Vital Signs: An Antibiotic Runs Amok

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A woman’s terrible stomach pain turns deadly.

by Tony Dajer

“How could she be so sick?” Mr. Kovacs implored, his eyes filling with tears. “We would have come in sooner.”

His wife of 40 years lay on a stretcher, barely conscious, moaning in pain, a large blue diaper wrapped around her lower body to capture the now-incessant diarrhea. Her blood pressure hovered around 80, and her skin had turned sallow and pasty.

The surgeon pressed softly on the patient’s abdomen. No matter where he probed, Mrs. Kovacs moaned louder. He stepped to the X-ray viewing screen. The abdominal CT scan showed a massively thickened large intestine.

“We need to get her to the operating room,” he said. “She’s obviously septic. Worse, the colon is probably dying.”

An x-ray shows a massively inflamed colon.

Mrs. Kovacs had complained of diarrhea and stomach cramps for four days, but what finally brought her in was the weakness. "She can barely move," her husband had told the triage nurse. A healthy 65-year-old, Mrs. Kovacs had seen the inside of a hospital only to deliver her babies. As for doctors, she had needed their services for mild high blood pressure.

The diarrhea had started out watery, not bloody, not too copious, with no fever. According to her husband, she didn't have any risk factors that might explain the persistent diarrhea. She hadn't been out of the country, she hadn't eaten any spoiled food, and she hadn't taken any antibiotics lately.

Two IVs dripped saline in, but her blood pressure would not rally.

“This morning she was walking around,” one of her daughters said fearfully. "We thought she had a stomach flu.”

The lab results had come back sky-high, with a white blood cell count of 25,000 (normal is 4,000 to 11,000). Her diarrhea had made her so dehydrated that her kidney function was one-third of normal.

The surgeon, still puzzled as to how a gastrointestinal infection could fell a healthy woman, went back over the history.
"No antibiotics in the past few months?" he asked. "You're sure?"

Another daughter had since arrived. "Oh, yes," she exclaimed. "She had a tooth infection about three weeks ago. The dentist gave her something. I brought the container."

She fished in her pocket and handed a plastic vial to the surgeon.

"Clindamycin," he read aloud.

Mr. Kovacs, understandably, had forgotten. His wife had finished the drug treatment two weeks earlier.

"This finally makes sense," the surgeon said. Then, as gently as he could, he addressed the family. "She's in for a very rough time."

In the 1960s, reports of a bizarre and sometimes lethal colon affliction appeared in the medical literature. Because the cell debris and inflammatory gunk that lined the colon looked like a yellow-green membrane, researchers called it pseudomembranous colitis, but its direct cause remained elusive. Clear from the start, however, was that antibiotics—clindamycin in particular—were implicated.

The human colon harbors a complex ecosystem of bacteria. By and large, our bacterial companions behave like a big happy family in which all mind their place and do their part. Some of the bacteria use oxygen; some don't. Many aid in digestion and make nutrients like vitamin K. The social order is fragile, however. Add antibiotics and the good bacteria die, allowing nasty competitors to move in. The most common side effect is diarrhea. Most cases occur because the bacteria-depleted intestine cannot fully digest carbohydrates, and the unabsorbed sugar provokes the runs.

A CT scan of the enlarged colon.

Pseudomembranous colitis is different. In 1978 researchers traced the cause to toxins made by the anaerobic bacterium Clostridium difficile. The toxins not only trick intestinal cells into secreting massive amounts of fluid but can also fatally gum up their protein-making machinery. Symptoms range from none (a healthy carrier state) to simple diarrhea to toxic mega-colon, where the colon balloons in size to become an inflammatory, necrotic cesspool. The older and more debilitated you are, the more likely you'll suffer the most severe effects.

Pain and fever caused by C. difficile may begin from 2 to 10 days after antibiotics are started or up to 10 weeks after they're stopped. Clindamycin leads the pack in terms of risk, probably because it's so good at wiping out the dominant, friendly anaerobic, or oxygen-shunning, bacteria (many antibiotics attack only aerobic bacteria). But common antibiotics like cephalosporins (Keflex and Rocephin) and penicillins (amoxicillin and ampicillin) also cause their share of cases. Recently another widely used class of antibiotic, the fluoroquinolones (which include Cipro and Levaquin), have shown worrisome signs of catching up. Adding to the dilemma are some studies suggesting that stomach acid—reducing drugs—among the most widely prescribed medications in the world—may also increase the risk of C. difficile disease.

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infects 3 million patients a year—including about 13 percent of all inpatients who spend up to two weeks in the hospital. Mrs. Kovacs was an unlucky outlier—only 20,000 outpatient cases are reported each year in the United States. That's the good news. The bad news: The prescribing of antibiotics for everything from colds to sinusitis and benign coughs seems to have spawned another superbug. Over the past five years, a new strain of \textit{C. difficile} that produces 20 times the usual amount of toxin has blitzkrieged through hospitals and nursing homes in Canada, the United States, and Europe, killing up to 10 percent of its elderly victims.

![Micrograph of the bacterium Clostridium difficile](image), courtesy of the Centers for Disease Control and Prevention.

In hospitals, alas, \textit{C. difficile} spreads mostly via health care workers. The new trend toward relying on regular squirts of alcohol-based gels to clean the hands might be making things worse because the gels do not kill the bacterium's spores. Old-fashioned handwashing and isolation do. Among Quebec hospitals hard-hit by a recent outbreak, enforced washing with good old soap and water dropped the infection rate by half.

On the outpatient front, Great Britain has seen the incidence of \textit{C. difficile} infection skyrocket from less than one per 100,000 people in 1994 to 22 per 100,000 in 2004. The profile of the patient is changing too. In 2005 the Centers for Disease Control received reports of eight healthy outpatients in the United States who suffered serious \textit{C. difficile} disease and hadn't taken antibiotics in the preceding three months. In other words, some strains of the organism are muscling aside good gut bacteria even without our help.

Ironically, the treatment for \textit{C. difficile} disease is more antibiotics: The idea is to pare back the runaway intruder with anaerobic-specific antibiotics like metronidazole or vancomycin. Although they kill good anaerobic \textit{Bacteroides fragilis} as well, they allow normal aerobes like \textit{Escherichia coli} to regain a foothold and begin to restore ecological harmony.

For Mrs. Kovacs, the surgeons tried every intervention: high-dose antibiotics, fluids, and pressors—medications that boost blood pressure. Still, her vital signs continued deteriorating. The next morning, hoping to extinguish the source of bacterial toxins and the corrosive by-products of massive cell death, the surgical team removed her colon. But the defenses kept crumbling. Two days later they had to take out a portion of small intestine. Then came a grim procession of secondary complications: a gallbladder infection, pneumonia, and internal bleeding.

"I don't think she'll make it," the surgeon confessed to me about two weeks into her treatment. He fought a long, hard rearguard action, aggressively working up and treating every new complication. I didn't ask if he was fighting so hard because this once hale, vigorous woman was at death's door due to a prescription for a tooth infection.

Two weeks later, with her family on a round-the-clock vigil, she succumbed. Had she come in sooner, her death might have been averted. Maybe a more adamant warning from her dentist about clindamycin's potential dangers would have saved her life. But it would be hard to pin blame only on him, given that we American doctors still uselessly prescribe antibiotics—to the tune of over 10 million prescriptions a year—to patients with viral upper respiratory infections.

And we still think we're doing good.

\textit{Tony Dajer is interim chief of the emergency department at New York Downtown Hospital. The cases described in Vital Signs are real, but the authors have changed patients' names and other details to protect their privacy.}
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