DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2003 Budget Request

Witness appearing before the House and Senate
Subcommittees on Labor-HHS-Education Appropriations

Allen M. Spiegel, M.D., Director
National Institute of Diabetes and Digestive and Kidney Diseases

March 13, 2002
March 21, 2002

Kerry N. Weems, Acting Deputy Assistant Secretary for Budget

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) for FY 2003, a sum of $1,609,292,000, which reflects an increase of $138,477,000 over the comparable Fiscal Year 2002 appropriation. The NIH budget request includes the performance information required by the Government Performance and Results Act (GPRA) of 1993. Prominent in the performance data is NIH's second annual performance report, which compared our FY 2001 results to the goals in our FY 2001 performance plan. I appreciate the opportunity to testify on behalf of the NIDDK, which supports research on a wide range of chronic, debilitating diseases. My testimony will highlight some examples of research progress, opportunities and plans.

DIABETES

In type 1 diabetes, immune system destruction of insulin-producing beta cells leads to lifelong dependence on insulin injections for survival. Last year, I told you that a team of researchers from Edmonton, Canada, had restored natural insulin production in a small number of patients by transplanting clusters of insulin-producing beta cells, called islets, taken from donor cadaver pancreases. This year, I am very pleased to report that scientists in a recently-established NIDDK intramural Transplantation and Autoimmunity Branch have achieved similar positive results in several patients. While we must closely monitor these patients to weigh the long-term effects of therapy, these early results are very encouraging. They provide an important "proof of principle" that islet transplantation can develop into a viable treatment for type 1 diabetes. The current shortage of cadaver pancreases, however, poses a beta-cell supply problem that must be solved if islet transplantation is to become a widely available treatment option. To address this problem, we have launched a multifaceted initiative to learn all we can about insulin-producing cells through a revolutionary "Comprehensive Beta Cell Project." This project will reveal the intricacies of beta cell biology, and define the

patterns of gene expression at every stage of beta cell development within the pancreas. These studies will help researchers find ways to generate an unlimited supply of new beta cells for transplantation therapy in type 1 diabetes. Moreover, they should help clarify the basis for the failure of beta cells to secrete adequate amounts of insulin in type 2 diabetes. As we strive to develop a cure for type 1 diabetes, we are also working diligently to prevent new cases in those at risk. Building on expanded knowledge of the immune system, we have launched a nimble clinical TrialNet to ensure rapid pilot testing of innovative ways to prevent disease onset. In this way, the most promising approaches can be readily propelled into larger multi-center clinical trials.

In parallel with our beta cell efforts, we are pursuing stem cell biology--not only as a source of islets for cell-based therapy of type 1 diabetes, but also for its application to a host of other diseases, such as end stage liver disease, in which transplantation is curative, but inadequate organ supply limits the number of patients who can receive transplants. Our initiatives are consonant with extensive previous work on bone-marrow-derived and other adult stem cells, and with the President's decision to permit NIH funding of research using certain existing human embryonic stem-cell lines. With advice from an external strategic planning group, we have developed a linked series of initiatives and planned genomics projects to capitalize on the enormous promise that stem cells hold for restoring tissues and organs ravaged by disease. These initiatives will explore the versatility of progenitor stem cells to differentiate into virtually any specific cell type in the body.

In type 2 diabetes, we are tackling a public health problem of epidemic proportions, fueled by the rising tide of obesity in the U.S. The prevalence of diabetes in adults is eight percent, equating to about 16 million people.[1] The number of Americans who have diabetes has increased 49 percent from 1990 to 2000 and is expected to burgeon further in the decade ahead.[2] Compounding today's grim statistics are particularly troublesome reports that both type 2 diabetes and obesity are on the rise in children and

teens. This trend is especially strong among minority groups, such as Native Americans, Mexican Americans and African Americans, in whom adults are already disproportionately affected by both conditions. Thus, today's epidemic may well be the tip of an iceberg that will surface--with great menace for our health care system--as these newly affected youngsters grow into adulthood.

