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INSIDE

Conference Focuses on Emerging Microbes

In the 1950s and 1960s, the successful use of antibiotics and vaccines to combat the main microbial killers that plagued humanity led many people to assume that the war on infectious diseases had been won. At a recent conference, however, presenters showed that—because of changes in human behavior, the microbes themselves, or both—the war is still on, and the medical community should be on the lookout for future battles. The conference on emerging microbes and microbial diseases, cosponsored by NIAID and the NIH Fogarty International Center, was held in Washington, DC, in November.

Among the more alarming infectious diseases now laying siege to humans are tuberculosis (TB), malaria, rheumatic fever, several sexually transmitted diseases (STDs), and disorders caused by antibiotic-resistant strains of bacteria.

"We are currently witnessing dramatic changes in TB," said Samuel Dooley, M.D., an epidemiologist with the Centers for Disease Control. After a 30-year period of decline in this country, he noted, the number of TB cases is on the upswing. Worldwide, TB also continues to take its toll. One-third of the world's population is now infected with TB, which causes 3 million deaths each year, according to the World Health Organization.

A chief cause of TB's increased prevalence is the epidemic spread of the AIDS virus, HIV. HIV disables the immune system, allowing symptom-free infections of TB to flare up and become life-threatening. HIV infection also makes people susceptible to infection with new and deadly strains of TB. In some clinics, nearly half of all TB patients are also infected with HIV, according to Dr. Dooley.

An increased understanding of the microbes that cause human disease is critical to keeping them in check.

Also perturbing is the recent emergence of TB strains that do not respond to the standard antibiotics used to treat the disorder. Such drug resistance is particularly common in patients previously treated for TB, and outbreaks of strains resistant to several different drugs have been occurring throughout the country, according to Dr. Dooley.

In such outbreaks, even with treatment, 80 percent of the patients die, usually within 2 months after diagnosis. For those who survive, treatment can be required for up to 2 years rather than the standard period of 6 months. "Drug-resistant TB is an alarming problem, which is likely to increase in some areas," Dr. Dooley summarized.

"We must intensify our research efforts on tuberculosis in order to be able to apply the state-of-the-art diagnostic and therapeutic approaches to this extremely serious emerging problem," commented NIAID's Director Anthony S. Fauci, M.D.

Also emerging because of HIV infection are several other "opportunistic

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New Findings on Preventing Recurrent PCP

An inexpensive drug used to treat *Pneumocystis carinii* pneumonia (PCP) has been found to be superior to the only drug currently approved for PCP prophylaxis in preventing a second episode of PCP, according to an NIAID-sponsored study.

PCP is the most common, life-threatening opportunistic infection affecting Americans with AIDS.

The risk of recurrent PCP was 3.25 times greater in patients who received AZT plus preventive aerosolized pentamidine than in those patients who received AZT plus preventive therapy with the less costly drug, trimethoprim/sulfamethoxazole (TMP/SMX), which is marketed under the trade names Bactrim® or Septra®.

The study was carried out in 310 volunteers at 23 sites of the AIDS Clinical Trials Group, a network of clinical research centers funded by NIAID. The co-principal investigators on the study were Robert Holzman, M.D., of New York University School of Medicine, and W. David Hardy, M.D., of the University of California at Los Angeles.

The objective of the study, known as ACTG protocol 021, was to compare the toxicity and efficacy of TMP/SMX plus AZT versus aerosolized pentamidine plus AZT in preventing a second episode of PCP. The protocol also sought to determine whether one treatment regimen was better than the other in extending survival.

An interim review of clinical and laboratory data, conducted by the NIAID Data and Safety Monitoring Board on August 28, showed the TMP/SMX regimen to be more effective for preventing recurrent PCP. This finding prompted the board's recommendation to stop the study on August 30, 1991, 9 months earlier than originally scheduled.

"The results of our study apply only to those people with significantly compromised immune systems who have recovered from an episode of PCP," said Dr. Holzman. "Caution should be used in generalizing to patients who do not fit this profile."

"It is important that all people with HIV infection consider PCP prophylaxis," Dr. Hardy added. "Aerosolized pentamidine and trimethoprim/sulfamethoxazole are both effective drugs." While not approved for PCP prophylaxis, TMP/SMX is approved for treating PCP and other infections and is available by prescription.

"A striking finding of this study is that only 10 percent of those patients who developed recurrent PCP died, suggesting that since the earliest days of this devastating epidemic, we have substantially improved our management of PCP," said NIAID Director Anthony S. Fauci, M.D.

While TMP/SMX had a greater effect in reducing recurrent PCP, the study investigators are careful to point out these results do not mean that it is the drug of choice for all patients. In the study, 27 percent of the TMP/SMX patients and 4 percent of the aerosolized pentamidine patients were switched to the other therapy because of side effects presumed to be related to the study medications. For all statistical analyses, participants were grouped according to the originally assigned treatment.

Without prophylaxis, more than 60,000 HIV-infected persons in the United States would be expected to develop new or recurrent PCP infections in 1992. Unless they receive prophylaxis, about 65 percent of patients successfully treated for an initial episode of PCP and receiving AZT for their HIV infection would develop recurrent PCP.

A Note to Physicians with detailed information about this study can be obtained from the AIDS Clinical Trials Information Service, 1-800-TRIALS-A, open Monday through Friday, 9:00 a.m. to 7:00 p.m. eastern time. ♦

—by Laurie K. Doepel

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the new antibiotics. "It's naive to think we'll never have resistance to antibiotics," said microbiologist Brian Spratt, Ph.D., of The University of Sussex in England. Antibiotic-resistant genes are part of the natural endowment of bacteria, he claims, and the use of a new antibiotic fosters the survival of those strains that have genes that allow them to resist the new drug. "Antibiotic-resistant genes probably already exist even for those antibiotics not yet introduced," Dr. Spratt said.

Drug-resistant strains of malaria have also been a problem in recent years. "We're likely to be in a continual race to develop new drugs for malaria," said Thomas Wellems, M.D., Ph.D., a parasitology researcher with NIAID. "Knowledge of the genetics of resistance will hopefully allow us to keep one step ahead in the race." This knowledge should lead to an understanding of exactly how an organism eludes a drug and foster the design of new drugs that block or reverse such drug resistance.

An increased understanding of the microbes that cause human disease is critical to keeping them in check. "To anticipate disease," said Barry Bloom, Ph.D., of the Howard Hughes Medical Institute of Albert Einstein College of Medicine, "we need more people studying these bugs in detail. We can't prepare after the fact." ♦

—by Margie Patlak