Remembering Stuart Levy

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Colleagues, friends and family remember Stuart Levy as a gifted researcher and compassionate, humble human being.

"Stuart was a rare combination," said John Leong. "He had a far-reaching vision of the consequences of inappropriate use of antibiotics, a keen understanding of the need for public education and policy change, an ability to communicate effectively, and a cutting-edge lab that studied the mechanisms of bacterial resistance."

The son of a doctor, Levy grew up steeped in medicine and science. He, his identical twin brother Jay and sister Ellen all ended up pursuing careers in academic medicine.

The twin brothers enjoyed switching identities, pulling off a notable prank as undergraduates. They successfully executed a week-long switch with Jay attending classes at Williams while Stuart hung out at Wesleyan, his twin's university. More recently, at the 100th anniversary celebration of the American Society for Microbiology, of which Stuart was President, the brothers marched in identical attire. "Some people," Jay recalled, "wondered how Stuart could be in two places at once."

Levy enrolled in the University of Pennsylvania School of Medicine in 1960. While on leave as a visiting research fellow at the Institut Pasteur, he met noted Japanese scientist Tsutomu Watanabe, who introduced him to a breakthrough discovery: that resistance to antibiotics can transfer from one bacterium to another, even across species. "This was unheard of previously. It was the beginning of studies on transferrable drug-resistance genes and infectious drug resistance," Levy told *The Scientist*.

Levy joined the Tufts School of Medicine in 1971. He published a study in the *New England Journal of Medicine* showing chickens raised on feed containing low-doses of antibiotics developed intestinal bacteria that were highly resistant to antibiotics which could be transferred to farm workers. The agricultural industry was sceptical. Prevailing wisdom was that low-dose antibiotics, routinely fed to promote livestock growth rather than treat disease, would result in low-level resistance—and only in the animals themselves. Levy's work has been credited with prompting the FDA to shift its guidelines on the use of antimicrobial drugs in food-producing animals.

In 1978, Levy's lab showed that *E. coli* resistance to tetracycline is due to the bacteria actively pumping the antibiotic out of the cell. Controversial at the time, this "active efflux" mechanism is now an accepted paradigm for a critical class of antibiotic resistance and is also a mechanism for resistance to drugs that treat cancer.

Levy believed that professional and public education was essential to preventing a looming health crisis. He became a quotable expert sought out by leading news media.

"Bacteria have seen dinosaurs come and they've seen them go," he told Dan Rather. "So we aren't going to destroy the bacterial world. We live in the bacterial world." He repeatedly called for "prudent use" of antibiotics, which he termed "societal drugs" because use by one person affects others.

He lobbied for incentives to make development of new antibiotics economically feasible. Along with Nobel Prize winner Walter Gilbert, he founded Paratek Pharmaceuticals, which developed a new tetracycline derivative, omadacycline, to which target bacteria were not resistant. He also called for rigorous management of antibiotics at hospitals and for advanced diagnostics to identify diseases earlier and more accurately to better target appropriate antibiotic use.

In 1981, he co-founded APUA, now part of the International Society of Antimicrobial Chemotherapy, which brought together infectious disease specialists from more than 100 counties. "On a shoestring, he put together this worldwide network to call attention to the problem and document it. And finally, the world woke up," Berman said.

Levy never shied away from controversy. When he advocated prohibiting antimicrobials like triclosan from common products such as soap and hand sanitiser because they left behind a dangerous residue associated with antibiotic resistance, product manufacturers protested loudly. Changes in FDA regulations vindicated him and he had the satisfaction of seeing the US launch a National Action Plan for Combating Antibiotic-Resistant Bacteria and the World Health Organization name antimicrobial resistance as one of the top threats to global health.

Levy's work also inspired the new Tufts Center for Integrated Management of Antimicrobial Resistance which will tap researchers from across the university to work alongside colleagues at the medical centre.

"Stuart Levy was a towering figure," Ralph Isberg said, "not because of his physical stature but because of the force of his ideas."

Matching those ideas were his kindness, humility, integrity and love of life. Describing himself as "an optimist to my toes," he made friends all over the world, and his fluency in seven languages enabled him to support them through good times and bad, as well as meet his wife of 35 years, Cecile Pastel Levy, a native of France.

His children—Arthur, Suzanne, and Walter—recall a father who regularly tucked them into bed when they were small; read their schoolwork; taught them how to tie the perfect bow tie that was among his trademarks; shared his love of music, painting, and singing; and talked about his work without condescension whether he was invited into their elementary school classroom or college lecture hall.

Leong described Levy as "confident, as he needed to be." But, he continued, "he was always extremely gracious, never dismissive. When I arrived in 2012, I asked him what role he'd like, what he needed. Stuart had only one request. He wanted to lecture first-year medical students and educate them on antimicrobial resistance. He didn't ask for more space or money. I thought that was remarkable."