Prevention is a critical means of halting the dual burden of diabetes and obesity. While treatments exist for those already affected, no strategy can be better than preventing, from the very outset, the interlinked health problems of type 2 diabetes and obesity. Impressive proof that prevention really works comes from our major clinical trial in type 2 diabetes, the Diabetes Prevention Program or DPP. Last year, I testified that we were nearing this trial's completion--hopeful of positive results. Today, I can report that the final results have far surpassed our hopes. So strikingly positive are the findings that we ended the trial one year ahead of schedule. The results were announced by Secretary Thompson at a press conference held at NIH on August 8, 2001, and reported in detail in The New England Journal of Medicine on February 7, 2002. With a lifestyle intervention consisting of only modest changes in diet and exercise, the development of type 2 diabetes was reduced by 58 percent in individuals at high risk for developing the disease. The beneficial effect of the lifestyle intervention applied across all racial, ethnic and age groups. Minority groups comprised 45 percent of the study population, and 20 percent were 60 years of age or older--thus demonstrating that this prevention strategy can be realistically applied to the diverse U.S. population. In another arm of the study, the diabetes medication metformin was also effective, reducing the development of diabetes by 31 percent, but the drug was effective only in younger and heavier individuals. Now, armed with the impressive results of the DPP, we must translate these successful prevention approaches to the 20 million Americans with impaired glucose tolerance who are at high risk for the disease--with emphasis on the 10 million at greatest risk. To this end, we are launching an initiative to develop cost-effective methods to identify those at

high risk and to implement the lifestyle intervention on a wider scale. We are also supporting a network of centers to develop effective prevention strategies specifically targeting children at high risk for type 2 diabetes. At the same time, vigorous fundamental research provides a framework for combating obesity by providing insights into the processes regulating appetite and metabolism. Research on fat-cell hormones, such as the appetite-inhibiting hormone leptin, is proving that fat tissue is not a passive depot of energy, but an active participant in regulating metabolic processes. These findings may pave the way to the development of effective drugs to aid weight loss and prevent or reduce obesity. In addition, we will continue to support behavioral research and outcomes research with implications for public health policy--for example, the recent finding that breast feeding may help a mother prevent her child from becoming obese.

For diabetes patients, the major killer is heart disease. Our National Diabetes Education Program has therefore launched a new campaign urging Americans to know their "ABCs." The "A" stands for the hemoglobin "A" 1c test--an integrated measure of blood glucose levels. The "B" for blood pressure and the "C" for cholesterol levels emphasize important prevention strategies that are built on extensive research by the National Heart, Lung and Blood Institute. This "ABCs" program is designed to help reduce mortality from heart disease and stroke in patients with diabetes.

DIGESTIVE DISEASES

In digestive diseases research, I am pleased to announce the identification of the first gene that increases susceptibility to Crohn's disease, a debilitating form of inflammatory bowel disease or IBD. A new IBD Genetics Consortium will take full advantage of this discovery, and also speed the search for other culprit genes in this complex disease. Identification of novel susceptibility genes for Crohn's disease and ulcerative colitis should lead to improved diagnosis and treatments. We are convening

a meeting on therapeutic endpoints for clinical trials in IBD to facilitate efficient testing of innovative therapies. We are also augmenting our clinical research efforts in liver disease with a planned consensus conference for hepatitis C treatment, a cohort study of adult-to-adult liver transplantation, and two clinical trial networks-one for nonalcoholic steatohepatitis, a liver disease associated with insulin resistance and diabetes, and a second for biliary atresia, a serious pediatric disorder. We are developing plans for a hepatotoxicity network to apply advanced genomic methods to the serious problem of drug-induced liver injury.

KIDNEY, UROLOGIC AND BLOOD DISEASES

The incidence of end stage renal disease (ESRD) is increasing at an alarming rate with 300,000 patients currently on chronic dialysis and projections of 600,000 patients on dialysis by 2010.[3] Only 31 percent of dialysis patients survive five years.[4] We are taking multiple steps to address this problem. In addition to emphasizing primary prevention and effective treatment of diabetes--the cause of ESRD in 45 percent of patients--we are establishing a new National Kidney Disease Education Program (NKDEP), which will initially target high risk groups. The NKDEP will promote early recognition of chronic kidney disease, and implementation of treatment measures proven to slow progression to ESRD. For example, our major clinical trial, the African American Study of Kidney Disease (AASK), showed conclusively that treatment with angiotensin converting enzyme (ACE) inhibitors is more effective than calcium channel blockers in preventing hypertensive kidney disease from progressing to ESRD in high-risk African Americans. We are also launching treatment trials for other important causes of ESRD such as polycystic kidney disease and focal segmental glomerulosclerosis. Mortality of patients with chronic renal insufficiency, primarily from heart disease, is extremely high. A new cohort study of patients with chronic renal insufficiency will help shed light on the causes of the cardiovascular mortality that affects these patients, and a trial that lowers homocysteine levels in the blood of

kidney transplant patients will test whether this amino acid is responsible for increased heart disease in ESRD patients.

