

# Robert Webster

Like the mythological heroine Cassandra, Robert Webster seemed destined to remain a prophet who was never to be believed. His vision has since been validated but, fortunately for the world, his predictions of disaster—an influenza pandemic—have not yet reached the proportions of Greek tragedy.

Robert Webster likes to tell stories. Ask him how influenza spreads and he might launch into the tale of the New Zealand prime minister who visited Canada in 1918 and brought back the Spanish flu, killing thousands of Maoris. Inquire about his travels and you might hear about a never-used massive fort on the Dry Tortugas Islands off the coast of Florida. But Webster's favorite story by far goes something like this: a virus, harmless in wild aquatic birds, makes its way into domestic birds and eventually into humans. The human version of the virus spreads like wildfire between countries and continents, and soon millions worldwide are dead.

For decades, Webster has told this tale to scientists, politicians, regulatory agencies, the press and anyone else who will listen. Revered and ridiculed as he was for this obsession, he has now been vindicated: many experts agree it is just a matter of time before the world faces the next influenza pandemic.

"He's an international treasure," says James Crowe, a microbiologist at Vanderbilt University. "He's one of the giants. He's not only a scientist, but a person who thinks carefully about worldwide health."

Born and raised in New Zealand, Webster finished his Ph.D. in 1962 at the Australian National University in Canberra. He joined the faculty of St. Jude Children's Research Hospital in Memphis, Tennessee, on 1 January 1968, and has remained there ever since. He is a fellow of the Royal Society of London, a member of the US National Academy of Sciences and director of the US Collaborating Center of the World Health Organization. He also has the distinction of publishing the first color image in *Nature*.

Any one of Webster's accomplishments would satisfy someone less ambitious. As a graduate student, he discovered the Coomassie blue stain for quantitating proteins. Along with Stephen Fazekas, his graduate advisor, he established the theory of 'original antigenic sin'. He was a member of the team that discovered that detergents such as sodium dodecyl sulfate disrupt the flu virus, a finding that led to the first commercial flu 'subunit' vaccine.

Perhaps his most valued contribution is the idea that wild birds are a reservoir of influenza viruses. "Why do some strains kill lots of people, and others are rather benign?" says Webster. "With robust genetics, we're starting to understand what's going on."

When Webster first began working on influenza in the early 1960s, the idea that animals might harbor flu viruses had already been around for some time. But it was Webster and his colleagues who first suggested that pandemic strains of flu arise by a reassortment of genetic segments (antigenic shift) between viruses in humans and lower animals, and not by mutations (antigenic drift) in annual strains.

Not surprisingly, there are several stories behind that discovery. It all began when Webster and long-time friend and collaborator Graeme Laver went sea fishing. One weekend, they were walking on the southeastern coast of Australia. On the beach lay dead 'mutton birds', large birds full of fish-oil that live in burrows and migrate all around the Pacific. "I don't know if it was me or [Laver] that said, 'Wouldn't it be funny if flu was killing these birds?'" Webster recalls.

Despite widespread skepticism, they arranged a trip to a deserted coral

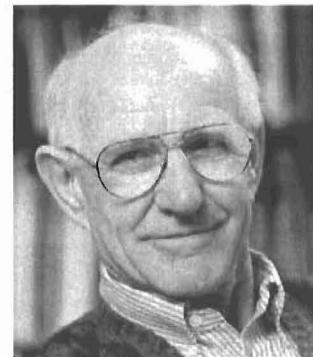
island off the coast of Queensland. They swam and snorkeled in the scorching sun by day and, at night, took swabs from the trachea and cloaca of birds. Some of those birds turned out to have antibodies to a flu virus. From samples isolated on a subsequent trip, Webster and Laver isolated the first influenza virus, which then led to the first anti-flu drug. "All from walking on the beach," Webster says.

Webster's obsession with flu took him to every corner of the world, from the Great Barrier Reef to Peru's Guano Islands, which have the world's highest concentration of birds. In the end, his quest led him back to Memphis, just two miles from his laboratory.

Webster and Virginia Hinshaw—now provost of the University of California, Davis—decided to test birds that had been shot dead by Memphis hunters. Every day, the two sat for hours in a feather machine and took swabs from hundreds of dead birds.

Webster says it never occurred to him to send a graduate student or

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technician to do the unpleasant work. "That's the difference between an American scientist and a New Zealand-trained scientist," he says. "We do it ourselves."

Webster's willingness to do anything it takes to find answers might be the key to his success. "Flu is a global problem and you have to be prepared to go out and see the source," he says. "The hypothetical epicenter for influenza is in Asia. That's where the work lies—that's why I go there."

At 71, he shows no signs of slowing down. In the matter of a few weeks this fall, he shuttled between Chicago, Okinawa, Memphis, Washington, DC, Hong Kong and Ames, Iowa. He still throws a legendary annual party where the star of the menu is home-grown corn, and spends three months every year as 'professor of excellence' at the University of Hong Kong.

During his career, Webster has collected more than 10,000 nonpathogenic viruses from ducks and shorebirds. So far this year, he has made more than 100 shipments of viruses worldwide. There are several researchers—including Albert Osterhaus and Yoshihiro Kawaoka—who might carry on the work Webster began. But none combine Webster's persistence in spreading the message, says Crowe.

Still, it may be time for Webster to slow down, says Laver, who recently reconciled with Webster after a decade-long rift. "The work [Webster] does is excellent," says Laver. But over the years, he says, Webster has become a bit too "preachy and pompous."

Webster may be preaching, but his gospel needs to be spread, counters Crowe. "Right now he seems [like] a 'St. John the Baptist' type," Crowe says. "But you know, when the pandemic comes, which is inevitable, he will appear prophetic."

*Apoorya Mandavilli, Chicago*