "for a second, says Dr. Meduri, who is now at the University of Tennessee Health Science Center in Memphis.

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Why Low-Cost Drugs That Might Halt Deadly Sepsis Go Unused

Continued From First Page

By all accounts, the prime skeptic is Gordon R. Bernard, a prominent Vanderbilt University critical-care specialist. He was the chief investigator both on a 1987 study showing steroids ineffective, and on the main large study of Lilly's Xigrist. Dr. Bernard has been sarcastic in his criticism of Dr. Meduri's work, attacking him in usually personal terms. In a medical-conference debate with Dr. Meduri at Chicago's Drake Hotel in 1996, for instance, Dr. Bernard seemed to question Dr. Meduri's "20 Act" name conference, a remark referring to one of the steroids. Dr. Bernard said, "I've never spent a night in Memphis—only three hours after Dr. Meduri was seen at the grave site of Dr. [Dr. Bernard] attached methylprednisolone to the grave."

Dr. Bernard says he regrets his IQ remark. As for whether steroids used the way Dr. Meduri proposes could help with sepsis, he says it "is a fair hypothesis—but give me some data."

Sepsis—which is often the culprit when a newspaper story says someone died of "complications" from surgery or illness—can ravage a young body as well as an old one. Shanta Cavel, a member of the pompous squad at the University of Memphis, went out for pizza one night in 1988 and fell ill. Twenty-four hours later, she was diagnosed with meningitis from airborne bacteria. It initially progressed to septic shock and acute respiratory distress syndrome.

Within hours, Ms. Cavel was on a ventilator, fighting for her life. Given four weeks of low-dose, intravenous steroids in one of Dr. Meduri's studies, she survived. She now is 34 and a nursing student.

Her story inspired Dr. Meduri's interest in the use of steroids. He had a heart attack in 1988, but during a cardiac procedure, he breathed in stomach contents he had coughed up, developing acute respiratory distress syndrome. Dr. Umberto Meduri, a retired accountant and lawyer in Germantown, Tenn., who had a heart attack in 1988, but during a cardiac procedure, he breathed in stomach contents he had coughed up, developing acute respiratory distress syndrome.

Dr. Meduri's research has been largely ignored for seven days on a ventilator. Then, given a low dose of methylprednisolone in a Meduri study, he improved enough to have heart surgery. Now the 80-year-old widower is back home and doing well. He says he has become a regular at a Baptist Church in Memphis, where "there's a lot of widows."

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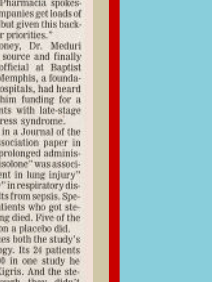
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How Sepsis Can Occur

What happens when an infection invades the body and how it can lead to sepsis, using the example of a respiratory infection.



1. Bacterial products or other inflammatory agents enter the lungs, activating a potent cascade of cytokines.

2. These cytokines act on the bloodstream to release the production of "fighting" proteins called cytokines.

3. When cytokines reach the brain's hypothalamus, it releases a hormone called ACTH.

4. ACTH flows through the bloodstream and stimulates the adrenal glands to produce cortisol.

5. Cortisol attaches to cell receptors, called glucocorticoid receptors, reducing the ability of white blood cells to produce cytokines. When the receptors occur in the lungs, inflammation subsides, healing begins.

6. Dr. Meduri contends additional cortisol-like steroids can ease the normal process.

By contrast, Lilly promotes Xigrist through a large sales force and also pays 20 critical-care specialists to speak to colleagues about it. Dr. Meduri, who has a rare pneumonia, which called for a low dose of steroids over many days. Last year, he had a heart attack in 1988, but during a cardiac procedure, he breathed in stomach contents he had coughed up, developing acute respiratory distress syndrome.

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The approach of Dr. Meduri and others such as Djillali Annane at the University of Paris is quite different. Instead of megadoses, they give steroids for days or weeks, intravenously, at doses of only 2% or less of those used in the 1980s. They believe synthetic steroids such as hydrocortisone and methylprednisolone can reactivate the cells' sensitivity to cortisol, curtailing inflammation.

This may have been what helped Grady Marlow Jr., a retired accountant and lawyer in Germantown, Tenn., who had a heart attack in late 1998. During a cardiac procedure, he breathed in stomach contents he had coughed up, developing sepsis and acute respiratory distress syndrome. He lingered for seven days on a ventilator. Then, given a low dose of methylprednisolone in a Meduri study, he improved enough to have heart surgery. Now the 80-year-old widower is back home and doing well. He says he has become a regular at a Baptist Church in Memphis, where "there's a lot of widows."



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WHAT HAPPENED

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Program

- * Within days after the WSJ publication, **UTHSC illegally removed the primary research funding source for Dr. Meduri's MLRP.**
- * **False charges of scientific misconduct** were leveled against Dr. Meduri.
- * These actions created lingering misperceptions about corticosteroids and shut down all research on corticosteroids for ARDS in the United States—even until today.

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THE IMPACT

The Destruction of the
Memphis Lung Research
Program

- From 2002-2020, ARDS killed 80 thousand patients each year in the U.S. alone—and ten times that globally. **A large percentage could have been saved with corticosteroid treatment.**
- In 2020, **COVID-related ARDS killed hundreds of thousands of patients** when they could have been saved with early corticosteroid treatment.
- Early treatment with corticosteroids would have mitigated the social and economic costs of the pandemic.
- Progress generated by **the MLRP's continued research could have prevented most of this.**

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