Our portfolio of urology research continues to flourish. This research is uncovering important knowledge about how bacteria attach to the bladder surface, and how we can use these insights to combat antibiotic resistance in the treatment of urinary tract infections. Major clinical initiatives in bladder disorders include clinical research networks to speed the testing of therapies for urinary incontinence and interstitial cystitis. Scientific recommendations of an expert panel, the Bladder Research Progress Review Group, will help guide our program development. Results of our major multi-center trial on Medical Therapy of Prostatic Symptoms (MTOPS) are to be announced later this year. We intend to bolster prostate research by making available biopsy tissue obtained in MTOPS for study by a network of investigators. We will also be launching a trial of saw palmetto and other phytotherapies widely used for symptoms of prostate enlargement.

In blood diseases, our strong portfolio in areas such as hematopoietic stem cell research and globin gene regulation is the basis for clinical advances. We are supporting studies on drugs to eliminate the toxic iron overload that is a byproduct of current treatment for Cooley's anemia. We are also supporting development of new non-invasive methods for accurate measurement of iron burdens in patients.

Mr. Chairman and Members of the Committee, these are just a few examples of our many research advances and initiatives. I would be pleased to answer any questions you may have.

[1] Harris MI: Diabetes in America: epidemiology and scope of the problem. *Diabetes Care* 1998;21 suppl 3: C11-C14.
[2] Mokdad AH, Bowman BA, Ford ES, Vinicor F, Marks JS, Koplan JP. The continuing epidemics of obesity and diabetes in the United States. *Journal of the American Medical Association* 286:1195, 2001.
[3] U.S. Renal Data System.
[4] U.S. Renal Data System.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases

Biographical Sketch

NAME: Allen M. Spiegel, M.D.

POSITION: Director, National Institute of Diabetes and Digestive and Kidney Diseases

BIRTHPLACE: Germany

DATE: May 18, 1946

EDUCATION: B.A., Columbia College, 1967
M.D., Harvard Medical School, 1971

EXPERIENCE:

1999-present	Director, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1999-present	Chief, Section on Molecular Pathophysiology, National Institute on Deafness and Other Communication Disorders, NIH
1990-1999	Director, Division of Intramural Research, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1988-1999	Chief, Metabolic Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, NIH
1985-1988	Chief, Section on Molecular Pathophysiology, Metabolic Diseases Branch, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, NIH
1977-1984	Senior Investigator, Metabolic Diseases Branch, National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH

1973-1976	Fellow, NIH Endocrinology Training Program, Clinical Associate, Metabolic Diseases Branch (Dr. G. D. Aurbach, Chief), National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH
1971-1973	Intern and Assistant Resident in Medicine, Massachusetts General Hospital, (Dr. Alexander Leaf, Chief)

HONORS AND AWARDS:

1966 - Elected to Phi Beta Kappa
1967 - B.A. Summa Cum Laude
1971 - Elected to Alpha Omega Alpha
1971 - M.D. Cum Laude
1988 - Outstanding Service Medal – U.S. Public Health Service
1990 - Meritorious Service Medal – U.S. Public Health Service
1990 - Jacobaeus Prize – Nordisk Insulin Foundation
1993 - Plenary Lecturer – Japan Endocrine Society
1993 - Aurbach Memorial Lecturer – American Society for Bone and Mineral Research
1994 - Harrison Memorial Lecturer – Endocrine Society of Australia
1996 - Komrower Memorial Lecturer – Society for the Study of Inborn Errors of Metabolism
1998 - Edwin B. Astwood Lecture Award – Endocrine Society (U.S.A.)

PROFESSIONAL ORGANIZATIONS:

American Federation for Clinical Research
The Endocrine Society
American Society for Bone and Mineral Research
American Society for Clinical Investigation
American Society for Biochemistry and Molecular Biology
Association of American Physicians

LICENSURE AND CERTIFICATION:

Diplomate American Board of Internal Medicine, 1974
Board Certified in Endocrinology, 1975
Licensed in Medicine, Maryland

DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE OF MANAGEMENT AND BUDGET
BIOGRAPHICAL SKETCH

NAME: Kerry N. Weems

POSITION: Acting Deputy Assistant Secretary for Budget

BIRTHPLACE: Portales, New Mexico

EDUCATION:
B.A., Philosophy, New Mexico State University, 1978
BBA, Management, New Mexico State University, 1978
MBA, University of New Mexico, 1981

EXPERIENCE:

2001 - present	Acting Deputy Assistant Secretary for Budget, HHS
1996 - present	Director, Division of Budget Policy, Execution and Management, HHS
1991 - 1996	Chief, Budget Planning Branch, HHS
1988 - 1991	Program Analyst, Office of Budget, HHS
1983 - 1988	Program and Budget Analyst, HHS (Social Security Administration)
1981 - 1983	Staff Member, United States Senate

HONORS AND AWARDS:

2001	Presidential Rank Award
1995	Secretary's Distinguished Service Award
1993	HHS Senior Management Citation