



Michael J. Dunn, MD

## Research in defense of terrorism will benefit medicine as a whole

By Michael J. Dunn, MD

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With human health already subject to myriad natural threats, the prospect of biological agents being used for malicious harm is particularly disconcerting. We work hard as physicians to prevent suffering and cure disease, and as new threats arise, I believe those with the expertise to protect our communities have a responsibility to do so.

Nationally recognized research programs led by Medical College of Wisconsin faculty members have attracted federal funding to establish research centers here dedicated to reducing the danger posed by bioterrorism and radiological terrorism. These new Medical College centers are poised to not only contribute substantially to national biodefense, but also protect the population against emerging infectious diseases and improve clinical care for current patients.

The Medical College's Center for Biopreparedness and Infectious Disease (CBID) is advancing research in the detection and prevention of infectious diseases developed as weapons as well as new and exotic viral and bacterial organisms that present a danger to humans. Funded by a portion of the National Institutes of Health's \$35 million Region V Great Lakes Regional Center of Excellence award, the CBID is directed by Dara Frank,

PhD, professor of Microbiology and Molecular Genetics.

Coordinating their research through the Center, Medical College investigators are studying a number of organisms that either have been made into weapons in the past or pose a threat because they are highly contagious or nearly untreatable. Much of their work also has long-term clinical implications.

Joseph T. Barbieri, PhD, professor of Microbiology and Molecular Genetics, is studying botulinum toxin's mode of action and how it interacts with nerve cells. This information may guide physicians on how to use the toxin more effectively to relieve muscle spasms as well as provide basic information on its use as a vaccine.

Dr Frank and Thomas C. Zahrt, PhD, assistant professor of Microbiology and Molecular Genetics, are leading a project to find the factors that make the bacterium that causes tularemia so highly infectious. Although tularemia was manipulated into a bioweapon during World War II, very little is known as to why humans are so susceptible. Substantial progress has been made to genetically engineer this bacterium for the design of a new vaccine.

The highly transmissible nature of smallpox and the large population of unvaccinated individuals

will make it imperative to have new treatments on hand should the poxvirus be used as an agent of bioterrorism. Paula Traktman, PhD, chair and the Walter Schroeder Professor in Microbiology and Molecular Genetics, is conducting genetic research in search of new therapeutics to treat viral infections with specific applications for preventing the spread of smallpox.

Additionally, many scientists are attempting to understand what it will mean if avian influenza spreads to humans. Kelly Henrickson, MD, and Jack Gorski, PhD, have ongoing projects investigating the epidemiology of influenza and the immunological mechanisms mediating protection in people. Doctor Henrickson is professor of Pediatrics (Infectious Diseases). Dr Gorski is senior investigator at the Blood Research Institute, BloodCenter of Wisconsin, with faculty appointments at the Medical College in Microbiology and Molecular Genetics and Cell Biology, Neurobiology and Anatomy.

Making this research possible is a commitment to building an infrastructure at the Medical College that allows work on organisms requiring higher levels of containment. In addition to maintaining and enhancing an oversight structure for safety and government compliance, the CBID operates a Level 3 containment lab-

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oratory that enables scientists to handle toxic agents and infectious diseases in a secure, safe, and sealed environment.

Currently under construction, our new \$117 million biomedical research building will contain expanded facilities for Dr Frank's Center as well, including a new Level 3 containment lab. The building is a joint project of the Medical College and Children's Hospital and Health System.

The value of these efforts extends beyond biodefense. Anti-terrorism research can be equated to the fight against infectious disease in general. The more we know about how pathogens cause disease and how they spread, the better we can protect ourselves against new and emerging bacteria, viruses, and parasites. And understanding the basic biology of organisms is going to help us translate that into treatment of everyday types of infections.

Such added value also exists in a new center established in September at the Medical College. With a 5-year, \$18.5 million contract from the National Institute of Allergy and Infectious Diseases, we were designated a Center for Medical Countermeasures Against Radiological Terrorism, 1 of 8 such centers nationally. While the centers were launched to combat potential radiological attacks, their research could benefit hundreds of cancer and blood disease patients every day and radiation accident victims worldwide.

Directed by John Moulder, PhD, professor of Radiation Oncology, the Medical College Center consists of 13 faculty researchers in radiation oncology, surgery, medicine, and pediatrics who have formed a consortium with 7 scientists from other institutions. Their goal is to develop drugs to treat acute or long-term injuries to the gut, lung, kidney, and brain that could occur in victims who have received damaging doses of radiation but have avoided or

survived bone marrow injury. Dr Moulder leads the kidney project; Mary Otterson, MD, professor of Gastrointestinal Surgery and associate director of the Center, leads the gut injury project; and Meetha Medhora, PhD, associate professor of Pulmonary and Critical Care Medicine, leads one lung project. Another lung project and the brain injury project are being led by collaborators in Toronto and Detroit.

All of the drugs investigated in the Center are expected to also be useful for treating the side-effects of medical radiation. If a drug will work against terrorism, we are confident it will work equally well for patients.

Researchers are looking for agents that could be administered in a mass casualty situation—oral medications, for example, would be easier than an injection in an attack scenario. Cancer patients would benefit from either delivery system.

Experimental work is already underway in the College's Center. Dr Moulder expects to have proven efficacy in at least 1 animal model for several agents later this year. Several new agents have been synthesized and are in trial, and Center results have already been published in the scientific literature.

The team is working with agents already approved for human use by the Food and Drug Administration (FDA) for other purposes, and with new agents not previously approved for efficacy and safety in humans. Those FDA-approved drugs found successful for treating radiation could be available for radiation countermeasures in as little as 2 years. Others might be 4 years away from the marketplace.

Center researchers are interested in developing drugs for radiation injuries that can be stockpiled and ready to use with simple instruction. Currently, hospitals and physicians are not equipped to handle a radiation attack—such an event has never

occurred. The hope is that preparation and knowledge of how to defend against radiological terrorism will not only diminish its impact but also make it less attractive to terrorists as a weapon.

It is unfortunate that the threat of terrorism has necessitated creation of these centers for biopreparedness and countermeasures against radiation, but the ensuing research is promising. Historically, the resources committed to medical research in times of war have resulted in great advances in medicine. We expect no less from our research in biological and radiological defense.

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