

news THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT DALLAS

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******Medical scientist to share high
German award for cholera research.*

DALLAS-- A Southwestern Medical School scientist will share one of Germany's highest medical awards for his work with cholera, an ancient scourge he feels may soon be defeated.

Dr. Richard A. Finkelstein, professor of microbiology at the medical school, has been notified that he and Dr. Mark H. Richmond, professor of bacteriology at the University of Bristol, have been chosen to share the Robert Koch Prize of approximately \$24,000.

The awards, which include the Robert Koch medal for each recipient, "are the highest honors that German science and medicine can submit to scientists in the biomedical field who, in addition, have done something for public health," according to the letter of notification. Award ceremonies will be held December 7 in Bonn with presentations by the German Ministry of Health. Dr. Richmond is being recognized for his work on antibiotic resistance.

Cholera, an acute infectious disease marked by severe vomiting and diarrhea, has been responsible for the deaths of countless persons through seven great worldwide epidemics.

Dr. Finkelstein has done fundamental work on the cholera organism and was responsible for the purification and crystallization of the "exo-enterotoxin" and a related toxoid which the organism secretes, in addition to research on the significance of cholera antigens in the immunology of cholera infections.

This work has enabled researchers across the world to zero in on the method by which cholera sickens and kills and on possible methods to combat the disease.

"Since 1961, the 'Seventh Great Pandemic' of cholera has raged worldwide," says Dr. Finkelstein, "It was widely seeded in Africa and invaded Europe for the first time in this century. There are occasional imported cases in the Western Hemisphere and even one in Texas in 1973."

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Cholera is a disease of violent vomiting and diarrhea. The cholera bacteria-- a curved rod-shaped organism called a vibrio--sticks tightly to the lining of the upper bowel and reproduces so rapidly that the surface soon gives the appearance of a shag carpet in highly-magnified electron micrographs.

The vibrios then excrete the toxin which activates the cells lining the bowel, causing them to produce "cyclic AMP," an important regulator of many bodily functions, including intestinal secretion of salts and water.

Indiscriminately produced, the cyclic AMP causes the victim to discharge great quantities of water and electrolytes (salts) through diarrhea or vomiting.

"A person can lose 20 liters a day and in places where there is poor sanitation, this can put two trillion vibrios into the environment," Dr. Finkelstein calculates.

This accounts for the rapid spread of the disease.

Before recent developments in research, mortality was as high as 60 to 80 per cent of all cases. Today, administration of the proper fluids by mouth or intravenously provides ideal treatment.

Yet, lacking proper treatment, thousands die in underdeveloped nations and so a form of immunization is badly needed.

Dr. Finkelstein became interested in cholera while doing research toward his Ph.D. with Professor C.E. Lankford in 1955 at UT Austin. This work led to development of a culture medium for vibrios which is in wide use. After post-doctoral work at Southwestern in virology, he went to Walter Reed Army Research Institute where he again worked on cholera because there were outbreaks in Thailand and the Philippines. He went to the Southeast Asia Treaty Organization's medical research laboratory in Bangkok for three years and returned to Southwestern in 1967.

Working with Dr. Joseph LoSpalluto, a Southwestern biochemist, Dr. Finkelstein isolated the single toxin protein which produced the disease. The protein was crystallized in 1972--giving opportunity for studying its structure with x-rays.

Actually, the researchers discovered two parts of the toxin molecule--one part responsible for binding to host cells and the other responsible for the biological activity.

"We've given the toxin and components to more than 200 other investigators around the world for their studies," noted the researcher.

A number of discoveries about the molecular mechanisms initiated by the toxin have resulted.

Currently, the only immunization against cholera is a rather inefficient method using killed vibrios. A chemically altered toxin is being tested in Bangladesh and the Philippines.

With Dr. Randall K. Holmes and Ph.D. student Michael Vasil, Dr. Finkelstein developed a mutant strain of cholera vibrios which did not produce much toxin and therefore did not cause the disease reaction.

The mutant was tested on volunteers in Maryland and was found to induce immunity but certain of the vibrios reverted to producing the original kind of toxin and it was deemed unsafe.

More recently he and Dr. Michele Ubelaker have been attempting to produce a mutant which would secrete a "safe" toxin. This would stimulate immunity to the toxin itself but not cause the disease. He feels this search may have a good chance of success and said that "I think this will be the ultimate weapon.

"Incidentally, some immunological 'relatives' of cholera toxin are produced by other intestinal bacteria which cause diarrhea. This includes the toxin produced by some strains of E. coli which cause diarrhea of travelers.

"So, if the mutant is successful, it probably would protect against 'turista'," he speculated.

Present studies include attempts to isolate and characterize the E. coli toxin with graduate student John Clements.

Dr. Finkelstein's other major interest is the study of gonorrhea. With National Science Foundation Fellow Shelley Payne, he is looking into the gonococci's ability to acquire iron as a determinant of its virulence and hopes to develop a vaccine against gonorrhea.

Dr. Finkelstein's work has been supported by grants from National Institute of Allergy and Infectious Diseases.

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