2011 Lasker~Bloomberg Public Service Award

The Clinical Center of the National Institutes of Health

For serving since its inception as a model research hospital – providing innovative therapy and high-quality patient care, treating rare and severe diseases, and producing outstanding physician-scientists whose collective work has set a standard of excellence in biomedical research.

The 2011 Lasker~Bloomberg Public Service Award honors an institution that has served since its inception as a model research hospital. Since 1953, **the Clinical Center of the National Institutes of Health** (NIH) has provided innovative therapy and high-quality patient care, treated rare and severe diseases, and produced outstanding physician-scientists whose collective work has set a standard of excellence in biomedical research. It has spearheaded major advances in a wide array of medical arenas, established an example for academic institutions across the world, and trained thousands of investigators, many of whom now lead those establishments.

On July 6, 1953, the NIH Clinical Center admitted its first patient and embarked on its mission to generate new ways to diagnose, treat, and prevent disease by connecting bedside observations with laboratory inquiries. Patterned after a similar design at the Rockefeller University Hospital (New York City), the NIH's Center scaled up the endeavor to create a larger institution with vastly more patient-recruiting power. By grappling with perplexing illnesses in a setting where laboratories and hospital beds share a building, the Center united basic-science researchers, clinicians, and patients in their shared goal of understanding and combating disease. Today, 18 of the 27 NIH Institutes and Centers, each of which focuses on a particular biomedical realm, rely on the Center. There, scientists can benefit human beings by applying knowledge they have gleaned from experiments on cells and animals. Specialists from all over the NIH join forces with each other, the highly skilled hospital staff, and the patients.

The Center has touched many conditions and countries. It tackles common plagues such as tuberculosis and rare ones such as cystinosis. Its patients suffer attacks on the entire range of the body's systems, from endocrine, neurological, blood, eye, and autoimmune disorders to adrenal problems, vitamin deficiencies, infectious diseases, and behavioral conditions such as schizophrenia and depression. The Center's success relies on patients as collaborators, and they have flocked there from 149 countries that stretch from Brazil to Bahrain to Botswana. In 2010, the Center treated 10,086 individuals and since it opened, it has ministered to almost 450,000. Its physicians are currently following 575 unique diseases. The Center provides state-of-the-art care at no cost to patients, thus facilitating their contributions to the research enterprise. Because of its geographical reach and financial resources, the Center's studies can accrue participants unusually quickly.

Medical innovations from the Center have spanned the full spectrum of human illness. For example, in the 1960s, Roscoe Brady and Elizabeth Neufeld uncovered the causes of several

rare diseases in which lipids or carbohydrates, respectively, accumulate and harm tissues. The researchers pinned down specific enzyme deficiencies that underlie the maladies and laid the groundwork for diagnosis, prenatal detection, and, in some cases—such as Gaucher's disease—enzyme-replacement therapies. At the same time, scientists at the Center developed and administered combination chemotherapy for a variety of cancers, including acute lymphocytic leukemia in children. In that era, the oncology community was skeptical of this new approach, as conventional wisdom held that chemotherapy could not cure advanced cancer. Fortunately, the Center provided an environment that allowed Emil Frei and Emil J. Freirich to pursue unorthodox methods, and many of their patients achieved complete remissions. Soon afterward, they and other NIH investigators made similar advances in other cancers, including Hodgkin's disease. The Center played a central role in studying and treating AIDS as well. In the 1980s, its scientists developed AZT, the first effective drug for the disorder, and discerned key pathological features of the disease.

Activities at the Center have also enhanced the health of people who do not suffer from severe or unusual illnesses. Work there on hepatitis B and C viruses as well as H.I.V. has radically improved the safety of blood supplies worldwide.

The Center continues to cultivate discoveries. For instance, in the last decade, Daniel Kastner has investigated a rare and devastating immunological disorder. This condition—neonatal-onset multisystem inflammatory disease—attacks the nervous system, skin, and joints. Kastner and his colleagues traced the ailment to defects in a gene that regulates inflammation and identified a compound that dramatically improves symptoms. Another recent therapeutic breakthrough involves a rare inherited disease, lipodystrophy, in which affected individuals lack fat tissue, which normally produces a hormone called leptin. The resulting leptin insufficiency leads to a severe form of type 2 diabetes, high lipid levels, and liver problems. Phillip Gorden and his colleagues reversed many of the metabolic abnormalities in these patients with leptin therapy.

New ventures at the Center include the Undiagnosed Diseases Program, launched in 2008 to recruit individuals whose conditions have stumped the medical community. More than 4000 patient charts already have arrived at the Center. Multidisciplinary teams are puzzling out who they can most likely help and what is happening in those people's bodies. The program is beginning to make headway. For instance, researchers traced one unusual condition to alterations in a gene that normally prevents calcium from depositing in blood vessels. Now that scientists know what instigates the illness, they are developing methods to treat it.

The NIH has long attracted some of the country's best and brightest early-career physician researchers, many of whom have played pivotal roles in the Center's activities and have since carried the fruits of their training elsewhere. During the Vietnam War in particular, when virtually all male doctors were drafted, the agency drew a tremendously talented group because it allowed physicians to discharge their military service while learning how to conduct first-class research. Many of those individuals got hooked on experimental clinical science and became some of the nation's most distinguished investigators at academic and other institutions.

For almost 60 years, the Center has excelled in patient care, research, and training. Its achievements have earned high accolades; Lasker Awards have honored numerous investigators who did their clinical work there. By intermingling clinicians with scientists who untangle basic biological processes, it has sparked insights and innovations, often on sicknesses that eluded diagnosis and treatment in conventional settings. The Center has offered hope to patients and provided a template for clinical research institutions across the globe.

By Evelyn Strauss